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Patterns of lymph node biopsy pathology Chris Hani Baragwanath academic hospital over a period of three years 2010-2012

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1.0 Introduction

1.1 Lymph node function and anatomy

Lymph nodes are secondary lymphoid organs, as opposed to the bone marrow and thymus, which are primary lymphoid organs responsible for production and development of lymphocytes, respectively. Immune responses are initiated and amplified in lymph nodes, with immunological memory persisting after infection (Kumar & Clark, 2009). Lymph nodes are small elliptical structures and are widely distributed, with groups of nodes in the axillae, groin, neck and abdomen, linked by lymphatic vessels.

Trabeculae are formed from extensions of the surrounding fibrous capsule, with the subcapsular sinus arising in between and allowing movement of lymphatic fluid. The architecture of the node comprises an outer cortex containing B cells arranged in follicles and a paracortex containing T cells (Kumar & Clark, 2009). Vessels and plasma cell-containing medullary cords are located in the inner medulla (Kumar & Clark, 2009).

Endothelial venules allow migration of circulating T lymphocytes, while the afferent lymphatic vessels allow entry of dendritic cells and macrophages into the lymph node. Antigen presentation to T cells occurs in the paracortex and results in activation of effector T cells, which exit the node via efferent lymphatics (Kumar & Clark, 2009). Once activated, B cells migrate to germinal centres within the follicles. Increased numbers of lymphocytes and activation of immune cells results in enlargement of the lymph node (Kumar & Clark, 2009).

1.2 Causes of lymphadenopathy

Lymphadenopathy is a common presentation of disease in South Africa (SA), particularly in the era of Human Immunodeficiency Virus (HIV) and tuberculosis (TB) co-infection. There are only a limited number of studies that have described lymph node pathology in Southern Africa. A retrospective study by Muthuphei (1998) at Ga-Rankuwa Hospital demonstrated that most patients with cervical lymph node biopsies had TB, lymphoproliferative disorders and metastatic tumours.

Similar findings were established in studies performed in Zimbabwe and Nigeria by Sibanda & Stanczuk (1993) and Olu-eddo & Omoti (2011), respectively. The Zimbabwean study by Sibanda & Stanczuk (1993) showed that the most common causes of lymphadenopathy in their setting were nonspecific reactive lymphoid hyperplasia, TB and malignancies including metastases, Kaposi sarcoma and lymphomas. The Nigerian study assessed cervical lymph node biopsies retrospectively over a period of twenty years at a single centre. They found that although malignancy constituted the largest group of pathology (including non-Hodgkin lymphoma, Hodgkin lymphoma and metastatic carcinoma), TB was the single most common cause of lymphadenopathy (Olu-eddo & Omoti, 2011).

A Zambian study by Bem et al (1996) furthermore suggested that primary HIV lymphadenopathy was a significant cause of superficial lymphadenopathy. HIV-associated lymphadenitis (reported in our setting as HIV reactive nodes) is likely due to the lymphotropism of HIV, and is characterized by a pattern of histological findings. Mahe et al (2011) described a pathological grading system for HIV-associated lymphadenitis: grade 1 is associated with hyperplastic features, enlargement of germinal

centres with increased apoptosis and phagocytosis by macrophages; grade 2 comprises a reduction in lymphoid follicles and mature lymphocytes, and an increase in plasma cells and perifollicular blood vessels; and grade 3 comprises sclerotic germinal centres.

In the United States of America, lymphadenopathy is mostly caused by common viral and bacterial infections (Kanwar & Sills, 2012). The pathogens include Epstein-Barr virus, cytomegalovirus, viral causes of upper respiratory tract infections, staphylococci and beta-haemolytic streptococci (Kanwar & Sills, 2012). Less common causes are HIV, malignancy and autoimmune diseases (Kanwar & Sills, 2012).

The list of diseases associated with lymphadenopathy is very broad. A summary adapted from Harrison's Principles of Internal Medicine is depicted in Table 1 (Longo et al, 2012).

Table 1. Diseases associated with lymphadenopathy (Longo et al, 2012)

Infectious Diseases	Viral- Epstein-Barr Virus, cytomegalovirus, Hepatitis, Herpes simplex
	Bacterial- streptococci, staphylococci, tuberculosis
	Fungal- histoplasmosis, coccidioidomycosis, paracoccidioidomycosis
	Chlamydial- lymphogranuloma venereum, trachoma
	Parasitic- toxoplasmosis, leishmaniasis, trypanosomiasis, filariasis
	Rickettsial- scrub typhus, rickettsialpox, Q fever
Immunologic diseases	Rheumatoid arthritis
	Juvenile Rheumatoid arthritis
	Mixed connective tissue disease
	Systemic lupus erythematosus
	Dermatomyositis
	Sjogren's syndrome
	Serum sickness
	Drug hypersensitivity- diphenylhydantoin, hydralazine, allopurinol
	Angioimmunoblastic lymphadenopathy
	Primary biliary cirrhosis
	Graft-vs.-host disease
	Silicone-associated
	Autoimmune Lymphoproliferative syndrome
Malignant disease	Haematologic- Hodgkin lymphoma, non-Hodgkin lymphoma, acute or chronic lymphocytic leukaemia, hairy cell leukaemia
	Metastatic
Lipid storage diseases	Gaucher's, Niemann-Pick, Fabry, Tangier
Endocrine diseases	Hyperthyroidism
Other disorders	Castleman disease
	Sarcoidosis
	Dermatopathic lymphadenitis
	Lymphomatoid granulomatosis
	Histiocytic necrotizing lymphadenitis (Kikuchi's disease)
	Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease)
	Mucocutaneous lymph node syndrome (Kawasaki's disease)
	Histiocytosis X
	Familial Mediterranean fever
	Severe hypertriglyceridaemia, Vascular transformation of sinuses, Inflammatory pseudotumour of lymph node

1.3 Malignancy in South Africa

"The World Health Organization estimates of the burden of disease in South Africa suggest that non-communicable diseases caused 28% of the total burden of disease measured by disability-adjusted life years (DALYs) in 2004" (Mayosi et al, 2009). According to the findings in the burden of non-communicable diseases in South Africa report by Mayosi et al (2009), malignancies, along with metabolic and lifestyle diseases, contribute 12% to the total burden of disease. Interestingly, although the proportions of these diseases have decreased relative to the proportions of communicable diseases (especially HIV), the incidence rates have not. These findings highlight the fact that the South African population, in both rural and urban areas, faces the dual epidemics of infectious diseases and non-communicable diseases, including malignancies.

Mayosi et al (2009) state that demographic change contributes to the high incidence of non-communicable disease, including malignancies, evidenced by an increase in the number of older people who are at greatest risk of developing these diseases. Other factors include tobacco use, sedentary lifestyle and poor diet (Mayosi et al, 2009). According to the 2009 Cancer registry, with the exclusion of skin cancers, the five leading causes of cancer in men were prostate, primary site unknown, Kaposi sarcoma, lung and colorectal. The five leading causes in women were breast, cervix, primary site unknown, Kaposi sarcoma and colorectal. In both groups, non-Hodgkin lymphoma was the seventh leading cause of cancer (2009 Cancer registry).

Interestingly, the pathology-based cancer registry has noted an increase in HIV-associated Kaposi sarcoma (KS). It has been projected that 8000 new cases of KS would be expected each year in South Africa if HIV trends follow those of other African

countries (Mayosi et al, 2009). Immunization against hepatitis B and human papilloma virus in children are expected to affect the prevalence of hepatocellular carcinoma and cervical cancer, respectively (Mayosi et al, 2009).

1.4 HIV and TB in South Africa

Studies by Martinson et al (2011), Schutz et al (2012) and Churchyard et al (2014) suggest that South Africa carries the highest global burden of HIV with an estimated 5.6 million people infected. These studies also suggest that TB is the most common serious opportunistic infection and the leading cause of death in patients both before and during antiretroviral treatment (Martinson et al, 2011; Schutz et al, 2012; and Churchyard et al, 2014). The association between HIV infection and TB is well described in South Africa, where HIV infection increases the risk of TB 20-fold, compared with HIV-negative individuals (Martinson et al, 2011). It has been estimated that up to a third of HIV-positive patients have coexistent TB (Wright, 2012).

TB and HIV enhance one another and together, accelerate immunological dysfunction. In a review article by Pawlowski et al (2012), it is stated that inborn errors of immunity and genetic polymorphisms may influence vulnerability to both HIV and TB infections. The effect of HIV on TB reactivation is complex and involves the depletion of CD4 cells, up-regulation of TB entry receptors on macrophages, HIV manipulation of macrophage bactericidal pathways including tumour necrosis factor, dysregulated chemotaxis and a T-helper 1 cell and T-helper 2 cell imbalance (Pawlowksi et al, 2012). The impaired CD4 function and tumour necrosis factor-mediated macrophage apoptotic response compromises granuloma formation in patients with advanced HIV, evidenced by

disseminated disease and a “dominant granulocytic infiltrate and necrosis without the typical caseous necrosis” seen in HIV-negative patients with TB granulomas (Pawlowski et al, 2012).

The effects of TB on HIV replication are less clear and involve a favourable microenvironment for facilitating HIV infection by increasing the expression of co-receptors which allow transmission of virus from monocyte-derived macrophages to T cells, and by increasing pro-inflammatory cytokines (Pawlowski et al, 2012).

In a review article by Martinson et al (2011), factors associated with an increased risk of TB in HIV-positive individuals can be divided into sociodemographic and clinical factors. The sociodemographic factors are residing or working in a high prevalence area or institution, recent exposure to an infectious case and tobacco smoking (Martinson et al, 2011). Clinical factors include a low body mass index, latent TB infection, silicosis, low CD4 count and high viral load (Martinson et al, 2011). Conversely, protective factors are a high body mass index, high CD4 count, low viral load, isoniazid preventive therapy and antiretroviral therapy (Martinson et al, 2011).

In a study performed at CHBAH by Edginton et al (2005), TB was diagnosed in 1291 patients over a period of two months. The global prevalence and death rates from TB are on the decline. However, in contrast, Africa is showing an increase in the tuberculous burden. Southern Africa, in particular, had an incidence of 330 cases per 100,000 population in 2012, according to the WHO Bulletin 2014. Factors contributing to this are inclusive of poverty, HIV infection, poor infrastructure, and programme management (WHO Bulletin, 2014).

1.5 Presentation of TB in our setting

According to the National Tuberculosis Management Guidelines, published by the Department of Health (2009), KwaZulu Natal had the highest TB caseload in 2006, with pulmonary TB accounting for 84% of cases and extrapulmonary TB for the remainder. In HIV-positive patients, as a result of disruption of granuloma structure and poor containment of infection, TB often presents as a systemic disease involving multiple organs that lack well-defined granulomas and instead develop diffuse lesions (Powlowski et al, 2012).

In a post-mortem study by Wong et al (2012), performed in Johannesburg, TB was found to be the cause of death in the majority of patients (69%) with advanced Acquired Immunodeficiency Syndrome (AIDS), both before and after starting antiretroviral therapy. Lymph nodes were the fourth most common site of positive mycobacterial cultures in this study (16%), following liver, spleen and lung (Wong et al, 2012). The study also suggested that TB often goes unrecognized in these patients, and can be accompanied by other infections or malignancies (Wong et al, 2012).

The clinical presentation of TB in our setting varies with immunological status in patients with HIV. The clinical presentation in patients with higher CD4 counts is similar to the HIV-negative population with subacute constitutional symptoms and features of cavitatory lung disease (Martinson et al, 2011). Conversely, in patients with lower CD4 counts, disseminated disease is common (Martinson et al, 2011). TB lymphadenitis is thought to be more common in women than men and more common in immunocompromised patients with a peak age range of 30-40 years (Fontanilla et al,

2011). According to the article by Martinson et al (2011), an increasing proportion of TB amongst HIV-positive patients is multidrug resistant or extremely drug resistant TB.

1.6 Importance of a correct diagnosis for lymphadenopathy

There is a wide differential diagnosis for peripheral TB lymphadenitis. The dangers of misdiagnosing TB, and subsequent empiric TB treatment, are progression of underlying disease (malignancy or other infection) and the toxicity of TB therapy. In a study conducted in KwaZulu Natal, Puvaneswaran & Shoba (2013) demonstrated the importance of an accurate diagnosis for lymphadenopathy. Patients with lymphoma in rural KZN were misdiagnosed based on clinical similarities to TB and were placed on empiric TB treatment, delaying the lymphoma diagnosis by a median of five months (Puvaneswaran & Shoba, 2013).

In a study done by Schutz et al (2012) at GF Jooste Hospital in Cape Town, TB treatment was found to be a frequent cause of drug-induced liver injury with a mortality of 35% at three months after presentation. They found that the risks of liver dysfunction due to TB therapy included direct morbidity and mortality from liver failure, disease progression due to interruption of optimal therapy, complications of prolonged hospitalization, a negative effect on adherence and therapy resistance related to interruptions (Schutz et al, 2012). In the aforementioned study, it was noted that 10% of patients were receiving both TB treatment and antiretroviral treatment, and a significant portion also received cotrimoxazole prophylaxis and were hepatitis B surface antigen positive (Schutz et al, 2012). These finding are relevant as patients with TB have additional, often indirect, risk factors for developing liver dysfunction.

1.7 Diagnostic procedures for establishing a cause of lymphadenopathy

Excisional biopsy of a clinically appropriate lymph node is traditionally favoured as a diagnostic procedure for a multitude of infectious and neoplastic disorders. However, studies by Fontanilla et al (2011) and Handa et al (2012) suggest that fine-needle aspiration (FNA) is replacing it as a first line diagnostic procedure, reserving excisional biopsy for non-diagnostic FNA results that require further investigation.

The South African TB guidelines are supported by the current literature, that suggests FNA as the first line procedure in the workup of TB lymphadenitis, with progression to excisional biopsy if no diagnosis has been made from FNA (Department of Health, 2009). "The WHO classification of lymphomas enabled primary diagnosis of lymphomas on FNA for the first time, as architecture was no longer as important for the diagnosis of lymphomas but on the basis of the morphology of the cells, the clinical presentation of the patient and the specific immunophenotyping and genetic abnormality of the malignant cells" (Wright, 2012).

FNA has reduced the number of excisional biopsies required in patients with metastatic carcinoma and melanoma in lymph nodes (Stewart et al, 1998). The complexity of previous lymphoma classifications and the prognostic value of architectural assessment in some lymphomas have limited the use of FNA, especially with regard to Hodgkin lymphoma and low-grade non-Hodgkin lymphoma (Stewart et al, 1998). However, accurate subtyping of lymphomas can be achieved with FNA when morphological assessment is complemented by ancillary studies (Stewart et al, 1998). A review by Wright (2012) emphasizes this point, stating that the diagnostic strength of the FNA

correlates with proper procedure technique, adequate clinical information and additional investigations such as TB culture, use of Xpert MTB/RIF, immunocytochemistry and flow cytometry.

Malignancies that can be diagnosed on FNA with additional flow cytometry are B-cell non-Hodgkin lymphomas that have specific immunophenotypic profiles, while follicular lymphoma, T-cell non-Hodgkin lymphoma and Hodgkin lymphoma require excision biopsy for diagnosis (Wright, 2012). Other lymphomas that prove difficult to diagnose with FNA include composite lymphomas, marginal-zone lymphomas, anaplastic large-cell non-Hodgkin lymphoma, polyclonal posttransplantation lymphoproliferative disorders and primary mediastinal large-cell lymphoma (Hehn et al, 2004).

The morphological difference between reactive and malignant lymphoid proliferation is a well-known area of difficulty in lymph node FNA cytology (Stewart et al, 1998; and Hehn et al, 2004). Whereas cells from high grade lymphomas may show an obvious abnormality, low grade lymphoma cells are relatively monomorphic and can lead to a false-negative lymphoma diagnosis, compared with the polymorphous cells seen in reactive hyperplasia, which can lead to a false-positive lymphoma diagnosis (Stewart et al, 1998).

In the series by Stewart et al (1998), half the number of false negative cases was of follicular lymphoma. The smears revealed a “mixed lymphoid pattern with histiocytes, and even on review it was considered that the morphological appearances favoured a reactive rather than a neoplastic process” (Stewart et al, 1998). The challenges of FNA diagnosis of follicular lymphoma also involve grading the lymphoma, and differentiating between a grade three follicular lymphoma and diffuse large B-cell lymphoma (DLBCL)

(Amador-Oritz et al, 2011; and Wright, 2012). The importance of an adequate FNA sample is reflected by the potential false-negative diagnosis of Hodgkin lymphoma, as there may be relatively few Reed-Sternberg cells or they may be masked by an infiltrate mimicking reactive hyperplasia (Stewart et al, 1998).

The Scottish study by Stewart et al (1998) assessed diagnostic accuracy of FNA in distinguishing reactive lymphoid hyperplasia from lymphoma, and revealed sensitivity for lymphoma of 91% and a specificity of 95%. This study showed immunocytochemistry and fluorescent in-situ hybridization (FISH) to be the most beneficial ancillary investigations to FNA in subtyping lymphomas, and that biopsy is suggested in cases with clinical discrepancy, particularly if ancillary studies have shown equivocal results (Stewart et al, 1998).

A retrospective American study by Amador-Oritz et al (2011) assessed diagnostic accuracy of FNA in conjunction with core needle biopsy in patients with suspected lymphoma. Although FNA morphological findings were reviewed, most FNAs were performed to generate a sample for flow cytometry (Amador-Oritz et al, 2011). The results of this study showed that core needle biopsy and FNA, in association with ancillary studies provided a diagnosis in 90% of cases, however a specific lymphoma subtyping was possible in only 75%, suggesting that architectural pattern is often necessary in complete subclassification (Amador-Oritz et al, 2011).

A small retrospective study conducted in Arizona by Hehn et al (2004) aimed to assess the diagnostic value of FNA from a clinician perspective in establishing a diagnosis of lymphoma using the WHO classification of lymphomas. There were many limitations to the study including relatively small numbers, lack of standardization evidenced by the

use of many different laboratories and pathologists, lack of information regarding the technique of FNA and the adequacy of samples, information regarding the site of FNA versus the site of biopsy, single patients having had multiple FNAs without a known indication and the paucity of ancillary studies done (Hehn et al, 2004). These limitations may have contributed to the seemingly poor outcome of FNA in this study, with only 29% of FNAs generating an accepted diagnostic classification (Hehn et al, 2004). The most common excisional biopsy diagnoses were follicular lymphoma and DLBCL, whereas the most common FNA diagnoses were atypical, non-diagnostic and lymphoma without subtype (Hehn et al, 2004).

1.8 FNA and the history of the procedure

Needle aspiration for diagnostic purposes was first described in 1847 (Ansari & Derias, 1997). In the late 1800s and early 1900s, the technique was used experimentally to isolate pneumonia-causing bacteria from cells, to diagnose pulmonary carcinoma, and to isolate trypanosomiasis in lymph node aspirates. Clinicians mainly used these techniques as tools to a rapid diagnosis (Ansari & Derias, 1997). Only in 1927, was aspiration cytopathology practically implemented in the United Kingdom, as a means of rapid diagnosis of tumours (Ansari & Derias, 1997).

Considered a pioneer in the field, Fred W Stewart was the American surgical pathologist responsible for interpretation of smears done during the 1930s at the Memorial Hospital for Cancer and Allied Diseases in New York (Ansari & Derias, 1997). Interestingly, Stewart noted certain points regarding the optimization of needle aspiration results that still ring true in modern pathology. He emphasized “the technique of aspiration and

preparation of the sample, and the importance of correlating clinical information with interpretation of the aspirated material" (Ansari & Derias, 1997).

The use of FNA waned in the United States in the 1960s as open biopsy was preferred, but became popular again in Europe in the 1950s, where thin 22 gauge needles were used (Ansari & Derias, 1997). This technique is now known as fine needle aspiration cytology (FNA). Diagnostic criteria for FNAs were defined for a variety of conditions by a group of Swedish pathologists who sampled, prepared and interpreted the aspirates in a direct referral clinic setting, thereby also providing a model for FNA services (Ansari & Derias, 1997).

1.9 FNA: the procedure

The procedure of FNA involves "aspirating cells and attendant fluid with a small-bore needle, followed by cytologic examination of the stained smear" (Kumar et al, 2010). As outlined in a review article on FNA of lymph nodes by Wright (2012), the indications for FNA of lymph nodes are to confirm suspected reactive hyperplasia, or to diagnose a specific infection or neoplastic infiltrate. Extra caution should be taken with FNA in a patient predisposed to bleeding or respiratory compromise, as complications of bleeding or pneumothorax may follow, respectively (Wright, 2012). In our setting, FNAs are performed by clinicians, pathologists, registered professional nurses and cytotechnologists (under medical supervision).

In addition to gloves and disinfectant, materials required for performance of an FNA include a twenty two gauge cutting needle, a ten cc syringe, glass slides, alcohol based

spray fixative, slide holders and material for ancillary studies (Wright, 2012). The process of FNA of lymph nodes has been described and illustrated in the review by Wright (2012). Personal protective equipment should be used during the aspiration of suspected tuberculous lymph nodes.

In adult patients, after consent has been obtained, the patient is positioned lying down, the node stabilized with one hand, and the needle is introduced while maintaining constant one to two cc suction throughout (Wright, 2012). Aspiration should be done using a cutting motion until material appears in the hub of the needle, after which suction should be released before withdrawing the needle and compressing the site (Wright, 2012). The needle should then be removed from the syringe, five to ten cc of air introduced into the syringe and the needle should be re-applied before expressing the material from the needle onto the glass slide (Wright, 2012). A second slide should be placed on the first and the two slides pulled apart, while maintaining gentle pressure. The first slide should be air-dried and the second spray fixed, with each FNA yielding four slides, as a minimum of two passes should be made during each procedure (Wright, 2012). If TB is suspected, the needle and syringe should be rinsed in TB culture medium (Wright, 2012).

1.10 Advantages and disadvantages of FNA and biopsy

According to Wright (2012), FNA has specific advantages to the patient, the clinician and the healthcare system as a whole. Patient advantages of FNA include it being a relatively brief outpatient procedure, with the absence of sutures or scars, minimal pain and inexpensive (Wright, 2012). Clinician advantages often overlap with patient advantages, in that it is an outpatient procedure due to the low risk of complications, and lack of scarring prevents interference with subsequent imaging (Ansari and Derias, 1997; and Wright, 2012). Additionally, ancillary material is available for additional investigations, results are rapid and minimal infrastructure is required (Wright, 2012). FNA has been suggested as a suitable diagnostic practice in resource poor countries with limited access to surgical teams (Ansari & Derias, 1997). It is also of benefit for use in debilitated patients, is repeatable and useful for evaluation of multiple lesions (Ansari & Derias, 1997).

Rare complications following FNA have been reported in older articles, such as haemorrhage after FNA of solid vascularized organs, septicaemia, peritonitis, and acute pancreatitis (Ansari & Derias, 1997). Seeding of tumour following FNA is rare and the risk increases with "multiple passes, larger needles and the absence of normal parenchyma covering the lesion" (Ansari & Derias, 1997). Contraindications to FNA are deep aspirations in patients predisposed to bleeding and FNA of phaeochromocytomas (risk of inducing a hypertensive crisis), while caution should be taken when performing a transthoracic FNA in patients with respiratory disease as the complication of pneumothorax may prove fatal, as mentioned previously (Ansari & Derias, 1997).

The advantages and disadvantages of FNA and biopsy have been outlined in many articles assessing the efficacy of FNA as a diagnostic procedure and are summarized in Tables 2 and 3 (Ansari & Derias, 1997; Stewart et al, 1998; Kumar et al, 2010; Amador-Oritz et al, 2011; and Wright, 2012). Table 2 illustrates the advantages and disadvantages of FNA. Table 3 shows the advantages and disadvantages of incisional, core or excisional biopsies.

Table 2. Advantages and disadvantages of FNA

Advantages	Disadvantages
Less invasive, fewer complications	Small sample size increases chance of specimen being non-representative
Small amount of tissue required	Sampling errors: the diagnostic value is dependent on sampling technique and preparation of slides
Can be used in surgically inaccessible sites	Risk of tumour cells spreading along FNA needle track
More rapidly performed	Limited architectural information
Obviates surgery and the risks associated with it	
Reliable in experienced hands	
Ancillary tests can be performed (immunocytochemistry, flow cytometry)	
Less expensive	
Can be used in patients too unstable for general anaesthetic or open surgical biopsy	

Table 3. Advantages and disadvantages of biopsy (incisional, core or excisional)

Advantages	Disadvantages
More likely to be representative	Surgical complications: bleeding, pain at incision site, scar
Ability to evaluate tissue architecture	Longer procedure
More likely to evaluate multiple pathologies in a single node	Slower turnaround time (specimen requires preparation)
More tissue available for further investigation or staining if required	More expensive

1.11 Aim of the study

The author conducted a retrospective review of the lymph node pathology identified at CHBAH to contribute to medical knowledge of common causes of lymphadenopathy requiring biopsy in South Africa, and the role of FNA as an adjunct to lymph node biopsy. The aims of the study were to describe, at CHBAH: the demographics of patients undergoing lymph node biopsy; the indications for lymph node biopsy; and the pathology identified. With regard to the pathology identified, comparison was made between HIV-negative and HIV-positive patients, to ascertain any pertinent differences in presentation and frequency of disease.

2.0 Materials and Methods

2.1 Study design and site

The study was a retrospective descriptive audit conducted at CHBAH, Johannesburg, South Africa. CHBAH which is a provincial tertiary hospital in Soweto, Johannesburg, contains close to 3300 beds and is the largest hospital in Africa (Edginton et al, 2005).

2.2 Study population

The study population consisted of all patients over the age of 12 years who underwent lymph node biopsies at CHBAH between 1 January 2010 and 31 December 2012, and had data available in the National Health Laboratory Service (NHLS) database.

2.3 Methods

Lymph node biopsy reports were extracted from the database of the NHLS Division of Anatomical Pathology. Patient demographic details such as gender, race and age were obtained from the laboratory requisition forms submitted by attending clinicians and from pathology reports. Further information regarding HIV status (determined with antibody testing using fourth generation HIV enzyme-linked immunosorbent assay), CD4 count (cells/ul), if relevant, and FNAs performed were accessed through the NHLS DisaLab system, using the patients' name and hospital number. Consent was not required from participants for their records to be used, as agreed by the Human Research Ethics committee at the University of the Witwatersrand. Patient information was anonymized and de-identified prior to analysis.

All lymph node biopsy and FNA biopsy specimens were previously analyzed, for diagnostic purposes, by pathologists employed by the NHLS at CHBAH. Histopathologic diagnoses were based on morphologic findings and, in the appropriate context, ancillary tests including Mycobacterial staining and culture, immunohistochemistry, FISH (fluorescent in-situ hybridization) techniques, and flow cytometry. The diagnosis of tuberculous lymphadenitis was confirmed by Ziehl-Neelsen stain for acid-fast bacilli and positive Mycobacterial culture. Mycobacterial culture and Mycobacterial PCR testing using Xpert MTB/RIF are performed in cases of clinically and histopathologically (granulomatous) suspected Mycobacterial lymphadenitis. Ziehl-Neelsen stains for acid-fast bacilli were routinely performed on all lymph node biopsies and FNA biopsies that displayed granulomatous inflammation (necrotizing and non-necrotizing). A total of 203 reports of FNAs preceding lymph node biopsy were evaluated. Findings of the FNA

were analyzed in conjunction with adequacy of FNA samples submitted for cytology, prior to comparison with biopsy.

2.4 Exclusion criteria

Specimens deemed unsuitable for histopathologic or cytologic analysis by the pathologist were excluded. Unsuitable samples were attributed to tissue samples not representative of lymphoid tissue or poor quality specimens that could not be evaluated. Non-diagnostic specimens were included in the analysis.

2.5 Separate Analysis

In cases where a single patient had more than one lymph node biopsy during the period of the study, the repeat biopsies were evaluated as a subset.

2.6 Statistical Analysis

Statistical analysis was performed using STATA version 12 for Windows (StataCorp LP, Texas; www.stata.com) and GraphPadQuickCalcs (GraphPad Software Inc, California; www.graphpad.com). A statistician was consulted. A p-value of less than 0.05 was considered statistically significant. A kappa co-efficient was used to measure the agreement between FNA and lymph node biopsy. Kappa values were interpreted as follows: <0.40= poor, >0.40 to <0.75= fair to good, and >0.75= excellent.

2.7 Ethical approval

The Human Research Ethics committee at the University of the Witwatersrand granted ethical approval for this study (Clearance Certificate number M130626).

3.0 Results

3.1 Demographic characteristics

The majority of patients (55%) who had lymph node biopsies were female [Table 4]. Over 90% of patients were of the African/black racial group, in keeping with the racial demographic distribution in SA, and the attendance pattern of patients at CHBAH. The median age of patients was 40 years, with a minimum of 12 and a maximum of 94.

Table 4. Biopsy Diagnosis in relation to Demographics

Demographic		Malignancy n=219						Necrotizing granulomatous inflammation n=125	HIV[1] reactive nodes n=46	Not definitive n=170	TOTAL n=560
		KS[2]	NHL[3]	CHL[4]	Car[5]	Other	Subtotal				n (%)
GENDER	Male	9	29	27	21	11	97	58	17	80	252 (45)
	Female	5	31	22	58	6	122	67	29	90	308 (55)
RACE	Asian				1		1	2			3 (1)
	Black	14	58	46	69	16	203	116	44	160	523 (93)
	White			2	9		11	3	1	9	24 (4)
	Mixed Race		2	1		1	4	4	1	1	10 (2)
AGE	Median 40 (12-94)										
AGE BAND	12-20yr		4	5	2		11	11	1	18	41 (7)
	21-35yr	11	13	20	13	9	66	59	22	40	187 (34)
	36-50yr	3	25	17	31	6	82	46	20	53	201 (36)
	51-65yr		15	7	25	1	48	8	3	48	107 (19)
	>65yr		3		8	1	12	1		11	24 (4)

[1]HIV: Human Immunodeficiency Virus
[2]KS: Kaposi sarcoma
[3]NHL: non-Hodgkin Lymphoma
[4]CHL: Classical Hodgkin Lymphoma
[5]Car: carcinoma

3.2 Indications for biopsy and topographic site of biopsies

The most common indication for biopsy was an uncertain diagnosis (more than two differential diagnoses entertained), followed by a suspicion for lymphoma, carcinoma and TB [Table 5]. The most frequent site of biopsy was cervical lymph node, followed by "other" which included laparoscopic biopsies (of intra-abdominal nodes), axillary and inguinal nodal biopsies. Laparoscopic biopsies were performed as part of a staging or curative process for patients known to have carcinoma. In other instances, lymph nodes were found incidentally during laparotomy or laparoscopy and subsequently sampled.

Of the patients suspected to have lymphoma, 28% were diagnosed with non-Hodgkin lymphoma and 23% with Hodgkin lymphoma (classical Hodgkin lymphoma and nodular lymphocyte predominant Hodgkin lymphoma). Of the patients with suspected TB, 62% displayed necrotizing granulomatous inflammation as per biopsy, while 53% of patients with a biopsy indication of staging carcinoma had confirmed carcinoma on biopsy.

Table 5. Biopsy Diagnosis in relation to Indications and site of biopsy

		Malignancy n=219						Necrotizing Nodes n=125	HIV[1] reactive nodes n=46	Not definitive n=170	TOTAL n=560
		KS[2]	NHL[3]	CHL[4]	Car[5]	Other	Subtotal				n (%)
INDICATION FOR BIOPSY	Suspect TB[6]	1	5	2	2	1	11	46	9	8	74 (13)
	Suspect lymphoma	2	33	28	4	4	71	17	13	19	120 (22)
	Staging Car[5]				60		60		0	54	114 (20)
	Uncertain Diagnosis	9	16	14	12	9	60	45	20	77	202 (36)
	Unknown	2	6	5	1	3	17	17	4	12	50 (9)
SITE OF LYMPH NODE BIOPSY	Cervical	8	26	37	18	9	98	73	16	31	218 (40)
	Inguinal	2	10	2	10	1	25	5	9	19	58 (10)
	Axilla	2	11	7	35	6	61	18	12	38	129 (23)
	Other	2	13	3	16	1	35	29	9	82	155 (27)

[1]HIV: Human Immunodeficiency Virus
[2]KS: Kaposi sarcoma
[3]NHL: non-Hodgkin Lymphoma
[4]CHL: Classical Hodgkin Lymphoma
[5]Car: carcinoma
[6]TB: Tuberculosis

3.3 Patterns of lymph node biopsy pathology

Overall, malignancy was the largest biopsy pathology group (39%), with 36% of this group having carcinoma and 27% non-Hodgkin lymphoma [Figure 1]. 22% of the total sample comprised nodes that displayed necrotizing granulomatous inflammation (including histopathology demonstrating definite mycobacterial infection and suspicious for mycobacterial infection). 8% of the sample comprised HIV-associated lymphadenitis and in the remainder no specific pathology was identified (including nonspecific reactive lymphoid hyperplasia).

Kaposi sarcoma (KS) accounted for 3% of lymph node pathology in the sample. Concomitant lymph node pathology was diagnosed within four cases of nodal KS (29% of the subset). The co-existing pathologies were mycobacterial infection [Figure 2] in one patient, Castleman disease [Figure 3] in two patients, and a combination of mycobacterial infection and Castleman disease in the fourth patient.

Rare causes of lymphadenopathy in this study included one case of Cryptococcosis (microbiologically confirmed) in an HIV-positive male patient who had profound immunosuppression (CD4 count of 8 cells/ul). In addition, there was a case of myeloid sarcoma (extramedullary counterpart of chronic myeloid leukaemia) in an HIV-positive female who had a CD4 count of 1626 cells/ul.

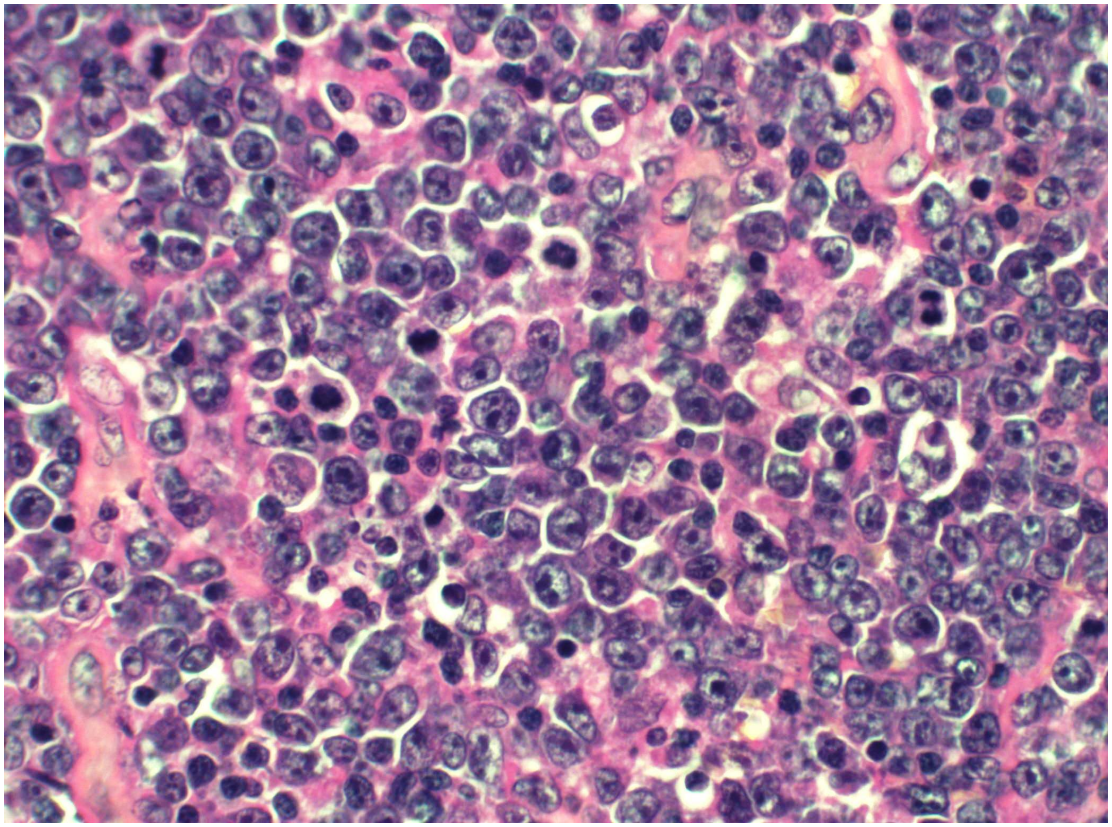


Figure 1. Diffuse large B-cell lymphoma, H&E stain x400 magnification

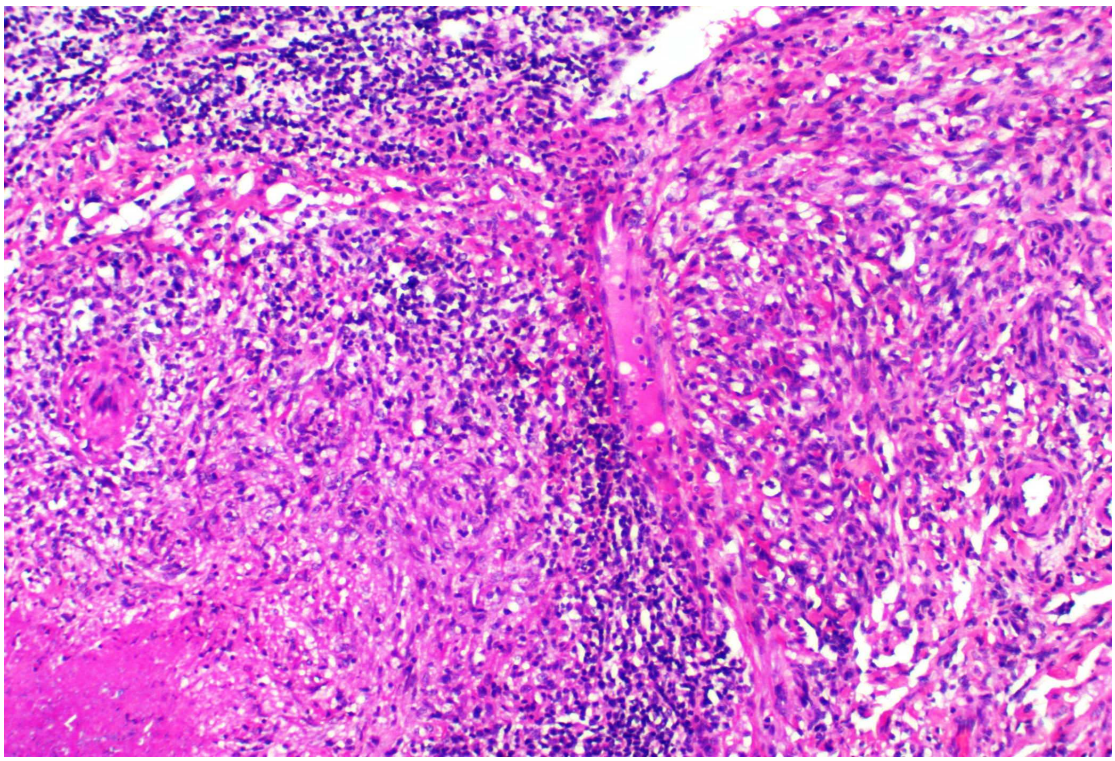


Figure 2. Kaposi sarcoma (right side of image) and necrotizing granulomatous inflammation (left side of image), H&E stain x100 magnification

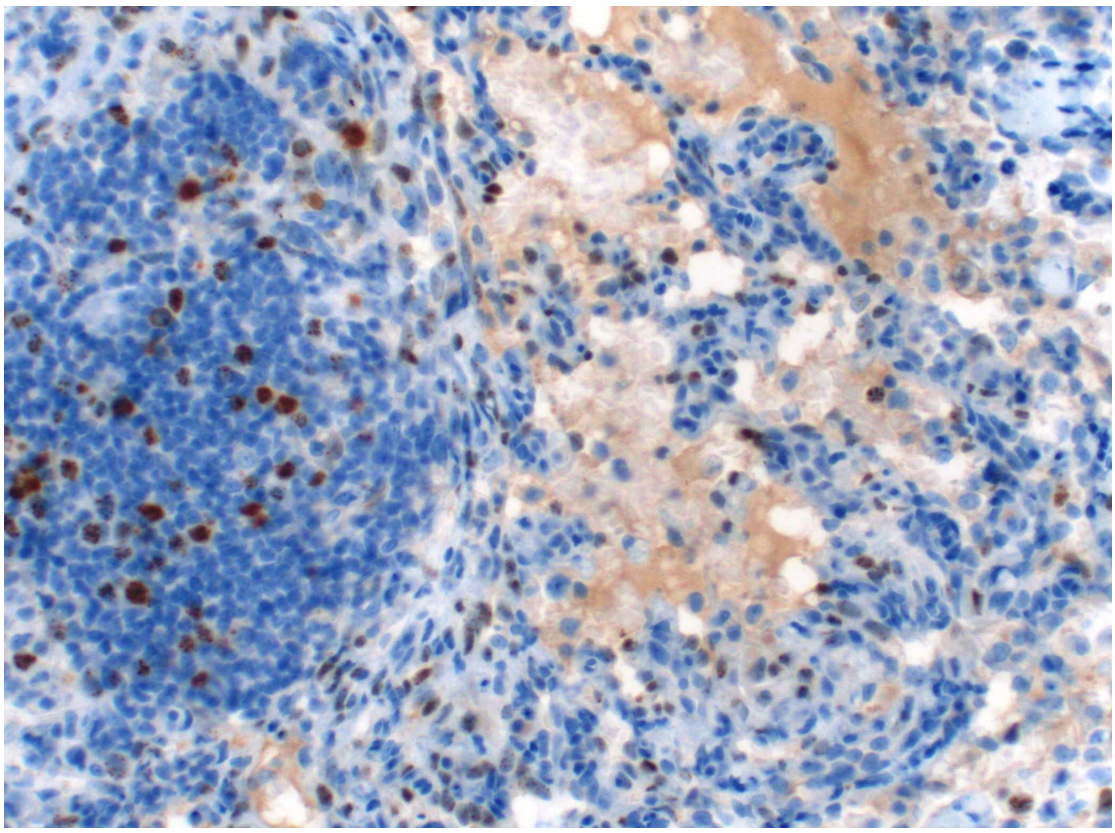


Figure 3. HHV8 immunohistochemistry demonstrating Castleman disease (left side of image) and Kaposi sarcoma lymphangiectatic variant (right side)

3.4 Distribution of disease according to HIV status

HIV-positive patients constituted 49% of the sample, with the majority of patients in this subset (64%) having a CD4 count below 350 cells/ul. 27% were HIV-negative and in the remaining 24%, the HIV status of patients was unknown. The most common lymph node pathologies in HIV-positive patients were mycobacterial infection (31%), HIV-associated lymphadenitis (15%), non-Hodgkin lymphoma (15%) and non-specific reactive lymphoid hyperplasia (15%) [Table 6]. Only 9% were of Hodgkin lymphoma.

In contrast, the most common lymph node pathologies in HIV-negative patients were nonspecific reactive lymphoid hyperplasia (45%), carcinoma (25%) and Mycobacterial infection (11%). In this group, non-Hodgkin lymphoma and Hodgkin lymphoma constituted 9% and 8%, respectively.

Only one HIV-negative case was classified as HIV lymphadenitis. This diagnosis was erroneously influenced by incorrectly specified clinical information regarding HIV status in the laboratory request form.

The diagnosis of TB and of carcinoma in the HIV-positive group versus the HIV-negative group had odds ratios of 3.52 (1.99-6.19) $p<0.001$ and 0.16 (0.09-0.32) $p<0.001$, respectively. However, the diagnosis of non-Hodgkin lymphoma and of Hodgkin lymphoma in the HIV-positive group versus the HIV-negative group had odds ratios of 1.66 (0.87-3.16) $p=0.12$ and 1.10 (0.54-2.28) $p=0.79$, respectively.

Table 6. Biopsy diagnosis in relation to HIV status

HIV status		Malignancy n=219						Necrotizing Nodes n=125	HIV[1] reactive nodes n=46	Not definitive n=170	TOTAL n=560
		KS[2]	NHL[3]	CHL[4]	Car[5]	Other	Subtotal				n (%)
	Subtotals	14	60	49	79	17	219	125	46	170	560 (100)
HIV[1] NEGATIVE			14	12	37	1	64	17	1	68	150 (27)
HIV[1] UNKNOWN		1	6	13	28	1	49	23	4	60	136 (24)
HIV[1] POSITIVE		13	40	24	14	15	106	85	41	42	274 (49)
CD4[6] BAND (cells/ul)	<100		7	4		3	14	35	2	6	57 (10)
	100-200	3	13	5	5	2	28	19	5	6	58 (11)
	201-350	5	8	8	1	6	28	10	12	11	61 (11)
	351-500	2	2	5	1		10	1	7	4	22 (4)
	>500	1	3		3	4	11	2	5	6	24 (4)
	Nil/ Unknown	2	7	2	4		15	18	10	9	52 (9)

[1]HIV: Human Immunodeficiency Virus
[2]KS: Kaposi sarcoma
[3]NHL: non-Hodgkin Lymphoma
[4]CHL: Classical Hodgkin Lymphoma
[5]Car: carcinoma
[6]CD4: Cluster of Differentiation 4 T-cells

3.5 Distribution of high-grade non-Hodgkin lymphoma according to HIV status

Amongst the patients with non-Hodgkin lymphoma, 66% were HIV-positive. In the HIV-positive subset, 50% of patients were diagnosed with DLBCL and 18% with Burkitt lymphoma. Plasmablastic lymphoma, B-cell lymphoma, unclassifiable with features intermediate between Burkitt lymphoma and DLBCL and anaplastic large cell lymphoma each contributed a further 10% to the HIV-positive group. In contrast, DLBCL was found in only 21% of the HIV-negative group.

3.6 Correlation of FNA and lymph node biopsies

There were 203 (36%) patients in our study sample who also underwent FNAs prior to biopsy. Of the FNAs, 23% were inadequate for assessment, 76% were adequate and in 1% adequacy was not commented on. When compared with the histopathology diagnosis as per lymph node biopsies, FNA was found to have excellent agreement with regards to Hodgkin lymphoma (K 0.774, SE 0.07, 95% CI 0.606-0.882, p=0.001), and good agreement with regards to non-Hodgkin lymphoma (K 0.640, SE 0.07, 95% CI 0.472-0.807, p=0.001), carcinoma (K 0.723, SE 0.069, 95% CI 0.528-0.918, p=0.001), and mycobacterial infection (K 0.726, SE 0.07, 95% CI 0.618-0.833, p=0.001) [Table 7].

Table 7. Statistical Agreement between LN FNA and LN Biopsy

Pathological Diagnosis	% observed agreements	% agreements expected by chance	Kappa	SE	95% Confidence Interval	P-value
CHL[1]	94.09	76.92	0.744	0.07	0.606-0.882	0.001
NHL[2]	92.61	79.50	0.640	0.07	0.472-0.807	0.001
Car[3]	96.55	87.55	0.723	0.069	0.528-0.918	0.001
Granulom inflam NOS[4]	97.04	95.20	0.385	0.07	-0.005-0.775	0.001
MI[5]	89.16	60.49	0.726	0.07	0.618-0.833	0.001
Non-specific reactive LH[6]	80.30	67.28	0.398	0.067	0.249-0.547	0.001

[1]CHL: Classical Hodgkin Lymphoma
[2]NHL: non Hodgkin Lymphoma
[3]Car: carcinoma
[4]Granulom inflam NOS: Granulomatous Inflammation not otherwise specified
[5]MI: Mycobacterial Infection
[6]Non-specific reactive LH: non-specific reactive lymphoid hyperplasia

3.7 Analysis of patients with more than one lymph node biopsy

There were two cases where a single patient had more than one lymph node biopsy during the period of the study. Both patients were HIV-positive with CD4 counts below 200 cells/ul. FNAs were performed prior to biopsy in both cases and were not definitive. The sites of the biopsies were, respectively, axillary and cervical in the first patient, and cervical both times, in the second patient. The definitive biopsies were both repeated due to a high index of clinical suspicion, and both subsequently confirmed to be non-Hodgkin lymphoma.

4.0 Discussion

4.1 Study findings

The majority of patients who underwent lymph node biopsy at CHBAH were middle-aged African/black females. Nodal pathology diagnoses at CHBAH include malignancy, necrotizing granulomatous inflammation and reactive nodes (due to HIV or other). The most common lymph node pathologies at CHBAH as per biopsy are in keeping with local African literature (Sibanda & Stanczuk, 1993; Muthuphei, 1998; and Olu-eddo & Omoti, 2011).

The most common indications for requesting a lymph node biopsy in our setting were an uncertain diagnosis and the suspicion of malignancy or TB, which reflects the relative dominance of the latter two diseases in Southern Africa.

In a study performed at CHBAH, by Edginton et al (2005), of the patients diagnosed with TB, 74% had pulmonary TB and of the patients with extrapulmonary TB, pleural and miliary were the most common forms. However, more recent publications by Fontanilla et al (2011), Ligthelm et al (2011), and Handa et al (2012) suggest that TB lymphadenitis is the most common form of extrapulmonary TB. The high prevalence of TB and TB suspicious lymphadenitis at CHBAH has been described by Karstaedt (2014), notably in the age band 25-44 years. In this study, 22% of lymph node biopsies and 27% of FNAs comprised nodes that displayed necrotizing granulomatous inflammation (including histopathology and cytology demonstrating definite mycobacterial infection and suspicious for mycobacterial infection), confirming the high prevalence of TB in CHBAH.

The study by Martinson et al (2011) stated that the risk of TB increases at lower CD4 counts, and suggested that early antiretroviral therapy reduced the population prevalence of TB in HIV-positive patients. This suggestion may also be evident in this study as the majority of HIV-positive patients in the sample had CD4 counts less than 350 cells/ul and the most common lymph node pathology in this group was confirmed and suspected TB. This study demonstrated statistically significant greater odds of diagnosing TB in an HIV-positive patient compared to an HIV-negative patient.

The findings in this study demonstrate the known significant correlation between HIV incidence and incidence of aggressive B-cell lymphomas and Hodgkin lymphoma (Wiggill et al, 2011; and Kaplan, 2012). However, the odds ratios in this study were not statistically significant in terms of diagnosing non-Hodgkin lymphoma and Hodgkin lymphoma in HIV-positive versus HIV-negative patients. Associated risk factors for the development of these malignancies are high HIV viral loads and low CD4 counts,

although malignancies may occur at any CD4 count (Kaplan, 2012). Of the HIV-infected patients with non-Hodgkin lymphoma in this study, 70% had CD4 counts under 350 cells/ul. The pathogenesis is thought to be immune dysregulation with loss of T-cell immunity against onco-viruses like Epstein-Barr Virus and human herpesvirus 8 (HHV8) (Kaplan, 2012).

The Zambian study by Bem et al (1996) suggested that primary HIV lymphadenopathy was a significant cause of superficial lymphadenopathy. This finding is also highlighted in this study, as HIV reactive nodes comprised 8% of the total sample, and was amongst the largest nodal pathology group in HIV-positive patients (15%), with the majority (29%) of these patients having CD4 counts in the range of between 201 and 350 cells/ul.

The association between KS and multicentric Castleman disease due to the common causal agent HHV8 is well described in the literature (Dupin et al, 1999). This association has been demonstrated by the co-existence of both these pathologies in lymph nodes in this study. Interestingly, two patients in this study with coexisting KS and Castleman disease had CD4 counts above 350 cells/ul. CD4 counts were not available for the remaining two patients who had concomitant lymph node pathology. A possible explanation for the relatively high CD4 counts may be immune reconstitution inflammatory syndrome.

This study affirmed a good correlation between FNA diagnosis and biopsy diagnosis on lymph node specimens, and has in turn raised questions regarding the implications for use of FNA as a first line diagnostic procedure in our resource limited but academic setting, and how it could be better implemented. The healthcare system advantages of FNA theoretically include optimal use of scarce resources, triage of patients at a primary

or regional level, improved turnaround time, and improved patient compliance (Wright, 2012). Perhaps, the most important role of FNA is in triaging reactive causes of lymphadenopathy from infectious and malignant aetiologies, allowing for appropriate follow up, referral and management (Wright, 2012; and Razack et al, 2014).

As emphasized in the literature and noted in the findings of this study, the benefits of FNA depend on an adequate, well-prepared specimen and analysis in a cytopathology laboratory experienced in examination of FNAs (Ansari & Derias, 1997; Stewart et al, 1998; and Wright, 2012). In the absence of such conditions, caution should be exercised when interpreting FNA results as they may be misleading and dangerous, as noted by Hehn et al (2004), clinicians working in a lymphoma centre, who found that 88% of patients in their study were given inadequate FNA diagnoses on which to base treatment, and 15% having been given the wrong diagnosis. Taking into account the findings of Hehn et al (2004) and the findings of this study, in the event of inadequate FNA samples, the result should be treated with reserve.

There are practical barriers to the use of FNA as a primary diagnostic modality for lymphadenopathy in our setting, as well as in first world countries. Amongst these is diagnostic delay in the event of a non-contributory FNA. The study by Hehn et al (2004) noted that the average time elapsed between inadequate FNA and eventual excisional biopsy diagnosis was more than 35 days. In addition to disease progression and treatment delay during this time, further disadvantages incurred by patients are cost of the second procedure, discomfort and additional costs such as transportation cost and time spent away from work.

Another impedance to the primary use of FNA in patients suspected to have lymphoma is a policy by haematologist-oncologist specialists in referral centres to only treat patients based on a diagnosis obtained from or confirmed by an excisional biopsy (Amador-Oritz, 2011). This is standard policy in CHBAH, and often influences clinicians to proceed directly to biopsy in cases of suspected lymphoma, in efforts to save valuable time in the case of high-grade lymphomas, and money in our resource limited setting.

The literature highlights the shortage of cytopathologists in South Africa, and the effect this has on the quality of FNAs done and the turnaround time of reporting (Wright, 2012). The NHLS was established in 2001 and is the largest diagnostic pathology service in South Africa, with 349 laboratories serving 80% of the population (South African government website). According to Pillay (2013), 3.5% of provincial budgets are allocated towards paying for pathology services in the state sector in South Africa. The National Health Insurance scheme is expected to place our already strained pathology service under increased pressure, as "improvement of access to healthcare will increase demand for diagnostic testing" (Pillay, 2013). Developments in new technology and inappropriate usage of laboratory tests are thought to add to costs overall, emphasizing the need for demand management protocols in laboratories (Pillay, 2013). In essence, a marriage between laboratory practices and clinician-directed testing behavior needs to be achieved, to ensure proper use of diagnostic testing and improved patient care (Pillay, 2013). Communication between pathologists and clinicians is necessary on a case-by-case basis as well, as clinical history and quality of specimen, often underestimated in value by clinicians, are essential for optimal pathologic diagnoses (Ansari & Derias, 1997; Kumar et al, 2010; and Wright, 2012).

Findings from this study and other studies locally and internationally support the use of FNA as a primary diagnostic procedure for the investigation of lymphadenopathy (Stewart et al, 1998; and Razack et al, 2014). Stewart et al (1998) reported a high sensitivity and specificity of FNA for diagnosis of lymphomas, when used in conjunction with ancillary testing, especially immunocytochemistry and FISH.

From a South African clinician point of view, the focus should be on submitting an optimal quality FNA with adequate clinical information. In CHBAH, nurses trained by the NHLS provide FNA services daily, during working hours. This is a means of assuring optimal quality samples, thereby generating reliable results. However, at the other two academic hospitals attached to the University of the Witwatersrand, Helen Joseph Hospital and Charlotte Maxeke Johannesburg Academic Hospital, FNA services are provided only twice a week, on Tuesdays and Thursdays. The negative impact of this on patients is prolonged hospitalization while awaiting the FNA procedure and results. Potential improvements to the existing structure of FNA services could include making FNA services available daily in all hospitals, workshops involving cytopathologists teaching clinicians the proper technique for performing and submitting FNAs with ancillary studies, and ensuring that materials required for FNA are readily available in the wards.

Regarding patient management, policies may need to be re-evaluated with the haematology-oncologist specialists regarding the need for biopsy-proven disease prior to initiation of treatment. Algorithms need to be developed to decide which lymphoproliferative malignancies require further subclassification on biopsy prior to treatment, and which can be treated based on results of FNA cytomorphology and ancillary studies.

The use of FNA in combination with core needle biopsy, as used in the study by Amador-Oritz et al (2011) may be a future consideration for investigation of patients suspected to have lymphoma, as this employs use of FNA for ancillary studies such as flow cytometry and core needle biopsy for evaluation of tissue architecture. Radiologists or clinicians, obviating the need for surgery, can perform core needle biopsies. Although this method combines the advantages of both FNA and biopsy, the practical implementation and cost in our setting need to be considered.

4.2 Recommendations

An initial FNA is indicated for any suspicion of TB or malignancy in our setting, if it does not significantly contribute to a delay in establishing treatment. If there is a clinical concern for nodal-based mycobacterial disease or malignancy despite a non-contributory FNA, an appropriate lymph node should be submitted for histopathologic assessment. In the event of persistent clinical concern, despite a negative histopathology result, an incisional or excisional biopsy should be considered. The importance of a repeat biopsy where there is a high clinical suspicion for disease, particularly in HIV-positive patients, was highlighted in the two patients from this study, subsequently confirmed to have non-Hodgkin lymphoma. The findings suggest that negative biopsy results in HIV-positive patients should be treated with reserve if there is a high index of clinical suspicion for lymphoma.

In correlating FNA with lymph node biopsy, there is scope for prospective studies to directly compare the two modalities and develop clinical algorithms taking into account

the clinical and demographic profile of patients who should proceed directly to lymph node biopsy in order to expedite diagnosis and treatment.

4.3 Limitations of the study

Limitations of the study include its selection bias, retrospective nature, and possible information bias as data was extracted from a database in which variable SNOMED codes for nodes at different topographic sites may be used. However, the findings correlate well with both local and international literature on the subject.

5.0 Conclusion

This study showed that the most common lymph node pathologies occurring in patients who underwent biopsies at CHBAH are malignancies, nonspecific reactive lymphoid hyperplasia, necrotizing granulomatous inflammation due to mycobacterial infection, and HIV-associated lymphadenitis. The distribution of disease differed in HIV-positive patients. FNA was found to have good overall correlation with histopathology biopsy diagnoses in our setting. The diagnosis specified in an FNA report should be interpreted in conjunction with the comment/s about adequacy of the aspirated specimen for assessment. Due to the coexistence of nodal KS with other pathologies, patients who have suspected nodal KS would benefit from proceeding directly to have biopsies for histopathological assessment.

6.0 Appendices

6.1 Plagiarism Declaration form

Faculty of Health Sciences, Postgraduate Office
Phillip V Tobias Building, 2nd Floor
Cnr York & Princess of Wales Terrace, Parktown 2193
Tel: (011) 717 2745 | Fax: (011) 717 2119
Email: Mathoto.senamela@wits.ac.za

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I , Denasha Lavanya Reddy (Student number: 742452) am a student

registered for the degree of Master of Medicine in the academic year 2015.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: _____

6.2 Human Research Ethics Committee approval form

R14/49 Dr Denasha Lavanya Reddy

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130626

NAME: (Principal Investigator)	Dr Denasha Lavanya Reddy
DEPARTMENT:	Internal Medicine Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Patterns of Lymph Node Biopsy Pathology at Chris Hani Baragwanath Hospital over a period of three years 2010 - 2012
DATE CONSIDERED:	28/06/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof WD Venter/Dr S Pather
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	13/11/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

6.3 Protocol Approval form

Faculty of Health Sciences
Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172040

Reference: Ms Thokozile Nhlapo
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07 January 2014
Person No: 742452
PAG

Dr DL Reddy
PO Box 82
Newcastle
2940
South Africa

Dear Dr Reddy

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Patterns of lymph node biopsy pathology at Chris Hani Baragwanath Hospital over a period of three years 2010-2012* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

6.4 Data

Patient Numl	Age	Age Band	Sex	Race	Indication	Indication2	Site of Lympl	HIV Status	CD4 Count	CD4 Band	Bio Diagnosis	Bio Diagnosis	FNA Diagnos	FNA Diagnosis2
Patient 1	30	21	M	B	4	Uncertain Dia	O	P	Nil	Nil	1	KS	11	Not done
Patient 2	44	36	M	B	2	Suspect Lymp	C	P	24	0	6	TB	11	Not done
Patient 3	29	21	F	B	2	Suspect Lymp	C	P	99	0	3	HL	2	NHL
Patient 4	50	36	F	B	4	Uncertain Dia	O	U	Nil	Nil	10	Not definitive	11	Not done
Patient 5	36	36	M	B	2	Suspect Lymp	A	P	247	201	3	HL	3	HL
Patient 6	31	21	F	B	1	Suspect TB	C	P	217	201	9	HIV reactive	11	Not done
Patient 7	52	51	F	B	4	Uncertain Dia	O	N	Nil	Nil	10	Not definitive	11	Not done
Patient 8	19	12	M	B	4	Uncertain Dia	O	N	Nil	Nil	10	Not definitive	11	Not done
Patient 9	29	21	M	B	5	Unknown	C	P	210	201	3	HL	7	TB Suspicious
Patient 10	52	51	M	B	2	Suspect Lymp	O	N	Nil	Nil	2	NHL	11	Not done
Patient 11	19	12	F	B	2	Suspect Lymp	C	N	Nil	Nil	2	NHL	10	Not definitive
Patient 12	35	21	F	B	4	Uncertain Dia	O	P	13	0	10	Not definitive	11	Not done
Patient 13	59	51	F	B	3	Staging Aden	I	N	Nil	Nil	10	Not definitive	11	Not done
Patient 14	22	21	F	B	2	Suspect Lymp	C	P	Nil	Nil	9	HIV reactive	11	Not done
Patient 15	31	21	M	B	1	Suspect TB	O	P	Nil	Nil	6	TB	11	Not done
Patient 16	40	36	F	B	5	Unknown	C	P	183	100	7	TB Suspicious	11	Not done
Patient 17	52	51	M	B	5	Unknown	A	P	120	100	7	TB Suspicious	7	TB Suspicious
Patient 18	64	51	F	B	3	Staging Aden	A	N	Nil	Nil	10	Not definitive	11	Not done
Patient 19	44	36	M	B	4	Uncertain Dia	C	P	27	0	6	TB	11	Not done
Patient 20	51	51	M	B	1	Suspect TB	O	P	47	0	2	NHL	11	Not done
Patient 21	31	21	F	B	1	Suspect TB	O	P	19	0	6	TB	11	Not done
Patient 22	30	21	F	B	2	Suspect Lymp	C	P	Nil	Nil	9	HIV reactive	10	Not definitive
Patient 23	17	12	M	B	4	Uncertain Dia	O	U	Nil	Nil	10	Not definitive	11	Not done
Patient 24	61	51	M	B	3	Staging Aden	O	N	Nil	Nil	4	Adenocarcino	5	Other
Patient 25	42	36	M	B	4	Uncertain Dia	I	P	342	201	7	TB Suspicious	11	Not done
Patient 26	33	21	M	B	1	Suspect TB	O	P	30	0	6	TB	11	Not done
Patient 27	42	36	F	B	4	Uncertain Dia	O	P	18	0	7	TB Suspicious	7	TB Suspicious
Patient 28	35	21	F	B	4	Uncertain Dia	A	U	Nil	Nil	3	HL	11	Not done
Patient 29	35	21	M	B	4	Uncertain Dia	O	P	Nil	Nil	6	TB	11	Not done
Patient 30	44	36	M	B	4	Uncertain Dia	O	U	Nil	Nil	8	Other	11	Not done
Patient 31	38	36	F	B	4	Uncertain Dia	I	N	Nil	Nil	10	Not definitive	10	Not definitive
Patient 32	41	36	M	B	1	Suspect TB	O	U	Nil	Nil	6	TB	7	TB Suspicious
Patient 33	59	51	M	B	2	Suspect Lymp	O	P	141	100	10	Not definitive	11	Not done
Patient 34	16	12	M	B	4	Uncertain Dia	O	U	Nil	Nil	10	Not definitive	11	Not done
Patient 35	54	51	F	C	4	Uncertain Dia	O	P	563	501	9	HIV reactive	10	Not definitive
Patient 36	40	36	F	B	4	Uncertain Dia	O	U	Nil	Nil	10	Not definitive	11	Not done
Patient 37	56	51	M	W	4	Uncertain Dia	C	N	Nil	Nil	4	Adenocarcino	5	Other
Patient 38	44	36	M	B	4	Uncertain Dia	I	N	Nil	Nil	8	Other	11	Not done
Patient 39	58	51	M	B	3	Staging Aden	C	N	Nil	Nil	10	Not definitive	7	TB Suspicious
Patient 40	46	36	M	B	1	Suspect TB	O	P	8	0	10	Not definitive	10	Not definitive
Patient 41	25	21	F	B	4	Uncertain Dia	A	N	Nil	Nil	10	Not definitive	11	Not done
Patient 42	18	12	M	B	2	Suspect Lymp	O	N	Nil	Nil	10	Not definitive	11	Not done
Patient 43	70	66 and greate	F	B	3	Staging Aden	O	U	Nil	Nil	4	Adenocarcino	11	Not done
Patient 44	37	36	F	B	1	Suspect TB	C	P	Nil	Nil	10	Not definitive	11	Not done
Patient 45	45	36	F	B	2	Suspect Lymp	A	P	Nil	Nil	12	Reactive Lym	11	Not done
Patient 46	43	36	M	B	1	Suspect TB	C	U	Nil	Nil	6	TB	7	TB Suspicious
Patient 47	36	36	M	B	4	Uncertain Dia	O	U	Nil	Nil	10	Not definitive	11	Not done
Patient 48	32	21	M	B	2	Suspect Lymp	O	P	130	100	10	Not definitive	11	Not done
Patient 49	34	21	M	B	1	Suspect TB	I	P	29	0	6	TB	11	Not done
Patient 50	45	36	F	B	1	Suspect TB	A	P	269	201	6	TB	11	Not done
Patient 51	28	21	M	B	1	Suspect TB	C	P	433	351	9	HIV reactive	10	Not definitive
Patient 52	34	21	F	B	2	Suspect Lymp	O	P	113	100	6	TB	11	Not done
Patient 53	44	36	M	B	2	Suspect Lymp	C	P	121	100	6	TB	11	Not done
Patient 54	18	12	F	B	2	Suspect Lymp	O	P	Nil	Nil	6	TB	11	Not done
Patient 55	49	36	M	B	4	Uncertain Dia	I	P	268	201	9	HIV reactive	11	Not done

Age Band	12	12 to 20
	21	21 to 35
	36	36 to 50
	51	51 to 65
	66	66 and greater
Sex	M	Male
	F	Female
	U	Unknown
Race	B	Black
	W	White
	C	Coloured
	A	Asian
	U	Unknown
Indication	1	Suspect TB
	2	Suspect Lymphoma
	3	Staging Adenocarcinoma
	4	Uncertain Diagnosis
	5	Unknown
Site of Lympl	C	Cervical
	I	Inguinal
	A	Axilla
	O	Other
HIV Status	P	Postive
	N	Negative
	U	U
CD4 Band	0	<100
	100	100 to 200
	201	201 to 350
	351	351 to 500
	501	501 and greater
Biopsy Diagn	1	KS
	2	NHL
	3	HL
	4	Adenocarcinoma
	5	Other
	6	TB
	7	TB Suspicious
	8	Other
	9	HIV reactive nodes
	10	Not definitive

Patient 56	48	36	M	C	2	Suspect Lym	O	P		21	0	2	NHL	10	Not definitive			12	Reactive lymphoid hyperplasia
Patient 57	44	36	F	B	2	Suspect Lym	C	P		43	0	6	TB	6	TB				
Patient 58	36	36	M	B	1	Suspect TB	A	P		255	201	12	Reactive Lym	11	Not done	FNA Diagnos		1	KS
Patient 59	40	36	M	B	4	Uncertain Di	A	P		103	100	6	TB	6	TB			2	NHL
Patient 60	31	21	F	B	2	Suspect Lym	C	P		126	100	3	HL	3	HL			3	HL
Patient 61	65	51	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11	Not done			4	Adenocarcinoma
Patient 62	63	51	F	B	4	Uncertain Di	C	N	Nil	Nil		10	Not definitive	11	Not done			5	Other
Patient 63	12	12	F	B	4	Uncertain Di	C	U	Nil	Nil		9	HIV reactive	11	Not done			6	TB
Patient 64	33	21	M	B	1	Suspect TB	A	U	Nil	Nil		6	TB	6	TB			7	TB Suspicious
Patient 65	32	21	F	B	4	Uncertain Di	O	P		173	100	7	TB Suspicious	11	Not done			8	Other
Patient 66	66	66 and great	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11	Not done			9	HIV reactive nodes
Patient 67	24	21	F	B	4	Uncertain Di	A	N	Nil	Nil		10	Not definitive	10	Not definitive			10	Not definitive
Patient 68	39	36	M	B	4	Uncertain Di	A	P		213	201	7	TB Suspicious	7	TB Suspicious			11	Not done
Patient 69	18	12	M	B	2	Suspect Lym	O	U	Nil	Nil		3	HL	11	Not done				
Patient 70	15	12	F	B	4	Uncertain Di	C	N	Nil	Nil		6	TB	10	Not definitive				
Patient 71	47	36	M	B	2	Suspect Lym	C	P		299	201	2	NHL	3	HL				
Patient 72	43	36	F	B	2	Suspect Lym	I	P		46	0	2	NHL	2	NHL				
Patient 73	26	21	F	B	4	Uncertain Di	O	P		320	201	10	Not definitive	11	Not done				
Patient 74	54	51	F	B	4	Uncertain Di	A	P		295	201	9	HIV reactive	10	Not definitive				
Patient 75	24	21	F	B	4	Uncertain Di	A	P	Nil	Nil		3	HL	3	HL				
Patient 76	35	21	M	B	2	Suspect Lym	C	P		215	201	6	TB	6	TB				
Patient 77	56	51	F	B	4	Uncertain Di	I	N	Nil	Nil		2	NHL	10	Not definitive				
Patient 78	61	51	F	B	3	Staging Aden	C	N	Nil	Nil		4	Adenocarcin	11	Not done				
Patient 79	56	51	M	W	4	Uncertain Di	O	U	Nil	Nil		10	Not definitive	11	Not done				
Patient 80	34	21	F	B	4	Uncertain Di	C	P		232	201	1	KS	10	Not definitive				
Patient 81	36	36	F	B	4	Uncertain Di	I	U		1364	501	2	NHL	11	Not done				
Patient 82	46	36	F	B	4	Uncertain Di	O	U		385	351	10	Not definitive	11	Not done				
Patient 83	64	51	F	W	4	Uncertain Di	C	U	Nil	Nil		6	TB	6	TB				
Patient 84	30	21	M	B	4	Uncertain Di	C	U	Nil	Nil		6	TB	7	TB Suspicious				
Patient 85	36	36	F	B	2	Suspect Lym	O	P		98	0	10	Not definitive	2	NHL				
Patient 86	35	21	F	B	2	Suspect Lym	C	P	Nil	Nil		2	NHL	11	Not done				
Patient 87	35	21	F	B	4	Uncertain Di	A	N	Nil	Nil		4	Adenocarcin	4	Adenocarcinoma				
Patient 88	33	21	M	B	1	Suspect TB	O	P	Nil	Nil		6	TB	11	Not done				
Patient 89	34	21	M	B	4	Uncertain Di	C	P		281	201	5	Other	9	HIV reactive nodes				
Patient 90	56	51	M	B	3	Staging Aden	O	N	Nil	Nil		10	Not definitive	11	Not done				
Patient 91	12	12	F	B	4	Uncertain Di	O	U	Nil	Nil		10	Not definitive	11	Not done				
Patient 92	30	21	F	B	2	Suspect Lym	I	P		86	0	2	NHL	2	NHL				
Patient 93	34	21	F	C	1	Suspect TB	A	P		194	100	6	TB	7	TB Suspicious				
Patient 94	61	51	F	B	4	Uncertain Di	C	N	Nil	Nil		3	HL	10	Not definitive				
Patient 95	35	21	M	B	4	Uncertain Di	O	P		135	100	12	Reactive Lym	11	Not done				
Patient 96	13	12	M	B	4	Uncertain Di	C	U	Nil	Nil		6	TB	11	Not done				
Patient 97	36	36	M	B	1	Suspect TB	A	P		236	201	2	NHL	11	Not done				
Patient 98	46	36	M	B	2	Suspect Lym	C	N	Nil	Nil		3	HL	11	Not done				
Patient 99	52	51	M	B	4	Uncertain Di	I	P		119	100	12	Reactive Lym	7	TB Suspicious				
Patient 100	42	21	M	W	4	Uncertain Di	C	U	Nil	Nil		3	HL	11	Not done				
Patient 101	59	51	M	B	4	Uncertain Di	C	N	Nil	Nil		4	Adenocarcin	10	Not definitive				
Patient 102	26	21	F	B	4	Uncertain Di	O	N	Nil	Nil		7	TB Suspicious	11	Not done				
Patient 103	58	51	M	B	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11	Not done				
Patient 104	45	36	M	W	4	Uncertain Di	I	P		392	351	9	HIV reactive	11	Not done				
Patient 105	26	21	F	B	2	Suspect Lym	C	P	Nil	Nil		6	TB	7	TB Suspicious				
Patient 106	53	51	F	B	2	Suspect Lym	C	U	Nil	Nil		2	NHL	11	Not done				
Patient 107	45	36	F	B	3	Staging Aden	I	N	Nil	Nil		4	Adenocarcin	11	Not done				
Patient 108	30	21	F	B	4	Uncertain Di	C	N	Nil	Nil		6	TB	11	Not done				
Patient 109	51	51	F	B	2	Suspect Lym	C	P	Nil	Nil		3	HL	3	HL				
Patient 110	39	36	M	B	1	Suspect TB	O	P	Nil	Nil		9	HIV reactive	11	Not done				
Patient 111	63	51	M	B	4	Uncertain Di	C	U	Nil	Nil		3	HL	10	Not definitive				

Patient 112	34	21	M	B	4	Uncertain Di	A	P		281	201	5	Other	9 HIV reactive nodes
Patient 113	61	51	F	B	2	Suspect Lym	A	P		409	351	9	HIV reactive	9 HIV reactive nodes
Patient 114	41	36	F	B	3	Staging Aden	O	P		349	201	10	Not definitive	11 Not done
Patient 115	49	36	M	B	4	Uncertain Di	C	N	Nil	Nil		8	Other	11 Not done
Patient 116	41	36	M	B	4	Uncertain Di	C	U	Nil	Nil		3	HL	11 Not done
Patient 117	58	51	F	B	3	Staging Aden	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 118	28	21	F	B	4	Uncertain Di	C	U	Nil	Nil		10	Not definitive	11 Not done
Patient 119	19	12	F	B	3	Staging Aden	O	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 120	63	51	F	B	4	Uncertain Di	C	N	Nil	Nil		3	HL	10 Not definitive
Patient 121	50	36	F	B	1	Suspect TB	A	P	Nil	Nil		9	HIV reactive	9 HIV reactive nodes
Patient 122	23	21	M	B	2	Suspect Lym	C	P		330	201	9	HIV reactive	10 Not definitive
Patient 123	38	36	F	B	1	Suspect TB	C	P		14	0	6	TB	11 Not done
Patient 124	44	36	M	B	2	Suspect Lym	C	P		139	100	9	HIV reactive	3 HL
Patient 125	31	21	M	B	4	Uncertain Di	C	U	Nil	Nil		3	HL	11 Not done
Patient 126	38	36	F	B	2	Suspect Lym	O	P		556	501	9	HIV reactive	2 NHL
Patient 127	45	36	M	B	2	Suspect Lym	C	U	Nil	Nil		2	NHL	11 Not done
Patient 128	51	51	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	4 Adenocarcinoma
Patient 129	43	36	M	B	4	Uncertain Di	O	P		693	501	5	Other	11 Not done
Patient 130	64	51	M	B	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11 Not done
Patient 131	36	36	F	B	2	Suspect Lym	C	P		263	201	10	Not definitive	10 Not definitive
Patient 132	50	36	M	W	3	Staging Aden	O	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 133	61	51	M	B	3	Staging Aden	O	N	Nil	Nil		10	Not definitive	11 Not done
Patient 134	40	36	M	B	4	Uncertain Di	C	N	Nil	Nil		6	TB	10 Not definitive
Patient 135	49	36	F	B	4	Uncertain Di	A	U	Nil	Nil		12	Reactive Lym	11 Not done
Patient 136	34	21	F	B	2	Suspect Lym	O	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 137	42	36	F	B	4	Uncertain Di	C	U	Nil	Nil		6	TB	7 TB Suspicious
Patient 138	54	51	M	B	2	Suspect Lym	O	N	Nil	Nil		2	NHL	11 Not done
Patient 139	40	36	M	B	2	Suspect Lym	C	P		564	501	4	Adenocarcin	11 Not done
Patient 140	36	36	F	B	1	Suspect TB	C	P		435	351	7	TB Suspicious	10 Not definitive
Patient 141	39	36	M	B	2	Suspect Lym	C	P		362	351	3	HL	3 HL
Patient 142	32	21	M	B	2	Suspect Lym	C	N	Nil	Nil		3	HL	3 HL
Patient 143	35	21	M	B	4	Uncertain Di	C	U	Nil	Nil		10	Not definitive	10 Not definitive
Patient 144	44	36	F	B	2	Suspect Lym	C	P		326	201	12	Reactive Lym	10 Not definitive
Patient 145	29	21	F	B	1	Suspect TB	C	P	Nil	Nil		6	TB	6 TB
Patient 146	29	21	F	B	2	Suspect Lym	C	P		182	100	6	TB	7 TB Suspicious
Patient 147	35	21	M	B	4	Uncertain Di	O	P		291	201	2	NHL	11 Not done
Patient 148	34	21	M	B	2	Suspect Lym	I	P		98	0	10	Not definitive	6 TB
Patient 149	35	21	M	B	2	Suspect Lym	C	P		77	0	3	HL	10 Not definitive
Patient 150	27	21	M	B	1	Suspect TB	A	P	Nil	Nil		6	TB	7 TB Suspicious
Patient 151	56	51	M	B	3	Staging Aden	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 152	48	36	F	B	2	Suspect Lym	C	P		346	201	3	HL	3 HL
Patient 153	27	21	F	B	4	Uncertain Di	A	U	Nil	Nil		12	Reactive Lym	9 HIV reactive nodes
Patient 154	50	36	M	W	3	Staging Aden	O	N	Nil	Nil		10	Not definitive	11 Not done
Patient 155	47	36	F	B	4	Uncertain Di	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 156	47	36	M	B	4	Uncertain Di	C	U	Nil	Nil		12	Reactive Lym	11 Not done
Patient 157	57	51	F	C	2	Suspect Lym	O	N	Nil	Nil		2	NHL	11 Not done
Patient 158	34	21	F	B	3	Staging Aden	A	P		193	100	4	Adenocarcin	4 Adenocarcinoma
Patient 159	55	51	F	B	4	Uncertain Di	I	P		42	0	7	TB Suspicious	11 Not done
Patient 160	32	21	M	B	4	Uncertain Di	A	P		188	100	1	KS	10 Not definitive
Patient 161	30	21	F	B	4	Uncertain Di	A	P		397	351	9	HIV reactive	9 HIV reactive nodes
Patient 162	21	21	M	B	4	Uncertain Di	C	U	Nil	Nil		12	Reactive Lym	11 Not done
Patient 163	34	21	M	B	4	Uncertain Di	A	P		287	201	9	HIV reactive	10 Not definitive
Patient 164	44	36	M	B	2	Suspect Lym	A	U	Nil	Nil		2	NHL	11 Not done
Patient 165	48	36	M	B	4	Uncertain Di	A	P		744	501	5	Other	11 Not done
Patient 166	70	66 and great	M	B	2	Suspect Lym	C	N	Nil	Nil		2	NHL	2 NHL
Patient 167	29	21	F	B	4	Uncertain Di	I	P	Nil	Nil		9	HIV reactive	11 Not done

Patient 168	24	21	F	B	4	Uncertain Di	I	P	Nil	Nil		1	KS	6	TB
Patient 169	58	51	M	B	2	Suspect Lym	C	U	Nil	Nil		4	Adenocarcin	11	Not done
Patient 170	29	21	F	B	2	Suspect Lym	A	P		80	0	2	NHL	2	NHL
Patient 171	47	36	F	B	4	Uncertain Di	O	U	Nil	Nil		8	Other	11	Not done
Patient 172	31	21	M	B	4	Uncertain Di	C	U	Nil	Nil		7	TB Suspicious	7	TB Suspicious
Patient 173	48	36	F	B	3	Staging Aden	O	N	Nil	Nil		10	Not definitive	11	Not done
Patient 174	36	36	F	B	2	Suspect Lym	C	P		195	100	2	NHL	11	Not done
Patient 175	55	51	M	B	1	Suspect TB	C	P		142	100	2	NHL	10	Not definitive
Patient 176	39	36	F	B	1	Suspect TB	C	P		11	0	6	TB	6	TB
Patient 177	59	51	F	B	4	Uncertain Di	C	N	Nil	Nil		10	Not definitive	11	Not done
Patient 178	55	51	M	B	1	Suspect TB	I	N	Nil	Nil		3	HL	11	Not done
Patient 179	36	36	M	B	4	Uncertain Di	A	P		385	351	3	HL	10	Not definitive
Patient 180	12	12	F	B	4	Uncertain Di	O	U	Nil	Nil		10	Not definitive	11	Not done
Patient 181	42	36	F	B	3	Staging Aden	O	P		329	201	10	Not definitive	11	Not done
Patient 182	28	21	M	B	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11	Not done
Patient 183	14	12	F	B	4	Uncertain Di	C	N	Nil	Nil		2	NHL	2	NHL
Patient 184	64	51	F	B	4	Uncertain Di	C	N	Nil	Nil		10	Not definitive	11	Not done
Patient 185	26	21	F	B	4	Uncertain Di	C	U	Nil	Nil		12	Reactive Lym	11	Not done
Patient 186	43	36	M	B	2	Suspect Lym	A	P		390	351	4	Adenocarcin	10	Not definitive
Patient 187	17	12	M	B	2	Suspect Lym	C	N	Nil	Nil		3	HL	3	HL
Patient 188	50	36	F	B	4	Uncertain Di	C	P		88	0	6	TB	11	Not done
Patient 189	35	21	M	B	2	Suspect Lym	O	P		238	201	2	NHL	11	Not done
Patient 190	48	36	M	B	1	Suspect TB	C	P	Nil	Nil		4	Adenocarcin	11	Not done
Patient 191	34	21	M	B	4	Uncertain Di	C	N	Nil	Nil		6	TB	10	Not definitive
Patient 192	34	21	F	B	1	Suspect TB	C	P		171	100	7	TB Suspicious	6	TB
Patient 193	25	21	M	B	1	Suspect TB	C	U	Nil	Nil		7	TB Suspicious	6	TB
Patient 194	33	21	M	B	2	Suspect Lym	O	P		242	201	10	Not definitive	2	NHL
Patient 195	38	36	M	B	4	Uncertain Di	A	P	Nil	Nil		2	NHL	11	Not done
Patient 196	61	51	M	B	2	Suspect Lym	A	U	Nil	Nil		6	TB	11	Not done
Patient 197	62	51	F	W	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11	Not done
Patient 198	63	51	M	B	4	Uncertain Di	C	U	Nil	Nil		4	Adenocarcin	11	Not done
Patient 199	39	36	M	B	4	Uncertain Di	C	P		139	100	5	Other	9	HIV reactive nodes
Patient 200	41	36	M	W	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11	Not done
Patient 201	42	36	F	B	4	Uncertain Di	O	P		343	201	9	HIV reactive	11	Not done
Patient 202	42	36	M	B	4	Uncertain Di	A	P		645	501	1	KS	9	HIV reactive nodes
Patient 203	47	36	F	B	4	Uncertain Di	I	U	Nil	Nil		12	Reactive Lym	9	HIV reactive nodes
Patient 204	18	12	F	B	4	Uncertain Di	I	P	Nil	Nil		12	Reactive Lym	11	Not done
Patient 205	17	12	M	B	2	Suspect Lym	C	U	Nil	Nil		3	HL	11	Not done
Patient 206	61	51	F	W	4	Uncertain Di	C	U	Nil	Nil		4	Adenocarcin	4	Adenocarcinoma
Patient 207	26	21	F	B	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11	Not done
Patient 208	76	66 and great	F	B	2	Suspect Lym	O	U	Nil	Nil		2	NHL	11	Not done
Patient 209	25	21	F	B	1	Suspect TB	C	P		316	201	7	TB Suspicious	11	Not done
Patient 210	77	66 and great	F	B	3	Staging Aden	I	N	Nil	Nil		4	Adenocarcin	11	Not done
Patient 211	27	21	F	B	1	Suspect TB	A	P	Nil	Nil		9	HIV reactive	10	Not definitive
Patient 212	41	36	M	B	1	Suspect TB	C	P		225	201	7	TB Suspicious	11	Not done
Patient 213	58	51	F	B	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11	Not done
Patient 214	17	12	M	B	1	Suspect TB	O	N	Nil	Nil		10	Not definitive	11	Not done
Patient 215	74	66 and great	M	W	3	Staging Aden	C	U	Nil	Nil		4	Adenocarcin	11	Not done
Patient 216	29	21	F	B	2	Suspect Lym	C	P		242	201	3	HL	3	HL
Patient 217	31	21	F	B	4	Uncertain Di	C	U	Nil	Nil		1	KS	11	Not done
Patient 218	50	36	F	B	3	Staging Aden	A	P	Nil	Nil		12	Reactive Lym	11	Not done
Patient 219	27	21	F	B	4	Uncertain Di	C	P		87	0	12	Reactive Lym	9	HIV reactive nodes
Patient 220	30	21	F	B	4	Uncertain Di	C	P		166	100	7	TB Suspicious	10	Not definitive
Patient 221	42	36	F	B	4	Uncertain Di	A	P		188	100	3	HL	3	HL
Patient 222	48	36	M	B	4	Uncertain Di	C	P		178	100	9	HIV reactive	10	Not definitive
Patient 223	46	36	M	B	4	Uncertain Di	O	N	Nil	Nil		10	Not definitive	11	Not done

Patient 224	26	21	M	B	4	Uncertain Di	C	P	Nil		Nil		9	HIV reactive	11	Not done
Patient 225	50	36	F	B	3	Staging Aden	C	N	Nil		Nil		4	Adenocarcin	4	Adenocarcinoma
Patient 226	51	51	M	B	2	Suspect Lym	C	P		277		201	2	NHL	2	NHL
Patient 227	27	21	F	B	4	Uncertain Di	O	P		154		100	6	TB	11	Not done
Patient 228	46	36	F	B	3	Staging Aden	I	N	Nil		Nil		4	Adenocarcin	11	Not done
Patient 229	39	36	F	B	2	Suspect Lym	C	P		150		100	3	HL	10	Not definitive
Patient 230	32	21	F	B	2	Suspect Lym	I	U	Nil		Nil		9	HIV reactive	2	NHL
Patient 231	43	36	M	B	4	Uncertain Di	A	P		447		351	9	HIV reactive	11	Not done
Patient 232	42	36	F	B	4	Uncertain Di	I	P		194		100	3	HL	11	Not done
Patient 233	36	36	F	B	1	Suspect TB	O	P	Nil		Nil		6	TB	11	Not done
Patient 234	63	51	M	B	4	Uncertain Di	A	U	Nil		Nil		2	NHL	11	Not done
Patient 235	49	36	M	B	4	Uncertain Di	I	P		302		201	9	HIV reactive	11	Not done
Patient 236	60	51	M	B	4	Uncertain Di	A	N	Nil		Nil		10	Not definitiv	11	Not done
Patient 237	34	21	M	B	4	Uncertain Di	O	P		25		0	6	TB	11	Not done
Patient 238	32	21	M	B	1	Suspect TB	C	U	Nil		Nil		10	Not definitiv	11	Not done
Patient 239	42	36	F	B	4	Uncertain Di	O	P		30		0	9	HIV reactive	11	Not done
Patient 240	28	21	F	C	1	Suspect TB	A	P		41		0	7	TB Suspicious	11	Not done
Patient 241	29	21	M	B	4	Uncertain Di	O	N	Nil		Nil		10	Not definitiv	11	Not done
Patient 242	38	36	M	B	2	Suspect Lym	C	P		110		100	2	NHL	2	NHL
Patient 243	55	51	M	B	4	Uncertain Di	O	N	Nil		Nil		10	Not definitiv	11	Not done
Patient 244	54	51	F	B	1	Suspect TB	A	P		18		0	6	TB	10	Not definitive
Patient 245	27	21	F	B	3	Staging Aden	O	N	Nil		Nil		4	Adenocarcin	11	Not done
Patient 246	46	36	M	B	2	Suspect Lym	I	P		357		351	2	NHL	2	NHL
Patient 247	33	21	F	B	2	Suspect Lym	A	P	Nil		Nil		2	NHL	11	Not done
Patient 248	18	12	F	B	4	Uncertain Di	C	N	Nil		Nil		12	Reactive Lym	9	HIV reactive nodes
Patient 249	27	21	F	B	1	Suspect TB	C	N	Nil		Nil		6	TB	7	TB Suspicious
Patient 250	50	36	M	W	4	Uncertain Di	I	U	Nil		Nil		10	Not definitiv	11	Not done
Patient 251	68	66 and great	F	W	3	Staging Aden	I	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 252	37	36	F	B	4	Uncertain Di	C	N	Nil		Nil		10	Not definitiv	10	Not definitive
Patient 253	16	12	M	B	4	Uncertain Di	C	P		136		100	6	TB	7	TB Suspicious
Patient 254	41	36	M	B	2	Suspect Lym	C	U	Nil		Nil		3	HL	11	Not done
Patient 255	37	36	M	B	4	Uncertain Di	I	U	Nil		Nil		10	Not definitiv	11	Not done
Patient 256	47	36	M	C	4	Uncertain Di	C	P		26		0	6	TB	11	Not done
Patient 257	36	36	M	B	2	Suspect Lym	C	P		222		201	3	HL	3	HL
Patient 258	23	21	F	B	2	Suspect Lym	C	P		574		501	9	HIV reactive	11	Not done
Patient 259	26	21	F	B	5	Unknown	O	U	Nil		Nil		12	Reactive Lym	11	Not done
Patient 260	74	66 and great	F	B	3	Staging Aden	O	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 261	47	36	F	B	3	Staging Aden	O	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 262	28	21	M	B	4	Uncertain Di	I	P		471		351	9	HIV reactive	11	Not done
Patient 263	16	12	M	B	5	Unknown	C	U	Nil		Nil		6	TB	11	Not done
Patient 264	39	36	M	B	4	Uncertain Di	I	N	Nil		Nil		5	Other	10	Not definitive
Patient 265	31	21	F	C	5	Unknown	C	P		36		0	5	Other	9	HIV reactive nodes
Patient 266	27	21	F	B	2	Suspect Lym	O	P		135		100	2	NHL	11	Not done
Patient 267	22	21	F	B	5	Unknown	C	P		340		201	9	HIV reactive	11	Not done
Patient 268	28	21	M	B	5	Unknown	A	P		143		100	5	Other	11	Not done
Patient 269	48	36	M	B	4	Uncertain Di	C	N	Nil		Nil		4	Adenocarcin	10	Not definitive
Patient 270	44	36	M	B	3	Staging Aden	O	P		274		201	12	Reactive Lym	11	Not done
Patient 271	40	36	M	B	5	Unknown	I	P		119		100	2	NHL	11	Not done
Patient 272	42	36	F	B	3	Staging Aden	I	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 273	35	21	M	B	5	Unknown	C	P		294		201	3	HL	11	Not done
Patient 274	77	66 and great	F	B	3	Staging Aden	O	N	Nil		Nil		10	Not definitiv	11	Not done
Patient 275	45	36	F	B	5	Unknown	C	U	Nil		Nil		7	TB Suspicious	11	Not done
Patient 276	28	21	F	B	5	Unknown	C	U	Nil		Nil		3	HL	11	Not done
Patient 277	37	36	F	B	1	Suspect TB	C	P	Nil		Nil		6	TB	11	Not done
Patient 278	38	36	F	B	2	Suspect Lym	A	P		305		201	2	NHL	2	NHL
Patient 279	28	21	F	B	5	Unknown	O	N	Nil		Nil		12	Reactive Lym	11	Not done

Patient 280	45	36	F	B	1	Suspect TB	C	P	Nil		Nil		6	TB	11	Not done
Patient 281	30	21	F	B	5	Unknown	C	P		178		100	7	TB Suspicious	7	TB Suspicious
Patient 282	35	21	F	B	1	Suspect TB	O	P	Nil		Nil		2	NHL	11	Not done
Patient 283	40	36	M	B	4	Uncertain Di	O	U	Nil		Nil		12	Reactive Lym	11	Not done
Patient 284	30	21	F	B	4	Uncertain Di	C	P		1057		501	2	NHL	11	Not done
Patient 285	38	36	M	B	5	Unknown	I	P	Nil		Nil		2	NHL	11	Not done
Patient 286	42	36	F	B	2	Suspect Lym	O	P		113		100	2	NHL	11	Not done
Patient 287	32	21	F	B	4	Uncertain Di	C	P	Nil		Nil		9	HIV reactive	10	Not definitive
Patient 288	35	21	M	B	1	Suspect TB	I	P		243		201	12	Reactive Lym	7	TB Suspicious
Patient 289	48	36	M	B	3	Staging Aden	I	P		107		100	4	Adenocarcin	11	Not done
Patient 290	14	12	M	B	2	Suspect Lym	I	N	Nil		Nil		10	Not definitive	11	Not done
Patient 291	28	21	F	B	4	Uncertain Di	I	P		141		100	4	Adenocarcin	11	Not done
Patient 292	47	36	M	B	4	Uncertain Di	O	U	Nil		Nil		12	Reactive Lym	11	Not done
Patient 293	64	51	F	B	3	Staging Aden	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 294	47	36	M	B	5	Unknown	O	N	Nil		Nil		4	Adenocarcin	10	Not definitive
Patient 295	44	36	F	B	2	Suspect Lym	O	U	Nil		Nil		3	HL	3	HL
Patient 296	47	36	F	B	3	Staging Aden	I	U	Nil		Nil		12	Reactive Lym	11	Not done
Patient 297	28	21	F	B	3	Staging Aden	I	P		141		100	4	Adenocarcin	11	Not done
Patient 298	50	36	F	B	3	Staging Aden	A	N	Nil		Nil		10	Not definitive	11	Not done
Patient 299	34	21	M	B	4	Uncertain Di	O	U	Nil		Nil		10	Not definitive	11	Not done
Patient 300	34	21	M	B	2	Suspect Lym	C	N	Nil		Nil		3	HL	10	Not definitive
Patient 301	30	21	M	B	2	Suspect Lym	O	P		99		0	7	TB Suspicious	6	TB
Patient 302	14	12	F	B	4	Uncertain Di	O	P		57		0	6	TB	11	Not done
Patient 303	17	12	M	B	4	Uncertain Di	O	N	Nil		Nil		12	Reactive Lym	11	Not done
Patient 304	26	21	M	B	4	Uncertain Di	O	U	Nil		Nil		10	Not definitive	11	Not done
Patient 305	44	36	F	B	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcin	11	Not done
Patient 306	42	36	F	B	4	Uncertain Di	C	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 307	12	12	F	B	5	Unknown	O	U	Nil		Nil		10	Not definitive	11	Not done
Patient 308	67	66 and great	F	B	3	Staging Aden	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 309	13	12	F	B	4	Uncertain Di	A	U	Nil		Nil		10	Not definitive	11	Not done
Patient 310	44	36	F	B	3	Staging Aden	I	P	Nil		Nil		4	Adenocarcin	11	Not done
Patient 311	54	51	F	B	3	Staging Aden	A	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 312	18	12	M	B	5	Unknown	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 313	33	21	M	B	4	Uncertain Di	C	P		9		0	6	TB	11	Not done
Patient 314	52	51	F	B	4	Uncertain Di	I	N	Nil		Nil		2	NHL	8	Other
Patient 315	60	51	F	B	3	Staging Aden	I	P		261		201	10	Not definitive	10	Not definitive
Patient 316	24	21	F	B	5	Unknown	O	U	Nil		Nil		12	Reactive Lym	10	Not definitive
Patient 317	42	36	M	B	4	Uncertain Di	C	P		428		351	2	NHL	11	Not done
Patient 318	18	12	M	B	5	Unknown	O	U	Nil		Nil		10	Not definitive	11	Not done
Patient 319	61	51	M	B	2	Suspect Lym	C	N	Nil		Nil		10	Not definitive	7	TB Suspicious
Patient 320	21	21	M	B	2	Suspect Lym	C	P		107		100	6	TB	11	Not done
Patient 321	24	21	M	B	4	Uncertain Di	C	U	Nil		Nil		10	Not definitive	10	Not definitive
Patient 322	19	12	F	B	2	Suspect Lym	C	N	Nil		Nil		2	NHL	10	Not definitive
Patient 323	42	36	M	B	4	Uncertain Di	C	P		384		351	1	KS	7	TB Suspicious
Patient 324	69	66 and great	F	B	3	Staging Aden	A	U	Nil		Nil		10	Not definitive	11	Not done
Patient 325	38	36	F	B	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcin	11	Not done
Patient 326	38	36	F	B	4	Uncertain Di	I	P		40		0	2	NHL	11	Not done
Patient 327	36	36	M	B	2	Suspect Lym	O	P		200		100	9	HIV reactive	11	Not done
Patient 328	48	36	F	B	2	Suspect Lym	C	P		40		0	5	Other	9	HIV reactive nodes
Patient 329	33	21	M	B	2	Suspect Lym	O	P		26		0	6	TB	11	Not done
Patient 330	38	36	M	B	3	Staging Aden	O	P		945		501	10	Not definitive	11	Not done
Patient 331	42	36	F	B	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcin	11	Not done
Patient 332	23	21	F	B	3	Staging Aden	O	U	Nil		Nil		4	Adenocarcin	11	Not done
Patient 333	42	36	F	B	4	Uncertain Di	O	P		520		501	2	NHL	11	Not done
Patient 334	27	21	F	B	4	Uncertain Di	O	P	Nil		Nil		7	TB Suspicious	11	Not done
Patient 335	32	21	F	B	1	Suspect TB	C	P		107		100	6	TB	7	TB Suspicious

Patient 336	56	51	M	B	5	Unknown	O	P	Nil		Nil		10	Not definitive	11	Not done
Patient 337	53	51	M	B	3	Staging Aden	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 338	57	51	M	B	3	Staging Aden	O	U	Nil		Nil		4	Adenocarcino	11	Not done
Patient 339	80	66 and great	F	B	3	Staging Aden	A	N	Nil		Nil		10	Not definitive	11	Not done
Patient 340	31	21	M	W	3	Staging Aden	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 341	27	21	M	B	5	Unknown	O	N	Nil		Nil		12	Reactive Lym	11	Not done
Patient 342	50	36	F	B	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcino	11	Not done
Patient 343	36	36	M	B	3	Staging Aden	C	P		525		501	10	Not definitive	11	Not done
Patient 344	43	36	F	B	2	Suspect Lym	C	P		336		201	5	Other	10	Not definitive
Patient 345	45	36	F	B	5	Unknown	C	U	Nil		Nil		9	HIV reactive	10	Not definitive
Patient 346	27	21	F	B	4	Uncertain Di	C	P		205		201	5	Other	11	Not done
Patient 347	34	21	F	B	4	Uncertain Di	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 348	26	21	F	B	1	Suspect TB	A	P	Nil		Nil		7	TB Suspicious	11	Not done
Patient 349	52	51	F	B	2	Suspect Lym	C	P		26		0	3	HL	2	NHL
Patient 350	27	21	M	B	2	Suspect Lym	C	N	Nil		Nil		2	NHL	11	Not done
Patient 351	36	36	F	B	2	Suspect Lym	C	P		228		201	2	NHL	2	NHL
Patient 352	57	51	M	B	3	Staging Aden	O	U	Nil		Nil		10	Not definitive	11	Not done
Patient 353	63	51	F	B	3	Staging Aden	A	U	Nil		Nil		4	Adenocarcino	11	Not done
Patient 354	15	12	M	B	1	Suspect TB	C	N	Nil		Nil		3	HL	11	Not done
Patient 355	15	12	F	B	2	Suspect Lym	C	P		292		201	2	NHL	2	NHL
Patient 356	26	21	F	B	2	Suspect Lym	I	U	Nil		Nil		12	Reactive Lym	11	Not done
Patient 357	34	21	F	B	4	Uncertain Di	C	P		115		100	4	Adenocarcino	7	TB Suspicious
Patient 358	56	51	F	B	3	Staging Aden	A	N	Nil		Nil		10	Not definitive	4	Adenocarcinoma
Patient 359	47	36	M	B	4	Uncertain Di	O	P	Nil		Nil		12	Reactive Lym	11	Not done
Patient 360	46	36	F	B	4	Uncertain Di	O	P		480		351	12	Reactive Lym	11	Not done
Patient 361	58	51	F	B	3	Staging Aden	O	N	Nil		Nil		12	Reactive Lym	11	Not done
Patient 362	53	51	F	B	1	Suspect TB	C	P		67		0	6	TB	6	TB
Patient 363	24	21	M	B	1	Suspect TB	I	P		271		201	9	HIV reactive	9	HIV reactive nodes
Patient 364	25	21	M	B	4	Uncertain Di	C	P		409		351	1	KS	9	HIV reactive nodes
Patient 365	25	21	F	B	1	Suspect TB	C	P	Nil		Nil		6	TB	11	Not done
Patient 366	43	36	M	B	2	Suspect Lym	C	P	Nil		Nil		2	NHL	2	NHL
Patient 367	35	21	M	B	1	Suspect TB	C	N	Nil		Nil		6	TB	7	TB Suspicious
Patient 368	77	66 and great	M	B	3	Staging Aden	O	U	Nil		Nil		4	Adenocarcino	11	Not done
Patient 369	49	36	F	B	4	Uncertain Di	C	N	Nil		Nil		2	NHL	10	Not definitive
Patient 370	52	51	F	B	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcino	11	Not done
Patient 371	65	51	M	B	3	Staging Aden	O	U	Nil		Nil		10	Not definitive	11	Not done
Patient 372	39	36	F	B	3	Staging Aden	C	P	Nil		Nil		10	Not definitive	11	Not done
Patient 373	34	21	F	B	1	Suspect TB	C	P		129		100	9	HIV reactive	9	HIV reactive nodes
Patient 374	50	36	M	B	4	Uncertain Di	C	P		45		0	6	TB	6	TB
Patient 375	55	51	F	B	2	Suspect Lym	C	P	Nil		Nil		6	TB	7	TB Suspicious
Patient 376	42	36	M	B	4	Uncertain Di	C	P	Nil		Nil		2	NHL	11	Not done
Patient 377	57	51	F	B	3	Staging Aden	I	U	Nil		Nil		12	Reactive Lym	11	Not done
Patient 378	12	12	F	B	4	Uncertain Di	C	N	Nil		Nil		10	Not definitive	10	Not definitive
Patient 379	43	36	F	W	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcino	11	Not done
Patient 380	15	12	F	B	4	Uncertain Di	O	N	Nil		Nil		10	Not definitive	11	Not done
Patient 381	33	21	M	B	5	Unknown	C	P		407		351	3	HL	11	Not done
Patient 382	23	21	F	C	4	Uncertain Di	C	N	Nil		Nil		3	HL	10	Not definitive
Patient 383	33	21	M	B	1	Suspect TB	C	P	Nil		Nil		6	TB	6	TB
Patient 384	21	21	F	B	4	Uncertain Di	O	P		466		351	9	HIV reactive	11	Not done
Patient 385	33	21	F	B	2	Suspect Lym	A	P		730		501	9	HIV reactive	11	Not done
Patient 386	27	21	M	B	5	Unknown	C	P		8		0	6	TB	11	Not done
Patient 387	40	36	F	B	4	Uncertain Di	C	P		111		100	2	NHL	11	Not done
Patient 388	56	51	F	B	3	Staging Aden	A	N	Nil		Nil		4	Adenocarcino	11	Not done
Patient 389	55	51	M	A	3	Staging Aden	I	U	Nil		Nil		4	Adenocarcino	11	Not done
Patient 390	49	36	F	B	1	Suspect TB	C	U	Nil		Nil		7	TB Suspicious	7	TB Suspicious
Patient 391	36	36	M	B	1	Suspect TB	A	P		328		201	6	TB	11	Not done

Patient 392	50	36	F	B	3	Staging Aden	A	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 393	50	36	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitiv	11 Not done
Patient 394	35	21	F	B	4	Uncertain Di	C	P	Nil	Nil		9	HIV reactive	11 Not done
Patient 395	46	36	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 396	24	21	F	B	1	Suspect TB	C	P		15	0	6	TB	6 TB
Patient 397	40	36	F	B	2	Suspect Lym	A	P		298	201	9	HIV reactive	9 HIV reactive nodes
Patient 398	55	51	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 399	42	36	F	B	1	Suspect TB	C	P		185	100	6	TB	6 TB
Patient 400	36	36	F	B	4	Uncertain Di	C	N	Nil	Nil		7	TB Suspicious	11 Not done
Patient 401	56	51	F	B	3	Staging Aden	A	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 402	21	21	M	B	4	Uncertain Di	O	U	Nil	Nil		10	Not definitiv	11 Not done
Patient 403	67	66 and great	F	B	3	Staging Aden	O	U	Nil	Nil		10	Not definitiv	11 Not done
Patient 404	47	36	M	B	1	Suspect TB	C	P		8	0	6	TB	6 TB
Patient 405	29	21	F	B	2	Suspect Lym	C	P		46	0	6	TB	6 TB
Patient 406	70	66 and great	F	W	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 407	30	21	F	B	1	Suspect TB	A	U	Nil	Nil		6	TB	10 Not definitive
Patient 408	53	51	F	B	2	Suspect Lym	C	P		491	351	12	Reactive Lym	2 NHL
Patient 409	38	36	F	B	4	Uncertain Di	C	P	Nil	Nil		6	TB	11 Not done
Patient 410	17	12	F	B	2	Suspect Lym	C	U	Nil	Nil		3	HL	3 HL
Patient 411	40	36	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitiv	11 Not done
Patient 412	34	21	M	B	5	Unknown	C	P		189	100	1	KS	10 Not definitive
Patient 413	40	36	F	B	3	Staging Aden	A	P		884	501	4	Adenocarcin	11 Not done
Patient 414	22	21	M	B	5	Unknown	C	P		83	0	6	TB	11 Not done
Patient 415	63	51	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 416	42	36	M	B	4	Uncertain Di	C	U	Nil	Nil		12	Reactive Lym	11 Not done
Patient 417	52	51	M	B	5	Unknown	C	P		321	201	5	Other	11 Not done
Patient 418	15	12	M	B	3	Staging Aden	O	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 419	50	36	M	B	3	Staging Aden	O	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 420	47	36	F	B	5	Unknown	I	P	Nil	Nil		9	HIV reactive	9 HIV reactive nodes
Patient 421	58	51	F	C	4	Uncertain Di	C	P		217	201	10	Not definitiv	10 Not definitive
Patient 422	46	36	M	B	4	Uncertain Di	O	U	Nil	Nil		12	Reactive Lym	11 Not done
Patient 423	40	36	M	W	4	Uncertain Di	O	U	Nil	Nil		12	Reactive Lym	11 Not done
Patient 424	39	36	F	B	1	Suspect TB	O	P		17	0	9	HIV reactive	11 Not done
Patient 425	35	21	F	B	5	Unknown	A	N	Nil	Nil		9	HIV reactive	11 Not done
Patient 426	30	21	M	B	4	Uncertain Di	C	U	Nil	Nil		7	TB Suspicious	6 TB
Patient 427	46	36	M	B	3	Staging Aden	I	N	Nil	Nil		10	Not definitiv	11 Not done
Patient 428	35	21	M	B	2	Suspect Lym	C	P		54	0	5	Other	9 HIV reactive nodes
Patient 429	23	21	F	B	1	Suspect TB	C	P		336	201	1	KS	7 TB Suspicious
Patient 430	38	36	M	B	4	Uncertain Di	O	P		627	501	12	Reactive Lym	11 Not done
Patient 431	30	21	M	B	1	Suspect TB	A	P		829	501	5	Other	11 Not done
Patient 432	35	21	F	B	2	Suspect Lym	A	P		288	201	5	Other	11 Not done
Patient 433	48	36	F	B	4	Uncertain Di	C	N	Nil	Nil		2	NHL	10 Not definitive
Patient 434	62	51	M	B	4	Uncertain Di	C	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 435	50	36	F	B	4	Uncertain Di	C	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 436	32	21	M	B	5	Unknown	C	P	Nil	Nil		6	TB	7 TB Suspicious
Patient 437	46	36	F	B	2	Suspect Lym	I	P		58	0	2	NHL	11 Not done
Patient 438	54	51	F	B	2	Suspect Lym	A	P		149	100	10	Not definitiv	10 Not definitive
Patient 439	94	66 and great	F	B	2	Suspect Lym	A	N	Nil	Nil		10	Not definitiv	11 Not done
Patient 440	32	21	M	B	1	Suspect TB	C	P		555	501	7	TB Suspicious	6 TB
Patient 441	36	36	F	B	4	Uncertain Di	C	P	Nil	Nil		10	Not definitiv	10 Not definitive
Patient 442	55	51	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 443	39	36	F	B	1	Suspect TB	A	P		297	201	6	TB	6 TB
Patient 444	45	36	F	B	4	Uncertain Di	O	P	Nil	Nil		6	TB	11 Not done
Patient 445	50	36	F	B	1	Suspect TB	C	U	Nil	Nil		7	TB Suspicious	11 Not done
Patient 446	52	51	F	B	3	Staging Aden	A	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 447	31	21	M	B	1	Suspect TB	O	P		32	0	6	TB	11 Not done

Patient 448	51	51	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 449	77	66 and greate	F	B	5	Unknown	A	N	Nil	Nil		2	NHL	11 Not done
Patient 450	15	12	M	B	1	Suspect TB	C	N	Nil	Nil		6	TB	6 TB
Patient 451	48	36	M	B	4	Uncertain Di	C	P		958	501	10	Not definitive	10 Not definitive
Patient 452	49	36	F	W	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcino	11 Not done
Patient 453	64	51	F	B	3	Staging Aden	A	U	Nil	Nil		10	Not definitive	11 Not done
Patient 454	51	51	F	B	3	Staging Aden	A	U	Nil	Nil		10	Not definitive	11 Not done
Patient 455	25	21	F	B	4	Uncertain Di	C	N	Nil	Nil		3	HL	7 TB Suspicious
Patient 456	32	21	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcino	11 Not done
Patient 457	22	21	M	B	2	Suspect Lym	C	P		294	201	1	KS	2 NHL
Patient 458	33	21	M	B	1	Suspect TB	C	P		115	100	6	TB	7 TB Suspicious
Patient 459	32	21	F	B	4	Uncertain Di	C	P		51	0	6	TB	11 Not done
Patient 460	36	36	F	B	3	Staging Aden	A	P	Nil	Nil		10	Not definitive	11 Not done
Patient 461	34	21	F	B	3	Staging Aden	A	U	Nil	Nil		10	Not definitive	11 Not done
Patient 462	30	21	M	B	5	Unknown	I	P		349	201	6	TB	6 TB
Patient 463	52	51	M	B	5	Unknown	C	P		142	100	2	NHL	11 Not done
Patient 464	26	21	F	B	4	Uncertain Di	C	P		88	0	6	TB	11 Not done
Patient 465	27	21	F	C	5	Unknown	C	U	Nil	Nil		7	TB Suspicious	8 Other
Patient 466	42	36	F	B	5	Unknown	C	P		101	100	6	TB	7 TB Suspicious
Patient 467	33	21	M	B	2	Suspect Lym	C	P		1	0	6	TB	11 Not done
Patient 468	35	21	M	B	4	Uncertain Di	C	P		290	201	3	HL	11 Not done
Patient 469	31	21	M	B	5	Unknown	O	N	Nil	Nil		10	Not definitive	11 Not done
Patient 470	52	51	M	B	1	Suspect TB	C	P		142	100	2	NHL	11 Not done
Patient 471	60	51	F	B	5	Unknown	O	P		107	100	2	NHL	11 Not done
Patient 472	68	66 and greate	F	B	5	Unknown	C	N	Nil	Nil		6	TB	7 TB Suspicious
Patient 473	40	36	M	B	2	Suspect Lym	A	P		26	0	3	HL	10 Not definitive
Patient 474	33	21	F	B	2	Suspect Lym	C	P		470	351	3	HL	3 HL
Patient 475	41	36	F	B	2	Suspect Lym	O	P		201	201	6	TB	6 TB
Patient 476	42	36	M	B	5	Unknown	A	P		224	201	3	HL	10 Not definitive
Patient 477	32	21	M	B	4	Uncertain Di	I	P		159	100	1	KS	10 Not definitive
Patient 478	29	21	M	B	5	Unknown	C	P		582	501	2	NHL	11 Not done
Patient 479	45	36	F	B	5	Unknown	O	P		267	201	1	KS	11 Not done
Patient 480	54	51	M	B	5	Unknown	I	P		362	351	12	Reactive Lym	11 Not done
Patient 481	19	12	F	B	5	Unknown	O	P		610	501	7	TB Suspicious	11 Not done
Patient 482	28	21	M	B	1	Suspect TB	C	U	Nil	Nil		10	Not definitive	10 Not definitive
Patient 483	73	66 and greate	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 484	17	12	F	A	5	Unknown	C	N	Nil	Nil		6	TB	6 TB
Patient 485	50	36	M	B	3	Staging Aden	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 486	48	36	M	B	2	Suspect Lym	O	P		51	0	6	TB	11 Not done
Patient 487	62	51	F	B	2	Suspect Lym	C	P		147	100	3	HL	3 HL
Patient 488	55	51	M	B	2	Suspect Lym	A	P		153	100	2	NHL	2 NHL
Patient 489	13	12	M	B	4	Uncertain Di	O	U	Nil	Nil		7	TB Suspicious	11 Not done
Patient 490	64	51	F	B	3	Staging Aden	A	U	Nil	Nil		4	Adenocarcino	11 Not done
Patient 491	28	21	F	B	4	Uncertain Di	A	P		1626	501	5	Other	5 Other
Patient 492	32	21	F	B	3	Staging Aden	A	P	Nil	Nil		4	Adenocarcino	11 Not done
Patient 493	56	51	M	B	3	Staging Aden	O	N	Nil	Nil		10	Not definitive	11 Not done
Patient 494	52	51	M	B	3	Staging Aden	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 495	52	51	F	B	4	Uncertain Di	A	U	Nil	Nil		10	Not definitive	11 Not done
Patient 496	44	36	M	W	4	Uncertain Di	A	U	Nil	Nil		6	TB	7 TB Suspicious
Patient 497	41	36	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcino	11 Not done
Patient 498	42	36	F	B	1	Suspect TB	A	N	Nil	Nil		7	TB Suspicious	11 Not done
Patient 499	43	36	F	B	1	Suspect TB	A	P		161	100	9	HIV reactive	11 Not done
Patient 500	50	36	M	B	3	Staging Aden	C	U	Nil	Nil		4	Adenocarcino	11 Not done
Patient 501	22	21	F	W	1	Suspect TB	A	U	Nil	Nil		6	TB	10 Not definitive
Patient 502	31	21	F	B	5	Unknown	C	P		809	501	12	Reactive Lym	9 HIV reactive nodes
Patient 503	62	51	M	B	2	Suspect Lym	A	P		153	100	2	NHL	3 HL

Patient 504	31	21	F	B	3	Staging Aden	A	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 505	25	21	M	B	2	Suspect Lym	O	N	Nil	Nil		3	HL	11 Not done
Patient 506	43	36	M	B	5	Unknown	O	P	53		0	6	TB	6 TB
Patient 507	35	21	F	B	2	Suspect Lym	C	P	7		0	10	Not definitive	11 Not done
Patient 508	40	36	F	B	5	Unknown	C	P	18		0	6	TB	11 Not done
Patient 509	53	51	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	10 Not definitive
Patient 510	25	21	F	B	3	Staging Aden	A	N	Nil	Nil		4	Adenocarcin	11 Not done
Patient 511	38	36	M	B	2	Suspect Lym	C	U	Nil	Nil		3	HL	3 HL
Patient 512	12	12	M	B	5	Unknown	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 513	66	66 and greate	M	B	4	Uncertain Di	C	U	Nil	Nil		5	Other	11 Not done
Patient 514	42	36	M	W	2	Suspect Lym	C	N	Nil	Nil		3	HL	10 Not definitive
Patient 515	26	21	M	B	3	Staging Aden	A	U	Nil	Nil		10	Not definitive	11 Not done
Patient 516	37	36	F	B	1	Suspect TB	A	U	Nil	Nil		10	Not definitive	11 Not done
Patient 517	51	51	M	B	4	Uncertain Di	C	N	Nil	Nil		10	Not definitive	11 Not done
Patient 518	46	36	F	B	3	Staging Aden	A	P	Nil	Nil		4	Adenocarcin	10 Not definitive
Patient 519	42	36	F	B	4	Uncertain Di	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 520	69	66 and greate	M	B	4	Uncertain Di	I	N	Nil	Nil		10	Not definitive	11 Not done
Patient 521	45	36	F	B	3	Staging Aden	O	P	138		100	12	Reactive Lym	11 Not done
Patient 522	37	36	M	B	2	Suspect Lym	C	U	Nil	Nil		9	HIV reactive	10 Not definitive
Patient 523	45	36	F	B	2	Suspect Lym	C	P	460		351	3	HL	3 HL
Patient 524	30	21	M	B	4	Uncertain Di	C	N	Nil	Nil		10	Not definitive	11 Not done
Patient 525	65	51	F	B	3	Staging Aden	A	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 526	62	51	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 527	43	36	M	B	4	Uncertain Di	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 528	58	51	F	B	5	Unknown	A	N	Nil	Nil		6	TB	11 Not done
Patient 529	49	36	M	B	4	Uncertain Di	O	P	1659		501	9	HIV reactive	11 Not done
Patient 530	39	36	F	B	4	Uncertain Di	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 531	46	36	M	B	3	Staging Aden	O	U	Nil	Nil		10	Not definitive	11 Not done
Patient 532	74	66 and greate	F	B	3	Staging Aden	A	U	Nil	Nil		10	Not definitive	10 Not definitive
Patient 533	62	51	M	B	4	Uncertain Di	C	U	Nil	Nil		4	Adenocarcin	4 Adenocarcinoma
Patient 534	73	66 and greate	F	W	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 535	73	66 and greate	F	W	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 536	53	51	M	B	2	Suspect Lym	O	P	450		351	10	Not definitive	11 Not done
Patient 537	54	51	F	B	4	Uncertain Di	A	N	Nil	Nil		10	Not definitive	10 Not definitive
Patient 538	64	51	M	W	4	Uncertain Di	I	N	Nil	Nil		10	Not definitive	11 Not done
Patient 539	29	21	F	B	1	Suspect TB	C	U	Nil	Nil		4	Adenocarcin	10 Not definitive
Patient 540	46	36	F	B	3	Staging Aden	O	P	673		501	4	Adenocarcin	11 Not done
Patient 541	53	51	F	B	4	Uncertain Di	A	N	Nil	Nil		10	Not definitive	10 Not definitive
Patient 542	40	36	F	B	3	Staging Aden	A	P	314		201	4	Adenocarcin	11 Not done
Patient 543	26	21	M	B	2	Suspect Lym	C	P	327		201	1	KS	11 Not done
Patient 544	47	36	M	B	4	Uncertain Di	I	P	266		201	9	HIV reactive	11 Not done
Patient 545	43	36	M	B	1	Suspect TB	C	P	133		100	7	TB Suspicious	10 Not definitive
Patient 546	53	51	F	B	3	Staging Aden	A	P	749		501	10	Not definitive	11 Not done
Patient 547	55	51	F	B	3	Staging Aden	A	N	Nil	Nil		10	Not definitive	11 Not done
Patient 548	21	21	M	B	2	Suspect Lym	C	N	Nil	Nil		2	NHL	11 Not done
Patient 549	30	21	M	B	2	Suspect Lym	A	U	Nil	Nil		10	Not definitive	10 Not definitive
Patient 550	31	21	F	B	2	Suspect Lym	A	P	243		201	9	HIV reactive	10 Not definitive
Patient 551	25	21	F	B	2	Suspect Lym	C	U	Nil	Nil		3	HL	11 Not done
Patient 552	29	21	F	B	4	Uncertain Di	C	N	Nil	Nil		7	TB Suspicious	7 TB Suspicious
Patient 553	29	21	M	B	4	Uncertain Di	O	P	33		0	6	TB	11 Not done
Patient 554	35	21	M	B	2	Suspect Lym	O	N	Nil	Nil		10	Not definitive	11 Not done
Patient 555	25	21	M	B	4	Uncertain Di	I	U	Nil	Nil		10	Not definitive	11 Not done
Patient 556	39	36	F	B	3	Staging Aden	O	U	Nil	Nil		4	Adenocarcin	11 Not done
Patient 557	15	12	F	B	4	Uncertain Di	C	U	Nil	Nil		7	TB Suspicious	10 Not definitive
Patient 558	25	21	M	B	4	Uncertain Di	C	P	29		0	6	TB	11 Not done
Patient 559	25	21	F	A	4	Uncertain Di	O	N	Nil	Nil		6	TB	11 Not done

Patient 560	28	21	F	B	4	Uncertain Di:	A	P	187	100	2	NHL	2

Patient Numb	Age	Age Band	Sex	Race	Indication	Indication2	Site of Lympl	HIV Status	CD4 Count	CD4 Band	Bio Diagnosis	Bio Diagnosis	FNA Diagnos	FNA Diagnos	Subtype NHL
Patient 10	52	51	M	B	2	Suspect Lymp	O	N	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 11	19	12	F	B	2	Suspect Lymp	C	N	Nil	Nil	2	NHL	10	Not definitiv	Tcell ALL
Patient 20	51	51	M	B	1	Suspect TB	O	P	47	0	2	NHL	11	Not done	ALCL
Patient 56	48	36	M	C	2	Suspect Lymp	O	P	21	0	2	NHL	10	Not definitiv	DLBCL
Patient 71	47	36	M	B	2	Suspect Lymp	C	P	299	201	2	NHL	3	HL	Plasmablastic
Patient 72	43	36	F	B	2	Suspect Lymp	I	P	46	0	2	NHL	2	NHL	DLBCL
Patient 77	56	51	F	B	4	Uncertain Di	I	N	Nil	Nil	2	NHL	10	Not definitiv	Tcell NHL
Patient 81	36	36	F	B	4	Uncertain Di	I	U	1364	501	2	NHL	11	Not done	DLBCL
Patient 86	35	21	F	B	2	Suspect Lymp	C	P	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 92	30	21	F	B	2	Suspect Lymp	I	P	86	0	2	NHL	2	NHL	DLBCL
Patient 97	36	36	M	B	1	Suspect TB	A	P	236	201	2	NHL	11	Not done	DLBCL
Patient 106	53	51	F	B	2	Suspect Lymp	C	U	Nil	Nil	2	NHL	11	Not done	Intermediate DLBCL/Burkitt
Patient 127	45	36	M	B	2	Suspect Lymp	C	U	Nil	Nil	2	NHL	11	Not done	Marginal zone lymphoma
Patient 138	54	51	M	B	2	Suspect Lymp	O	N	Nil	Nil	2	NHL	11	Not done	CLL
Patient 147	35	21	M	B	4	Uncertain Di	O	P	291	201	2	NHL	11	Not done	DLBCL
Patient 157	57	51	F	C	2	Suspect Lymp	O	N	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 164	44	36	M	B	2	Suspect Lymp	A	U	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 166	70	66 and great	M	B	2	Suspect Lymp	C	N	Nil	Nil	2	NHL	2	NHL	CLL
Patient 170	29	21	F	B	2	Suspect Lymp	A	P	80	0	2	NHL	2	NHL	Burkitt
Patient 174	36	36	F	B	2	Suspect Lymp	C	P	195	100	2	NHL	11	Not done	Plasmablastic
Patient 175	55	51	M	B	1	Suspect TB	C	P	142	100	2	NHL	10	Not definitiv	Burkitt
Patient 183	14	12	F	B	4	Uncertain Di	C	N	Nil	Nil	2	NHL	2	NHL	ALCL
Patient 189	35	21	M	B	2	Suspect Lymp	O	P	238	201	2	NHL	11	Not done	DLBCL
Patient 195	38	36	M	B	4	Uncertain Di	A	P	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 208	76	66 and great	F	B	2	Suspect Lymp	O	U	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 226	51	51	M	B	2	Suspect Lymp	C	P	277	201	2	NHL	2	NHL	Plasmablastic
Patient 234	63	51	M	B	4	Uncertain Di	A	U	Nil	Nil	2	NHL	11	Not done	CLL
Patient 242	38	36	M	B	2	Suspect Lymp	C	P	110	100	2	NHL	2	NHL	Plasmablastic
Patient 246	46	36	M	B	2	Suspect Lymp	I	P	357	351	2	NHL	2	NHL	Tcell NHL
Patient 247	33	21	F	B	2	Suspect Lymp	A	P	Nil	Nil	2	NHL	11	Not done	Burkitt
Patient 266	27	21	F	B	2	Suspect Lymp	O	P	135	100	2	NHL	11	Not done	Burkitt
Patient 271	40	36	M	B	5	Unknown	I	P	119	100	2	NHL	11	Not done	DLBCL
Patient 278	38	36	F	B	2	Suspect Lymp	A	P	305	201	2	NHL	2	NHL	Burkitt
Patient 282	35	21	F	B	1	Suspect TB	O	P	Nil	Nil	2	NHL	11	Not done	Intermediate DLBCL/Burkitt
Patient 284	30	21	F	B	4	Uncertain Di	C	P	1057	501	2	NHL	11	Not done	DLBCL
Patient 285	38	36	M	B	5	Unknown	I	P	Nil	Nil	2	NHL	11	Not done	Burkitt
Patient 286	42	36	F	B	2	Suspect Lymp	O	P	113	100	2	NHL	11	Not done	Intermediate DLBCL/Burkitt
Patient 314	52	51	F	B	4	Uncertain Di	I	N	Nil	Nil	2	NHL	8	Other	Follicular
Patient 317	42	36	M	B	4	Uncertain Di	C	P	428	351	2	NHL	11	Not done	ALCL
Patient 322	19	12	F	B	2	Suspect Lymp	C	N	Nil	Nil	2	NHL	10	Not definitiv	DLBCL
Patient 326	38	36	F	B	4	Uncertain Di	I	P	40	0	2	NHL	11	Not done	DLBCL
Patient 333	42	36	F	B	4	Uncertain Di	O	P	520	501	2	NHL	11	Not done	DLBCL
Patient 350	27	21	M	B	2	Suspect Lymp	C	N	Nil	Nil	2	NHL	11	Not done	Tcell NHL
Patient 351	36	36	F	B	2	Suspect Lymp	C	P	228	201	2	NHL	2	NHL	DLBCL
Patient 355	15	12	F	B	2	Suspect Lymp	C	P	292	201	2	NHL	2	NHL	DLBCL
Patient 366	43	36	M	B	2	Suspect Lymp	C	P	Nil	Nil	2	NHL	2	NHL	DLBCL
Patient 369	49	36	F	B	4	Uncertain Di	C	N	Nil	Nil	2	NHL	10	Not definitiv	Marginal zone lymphoma
Patient 376	42	36	M	B	4	Uncertain Di	C	P	Nil	Nil	2	NHL	11	Not done	DLBCL
Patient 387	40	36	F	B	4	Uncertain Di	C	P	111	100	2	NHL	11	Not done	DLBCL
Patient 433	48	36	F	B	4	Uncertain Di	C	N	Nil	Nil	2	NHL	10	Not definitiv	CLL
Patient 437	46	36	F	B	2	Suspect Lymp	I	P	58	0	2	NHL	11	Not done	Burkitt
Patient 449	77	66 and great	F	B	5	Unknown	A	N	Nil	Nil	2	NHL	11	Not done	CLL
Patient 463	52	51	M	B	5	Unknown	C	P	142	100	2	NHL	11	Not done	ALCL
Patient 470	52	51	M	B	1	Suspect TB	C	P	142	100	2	NHL	11	Not done	ALCL
Patient 471	60	51	F	B	5	Unknown	O	P	107	100	2	NHL	11	Not done	DLBCL
Patient 478	29	21	M	B	5	Unknown	C	P	582	501	2	NHL	11	Not done	DLBCL
Patient 488	55	51	M	B	2	Suspect Lymp	A	P	153	100	2	NHL	2	NHL	Intermediate DLBCL/Burkitt
Patient 503	62	51	M	B	2	Suspect Lymp	A	P	153	100	2	NHL	3	HL	DLBCL
Patient 548	21	21	M	B	2	Suspect Lymp	C	N	Nil	Nil	2	NHL	11	Not done	Burkitt
Patient 560	28	21	F	B	4	Uncertain Di	A	P	187	100	2	NHL	2		Intermediate DLBCL/Burkitt

Patient Num	Age	Age Band	Sex	Race	Indication	Indication2	Site of Lymp	HIV Status	CD4 Count	CD4 Band	Biopsy Diagn	FNA Diagnosis
Patient 3	29	21	F	B	2	Suspect Lym	C	P	99	0	CHL	CHL
Patient 5	36	36	M	B	2	Suspect Lym	A	P	247	201	CHL	CHL
Patient 9	29	21	M	B	5	Unknown	C	P	210	201	CHL	Mycobacterial infection
Patient 11	19	12	F	B	2	Suspect Lym	C	N	Nil	Nil	NHL	Other (Atypical lymphoid cells)
Patient 17	52	51	M	B	5	Unknown	A	P	120	100	Mycobacteri	Mycobacterial infection
Patient 22	30	21	F	B	2	Suspect Lym	C	P	Nil	Nil	HIV Lymphac	Non-specific reactive lymphoid hyperplasia
Patient 24	61	51	M	B	3	Staging Aden	O	N	Nil	Nil	Carcinoma	Carcinoma
Patient 27	42	36	F	B	4	Uncertain Di	O	P	18	0	Mycobacteri	Mycobacterial infection
Patient 31	38	36	F	B	4	Uncertain Di	I	N	Nil	Nil	Non-specific	Other (No abnormalities)
Patient 32	41	36	M	B	1	Suspect TB	O	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 35	54	51	F	C	4	Uncertain Di	O	P	563	501	HIV Lymphac	Other (No abnormalities)
Patient 37	56	51	M	W	4	Uncertain Di	C	N	Nil	Nil	Carcinoma	Carcinoma
Patient 39	58	51	M	B	3	Staging Aden	C	N	Nil	Nil	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 40	46	36	M	B	1	Suspect TB	O	P	8	0	Other (Crypt	Other (Cryptococcosis)
Patient 46	43	36	M	B	1	Suspect TB	C	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 51	28	21	M	B	1	Suspect TB	C	P	433	351	HIV Lymphac	Non-specific reactive lymphoid hyperplasia
Patient 56	48	36	M	C	2	Suspect Lym	O	P	21	0	NHL	Other (Atypical lymphoid cells)
Patient 57	44	36	F	B	2	Suspect Lym	C	P	43	0	Mycobacteri	Mycobacterial infection
Patient 59	40	36	M	B	4	Uncertain Di	A	P	103	100	Mycobacteri	Mycobacterial infection
Patient 60	31	21	F	B	2	Suspect Lym	C	P	126	100	CHL	CHL
Patient 64	33	21	M	B	1	Suspect TB	A	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 67	24	21	F	B	4	Uncertain Di	A	N	Nil	Nil	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 68	39	36	M	B	4	Uncertain Di	A	P	213	201	Granulomatc	Mycobacterial infection
Patient 70	15	12	F	B	4	Uncertain Di	C	N	Nil	Nil	Mycobacteri	Other (Atypical lymphoid cells)
Patient 71	47	36	M	B	2	Suspect Lym	C	P	299	201	NHL	CHL
Patient 72	43	36	F	B	2	Suspect Lym	I	P	46	0	NHL	NHL
Patient 74	54	51	F	B	4	Uncertain Di	A	P	295	201	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 75	24	21	F	B	4	Uncertain Di	A	P	Nil	Nil	CHL	CHL
Patient 76	35	21	M	B	2	Suspect Lym	C	P	215	201	Mycobacteri	Mycobacterial infection
Patient 77	56	51	F	B	4	Uncertain Di	I	N	Nil	Nil	NHL	NHL
Patient 80	34	21	F	B	4	Uncertain Di	C	P	232	201	Other (KS)	CHL
Patient 83	64	51	F	W	4	Uncertain Di	C	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 84	30	21	M	B	4	Uncertain Di	C	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 85	36	36	F	B	2	Suspect Lym	O	P	98	0	HIV Lymphac	NHL
Patient 87	35	21	F	B	4	Uncertain Di	A	N	Nil	Nil	Carcinoma	Carcinoma
Patient 89	34	21	M	B	4	Uncertain Di	C	P	281	201	Other (Castle	Non-specific reactive lymphoid hyperplasia
Patient 92	30	21	F	B	2	Suspect Lym	I	P	86	0	NHL	NHL
Patient 93	34	21	F	C	1	Suspect TB	A	P	194	100	Mycobacteri	Mycobacterial infection
Patient 94	61	51	F	B	4	Uncertain Di	C	N	Nil	Nil	CHL	Non-specific reactive lymphoid hyperplasia
Patient 99	52	51	M	B	4	Uncertain Di	I	P	119	100	Non-specific	Mycobacterial infection
Patient 101	59	51	M	B	4	Uncertain Di	C	N	Nil	Nil	Carcinoma	Carcinoma
Patient 105	26	21	F	B	2	Suspect Lym	C	P	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 109	51	51	F	B	2	Suspect Lym	C	P	Nil	Nil	CHL	CHL
Patient 111	63	51	M	B	4	Uncertain Di	C	U	Nil	Nil	CHL	CHL
Patient 112	34	21	M	B	4	Uncertain Di	A	P	281	201	Other (Castle	Non-specific reactive lymphoid hyperplasia
Patient 113	61	51	F	B	2	Suspect Lym	A	P	409	351	HIV Lymphac	Non-specific reactive lymphoid hyperplasia
Patient 120	63	51	F	B	4	Uncertain Di	C	N	Nil	Nil	Carcinoma	Carcinoma
Patient 121	50	36	F	B	1	Suspect TB	A	P	Nil	Nil	HIV Lymphac	Non-specific reactive lymphoid hyperplasia
Patient 122	23	21	M	B	2	Suspect Lym	C	P	330	201	HIV Lymphac	Other (Atypical lymphoid cells)
Patient 124	44	36	M	B	2	Suspect Lym	C	P	139	100	HIV Lymphac	CHL
Patient 126	38	36	F	B	2	Suspect Lym	O	P	556	501	Non-specific	NHL
Patient 128	51	51	F	B	3	Staging Aden	A	N	Nil	Nil	Carcinoma	Carcinoma
Patient 131	36	36	F	B	2	Suspect Lym	C	P	263	201	Other (No ab	Non-specific reactive lymphoid hyperplasia
Patient 134	40	36	M	B	4	Uncertain Di	C	N	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 137	42	36	F	B	4	Uncertain Di	C	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 140	36	36	F	B	1	Suspect TB	C	P	435	351	Mycobacteri	Other (No abnormalities)
Patient 141	39	36	M	B	2	Suspect Lym	C	P	362	351	CHL	CHL
Patient 142	32	21	M	B	2	Suspect Lym	C	N	Nil	Nil	CHL	CHL
Patient 143	35	21	M	B	4	Uncertain Di	C	U	Nil	Nil	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 144	44	36	F	B	2	Suspect Lym	C	P	326	201	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 145	29	21	F	B	1	Suspect TB	C	P	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 146	29	21	F	B	2	Suspect Lym	C	P	182	100	Mycobacteri	Non-specific reactive lymphoid hyperplasia
Patient 148	34	21	M	B	2	Suspect Lym	I	P	98	0	Non-specific	Mycobacterial infection
Patient 149	35	21	M	B	2	Suspect Lym	C	P	77	0	CHL	CHL
Patient 150	27	21	M	B	1	Suspect TB	A	P	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 152	48	36	F	B	2	Suspect Lym	C	P	346	201	CHL	CHL
Patient 153	27	21	F	B	4	Uncertain Di	A	U	Nil	Nil	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 158	34	21	F	B	3	Staging Aden	A	P	193	100	Carcinoma	Carcinoma
Patient 160	32	21	M	B	4	Uncertain Di	A	P	188	100	Other (KS)	Other (Atypical lymphoid cells)
Patient 161	30	21	F	B	4	Uncertain Di	A	P	397	351	HIV Lymphac	Non-specific reactive lymphoid hyperplasia
Patient 163	34	21	M	B	4	Uncertain Di	A	P	287	201	HIV Lymphac	Other (Atypical lymphoid cells)
Patient 166	70	66 and great	M	B	2	Suspect Lym	C	N	Nil	Nil	NHL	NHL
Patient 168	24	21	F	B	4	Uncertain Di	I	P	Nil	Nil	Other (KS)/ M	Mycobacterial infection
Patient 170	29	21	F	B	2	Suspect Lym	A	P	80	0	NHL	NHL
Patient 172	31	21	M	B	4	Uncertain Di	C	U	Nil	Nil	Mycobacteri	Mycobacterial infection
Patient 175	55	51	M	B	1	Suspect TB	C	P	142	100	NHL	Non-specific reactive lymphoid hyperplasia
Patient 176	39	36	F	B	1	Suspect TB	C	P	11	0	Mycobacteri	Mycobacterial infection
Patient 179	36	36	M	B	4	Uncertain Di	A	P	385	351	CHL	Mycobacterial infection
Patient 183	14	12	F	B	4	Uncertain Di	C	N	Nil	Nil	NHL	NHL
Patient 186	43	36	M	B	2	Suspect Lym	A	P	390	351	Carcinoma	Other (Atypical lymphoid cells)
Patient 187	17	12	M	B	2	Suspect Lym	C	N	Nil	Nil	CHL	CHL
Patient 191	34	21	M	B	4	Uncertain Di	C	N	Nil	Nil	Mycobacteri	Other (No abnormalities)
Patient 192	34	21	F	B	1	Suspect TB	C	P	171	100	Mycobacteri	Mycobacterial infection
Patient 193	25	21	M	B	1	Suspect TB	C	U	Nil	Nil	Granulomatc	Mycobacterial infection
Patient 194	33	21	M	B	2	Suspect Lym	O	P	242	201	Non-specific	NHL
Patient 199	39	36	M	B	4	Uncertain Di	C	P	139	100	Other (Castle	Non-specific reactive lymphoid hyperplasia
Patient 202	42	36	M	B	4	Uncertain Di	A	P	645	501	Other (Castle	Non-specific reactive lymphoid hyperplasia
Patient 203	47	36	F	B	4	Uncertain Di	I	U	Nil	Nil	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 206	61	51	F	W	4	Uncertain Di	C	U	Nil	Nil	Carcinoma	Carcinoma
Patient 211	27	21	F	B	1	Suspect TB	A	P	Nil	Nil	HIV Lymphac	Other (No abnormalities)
Patient 216	29	21	F	B	2	Suspect Lym	C	P	242	201	CHL	CHL
Patient 219	27	21	F	B	4	Uncertain Di	C	P	87	0	Non-specific	Non-specific reactive lymphoid hyperplasia
Patient 220	30	21	F	B	4	Uncertain Di	C	P	166	100	Mycobacteri	Non-specific reactive lymphoid hyperplasia
Patient 221	42	36	F	B	4	Uncertain Di	A	P	188	100	CHL	CHL
Patient 222	48	36	M	B	4	Uncertain Di	C	P	178	100	HIV Lymphac	Other (Atypical lymphoid cells)
Patient 225	50	36	F	B	3	Staging Aden	C	N	Nil	Nil	Carcinoma	Carcinoma
Patient 226	51	51	M	B	2	Suspect Lym	C	P	277	201	NHL	NHL
Patient 229	39	36	F	B	2	Suspect Lym	C	P	150	100	CHL	Other (Atypical lymphoid cells)
Patient 230	32	21	F	B	2	Suspect Lym	I	U	Nil	Nil	HIV Lymphac	NHL

Patient 242	38	36	M	B	2	Suspect Lym	C	P		110	100	NHL	NHL	
Patient 244	54	51	F	B	1	Suspect TB	A	P		18	0	Mycobacteri	Other (Atypical lymphoid cells)	
Patient 246	46	36	M	B	2	Suspect Lym	I	P		357	351	NHL	NHL	
Patient 248	18	12	F	B	4	Uncertain Di	C	N	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 249	27	21	F	B	1	Suspect TB	C	N	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 252	37	36	F	B	4	Uncertain Di	C	N	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 253	16	12	M	B	4	Uncertain Di	C	P		136	100	Mycobacteri	Granulomatous inflammation NOS	
Patient 257	36	36	M	B	2	Suspect Lym	C	P		222	201	CHL	CHL	
Patient 264	39	36	M	B	4	Uncertain Di	I	N	Nil	Nil		Other (Sarco	Other (Sarcoma)	
Patient 265	31	21	F	C	5	Unknown	C	P		36	0	Other (Castle	Non-specific reactive lymphoid hyperplasia	
Patient 269	48	36	M	B	4	Uncertain Di	C	N	Nil	Nil		Carcinoma	Other (Malignant cells)	
Patient 278	38	36	F	B	2	Suspect Lym	A	P		305	201	NHL	NHL	
Patient 281	30	21	F	B	5	Unknown	C	P		178	100	Granulomato	Granulomatous inflammation NOS	
Patient 287	32	21	F	B	4	Uncertain Di	C	P	Nil	Nil		Non-specific	Other (No abnormalities)	
Patient 288	35	21	M	B	1	Suspect TB	I	P		243	201	Non-specific	Mycobacterial infection	
Patient 294	47	36	M	B	5	Unknown	O	N	Nil	Nil		Carcinoma	Other (No abnormalities)	
Patient 295	44	36	F	B	2	Suspect Lym	O	U	Nil	Nil		CHL	CHL	
Patient 300	34	21	M	B	2	Suspect Lym	C	N	Nil	Nil		CHL	Other (Atypical lymphoid cells)	
Patient 301	30	21	M	B	2	Suspect Lym	O	P		99	0	Mycobacteri	Mycobacterial infection	
Patient 314	52	51	F	B	4	Uncertain Di	I	N	Nil	Nil		NHL	Granulomatous inflammation NOS	
Patient 315	60	51	F	B	3	Staging Aden	I	P		261	201	Non-specific	Other (No abnormalities)	
Patient 316	24	21	F	B	5	Unknown	O	U	Nil	Nil		Non-specific	Other (No abnormalities)	
Patient 321	24	21	M	B	4	Uncertain Di	C	U	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 322	19	12	F	B	2	Suspect Lym	C	N	Nil	Nil		NHL	Other (No abnormalities)	
Patient 323	42	36	M	B	4	Uncertain Di	C	P		384	351	Other (Castle	Granulomatous inflammation NOS	
Patient 328	48	36	F	B	2	Suspect Lym	C	P		40	0	Other (Castle	Non-specific reactive lymphoid hyperplasia	
Patient 335	32	21	F	B	1	Suspect TB	C	P		107	100	Mycobacteri	Mycobacterial infection	
Patient 344	43	36	F	B	2	Suspect Lym	C	P		336	201	Other (Castle	Non-specific reactive lymphoid hyperplasia	
Patient 345	45	36	F	B	5	Unknown	C	U	Nil	Nil		HIV Lymphad	Other (Atypical lymphoid cells)	
Patient 349	52	51	F	B	2	Suspect Lym	C	P		26	0	NHL	NHL	
Patient 351	36	36	F	B	2	Suspect Lym	C	P		228	201	NHL	NHL	
Patient 355	15	12	F	B	2	Suspect Lym	C	P		292	201	NHL	NHL	
Patient 357	34	21	F	B	4	Uncertain Di	C	P		115	100	Carcinoma	Other (Atypical lymphoid cells)	
Patient 358	56	51	F	B	3	Staging Aden	A	N	Nil	Nil		Other (No ab	Carcinoma	
Patient 362	53	51	F	B	1	Suspect TB	C	P		67	0	Mycobacteri	Mycobacterial infection	
Patient 363	24	21	M	B	1	Suspect TB	I	P		271	201	HIV Lymphad	Non-specific reactive lymphoid hyperplasia	
Patient 364	25	21	M	B	4	Uncertain Di	C	P		409	351	Other (KS)	Non-specific reactive lymphoid hyperplasia	
Patient 366	43	36	M	B	2	Suspect Lym	C	P	Nil	Nil		NHL	NHL	
Patient 367	35	21	M	B	1	Suspect TB	C	N	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 369	49	36	F	B	4	Uncertain Di	C	N	Nil	Nil		NHL	Non-specific reactive lymphoid hyperplasia	
Patient 373	34	21	F	B	1	Suspect TB	C	P		129	100	HIV Lymphad	Non-specific reactive lymphoid hyperplasia	
Patient 374	50	36	M	B	4	Uncertain Di	C	P		45	0	Mycobacteri	Mycobacterial infection	
Patient 375	55	51	F	B	2	Suspect Lym	C	P	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 382	23	21	F	C	4	Uncertain Di	C	N	Nil	Nil		CHL	Other (No abnormalities)	
Patient 383	33	21	M	B	1	Suspect TB	C	P	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 390	49	36	F	B	1	Suspect TB	C	U	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 396	24	21	F	B	1	Suspect TB	C	P		15	0	Mycobacteri	Mycobacterial infection	
Patient 397	40	36	F	B	2	Suspect Lym	A	P		298	201	HIV Lymphad	Non-specific reactive lymphoid hyperplasia	
Patient 399	42	36	F	B	1	Suspect TB	C	P		185	100	Mycobacteri	Mycobacterial infection	
Patient 404	47	36	M	B	1	Suspect TB	C	P		8	0	Mycobacteri	Mycobacterial infection	
Patient 405	29	21	F	B	2	Suspect Lym	C	P		46	0	Mycobacteri	Mycobacterial infection	
Patient 407	30	21	F	B	1	Suspect TB	A	U	Nil	Nil		Mycobacteri	Other (No abnormalities)	
Patient 408	53	51	F	B	2	Suspect Lym	C	P		491	351	Non-specific	NHL	
Patient 410	17	12	F	B	2	Suspect Lym	C	U	Nil	Nil		CHL	CHL	
Patient 412	34	21	M	B	5	Unknown	C	P		189	100	Other (KS)	Other (No abnormalities)	
Patient 420	47	36	F	B	5	Unknown	I	P	Nil	Nil		HIV Lymphad	Non-specific reactive lymphoid hyperplasia	
Patient 421	58	51	F	C	4	Uncertain Di	C	P		217	201	Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 426	30	21	M	B	4	Uncertain Di	C	U	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 428	35	21	M	B	2	Suspect Lym	C	P		54	0	Other (Castle	Non-specific reactive lymphoid hyperplasia	
Patient 429	23	21	F	B	1	Suspect TB	C	P		336	201	Other (KS)	Mycobacterial infection	
Patient 433	48	36	F	B	4	Uncertain Di	C	N	Nil	Nil		NHL	Non-specific reactive lymphoid hyperplasia	
Patient 436	32	21	M	B	5	Unknown	C	P	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 440	32	21	M	B	1	Suspect TB	C	P		555	501	Mycobacteri	Mycobacterial infection	
Patient 441	36	36	F	B	4	Uncertain Di	C	P	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 443	39	36	F	B	1	Suspect TB	A	P		297	201	Mycobacteri	Non-specific reactive lymphoid hyperplasia	
Patient 450	15	12	M	B	1	Suspect TB	C	N	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 451	48	36	M	B	4	Uncertain Di	C	P		958	501	Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 455	25	21	F	B	4	Uncertain Di	C	N	Nil	Nil		NHL	Mycobacterial infection	
Patient 458	33	21	M	B	1	Suspect TB	C	P		115	100	Mycobacteri	Mycobacterial infection	
Patient 462	30	21	M	B	5	Unknown	I	P		349	201	Mycobacteri	Mycobacterial infection	
Patient 465	27	21	F	C	5	Unknown	C	U	Nil	Nil		Granulomato	Granulomatous inflammation NOS	
Patient 466	42	36	F	B	5	Unknown	C	P		101	100	Mycobacteri	Mycobacterial infection	
Patient 472	68	66 and great	F	B	5	Unknown	C	N	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 473	40	36	M	B	2	Suspect Lym	A	P		26	0	CHL	CHL	
Patient 474	33	21	F	B	2	Suspect Lym	C	P		470	351	CHL	CHL	
Patient 476	42	36	M	B	5	Unknown	A	P		224	201	CHL	Other (Malignant cells)	
Patient 477	32	21	M	B	4	Uncertain Di	I	P		159	100	Other (KS)	Non-specific reactive lymphoid hyperplasia	
Patient 482	28	21	M	B	1	Suspect TB	C	U	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 484	17	12	F	A	5	Unknown	C	N	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 487	62	51	F	B	2	Suspect Lym	C	P		147	100	CHL	CHL	
Patient 488	55	51	M	B	2	Suspect Lym	A	P		153	100	NHL	NHL	
Patient 491	28	21	F	B	4	Uncertain Di	A	P		1626	501	other (CML)	other (CML)	
Patient 496	44	36	M	W	4	Uncertain Di	A	U	Nil	Nil		Mycobacteri	Mycobacterial infection	
Patient 501	22	21	F	W	1	Suspect TB	A	U	Nil	Nil		Mycobacteri	Other (Atypical lymphoid cells)	
Patient 502	31	21	F	B	5	Unknown	C	P		809	501	Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 503	62	51	M	B	2	Suspect Lym	A	P		153	100	NHL	CHL	
Patient 506	43	36	M	B	5	Unknown	O	P		53	0	Mycobacteri	Mycobacterial infection	
Patient 509	53	51	F	B	3	Staging Aden	A	N	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 511	38	36	M	B	2	Suspect Lym	C	U	Nil	Nil		CHL	CHL	
Patient 514	42	36	M	W	2	Suspect Lym	C	N	Nil	Nil		CHL	Other (No abnormalities)	
Patient 518	46	36	F	B	3	Staging Aden	A	P	Nil	Nil		Carcinoma	Non-specific reactive lymphoid hyperplasia	
Patient 522	37	36	M	B	2	Suspect Lym	C	U	Nil	Nil		HIV Lymphad	Non-specific reactive lymphoid hyperplasia	
Patient 523	45	36	F	B	2	Suspect Lym	C	P		460	351	CHL	CHL	
Patient 532	74	66 and great	F	B	3	Staging Aden	A	U	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 533	62	51	M	B	4	Uncertain Di	C	U	Nil	Nil		Carcinoma	Carcinoma	
Patient 537	54	51	F	B	4	Uncertain Di	A	N	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 539	29	21	F	B	1	Suspect TB	C	U	Nil	Nil		Carcinoma	Other (No abnormalities)	
Patient 541	53	51	F	B	4	Uncertain Di	A	N	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	
Patient 545	43	36	M	B	1	Suspect TB	C	P		133	100	Mycobacteri	Other (Atypical lymphoid cells)	
Patient 549	30	21	M	B	2	Suspect Lym	A	U	Nil	Nil		Non-specific	Non-specific reactive lymphoid hyperplasia	

Patient 550	31	21	F	B	2	Suspect Lym	A	P		243	201	HIV Lymphad	Non-specific reactive lymphoid hyperplasia
Patient 552	29	21	F	B	4	Uncertain Di	C	N	Nil	Nil		Mycobacteri	Mycobacterial infection
Patient 557	15	12	F	B	4	Uncertain Di	C	U	Nil	Nil		Granulomat	Mycobacterial infection
Patient 560	28	21	F	B	4	Uncertain Di	A	P		187	100	NHL	NHL

6.5 Turn it in Report

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RESEARCH ARTICLE

Patterns of Lymph Node Pathology; Fine Needle Aspiration Biopsy as an Evaluation Tool for Lymphadenopathy: A Retrospective Descriptive Study Conducted at the Largest Hospital in Africa

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Abstract

Background

Lymphadenopathy is a common clinical presentation of disease in South Africa (SA), particularly in the era of Human Immunodeficiency Virus (HIV) and tuberculosis (TB) co-infection.

Methods

Data from 560 lymph node biopsy reports of specimens from patients older than 12 years at Chris Hani Baragwanath Academic Hospital (CHBAH) between 1 January 2010 and 31 December 2012 was extracted from the National Health Laboratory Service (NHLS), division of Anatomical Pathology. Cytology reports of lymph node fine needle aspirates (FNAs) performed prior to lymph node biopsy in 203 patients were also extracted from the NHLS. Consent was not obtained from participants for their records to be used as patient information was anonymized and de-identified prior to analysis.

Results

The majority of patients were female (55%) and of the African/black racial group (90%). The median age of patients was 40 years (range12–94). The most common indication for biopsy was an uncertain diagnosis (more than two differential diagnoses entertained), followed by a suspicion for lymphoma, carcinoma and TB. Overall, malignancy constituted the largest biopsy pathology group (39%), with 36% of this group being carcinoma and 27% non-Hodgkin lymphoma. 22% of the total sampled nodes displayed necrotizing granulomatous inflammation (including histopathology and cytology demonstrating definite, and suspicious for

Competing Interests: Professor Venter is supported by PEPFAR. Dr. Pather was supported by SATBAT/FIC grant 3U2RTW007370-05S1. This does not alter the authors' adherence to PLOS ONE policies on sharing data and materials.

mycobacterial infection), 8% comprised HIV reactive nodes; in the remainder no specific pathology was identified (nonspecific reactive lymphoid hyperplasia). Kaposi sarcoma (KS) accounted for 2.5% of lymph node pathology in this sample. Concomitant lymph node pathology was diagnosed in four cases of nodal KS (29% of the subset). The co-existing pathologies were TB and Castleman disease. HIV positive patients constituted 49% of this study sample and the majority (64%) of this subset had CD4 counts less than 350 cells/ul. 27% were HIV negative and in the remaining nodes, the HIV status of patients was unknown. The most common lymph node pathologies in HIV positive patients were Mycobacterial infection (31%), HIV reactive nodes (15%), non-Hodgkin lymphoma (15%) and nonspecific reactive lymphoid hyperplasia (15%). Only 8.7% were of Hodgkin lymphoma. In contrast, the most common lymph node pathologies in HIV negative patients were nonspecific reactive lymphoid hyperplasia (45%), carcinoma (25%) and Mycobacterial infection (11%). In this group, non-Hodgkin lymphoma and Hodgkin lymphoma constituted 9% and 8%, respectively. There were more cases of high-grade non-Hodgkin lymphoma in the HIV positive group compared to the HIV negative group. FNA and lymph node biopsy had statistically significant good agreement with regard to Hodgkin lymphoma (K 0.774, SE 0.07, 95% CI 0.606-0.882, p=0.001), non-Hodgkin lymphoma (K 0.640, SE 0.07, 95% CI 0.472-0.807, p=0.001), carcinoma (K 0.723, SE 0.069, 95% CI 0.528-0.918, p=0.001), and mycobacterial infection (K 0.726, SE 0.07, 95% CI 0.618-0.833, p=0.001).

Conclusions

The most common lymph node pathologies in CHBAH are malignancies, nonspecific reactive lymphoid hyperplasia, necrotizing granulomatous inflammation and HIV reactive nodes. The distribution of disease differs in HIV positive patients. Overall, adequate FNA samples of lymph nodes have been found to have good correlation with lymph node biopsy findings in our setting.

Introduction

Lymphadenopathy is a common presentation of disease in South Africa (SA), particularly in the era of Human Immunodeficiency Virus (HIV) and tuberculosis (TB) co-infection. There are only a limited number of studies that have described lymph node pathology in Southern Africa. Chris Hani Baragwanath Academic Hospital (CHBAH) which is a provincial tertiary hospital in Soweto, Johannesburg, contains close to 3300 beds and is the largest hospital in Africa [1].

In a post-mortem study performed in Johannesburg, TB was found to be the cause of death in the majority of patients (69%) with advanced Acquired Immunodeficiency Syndrome (AIDS), both before and after starting antiretroviral therapy [2]. Lymph nodes were the fourth most common site of positive mycobacterial cultures in this study (16%), following liver, spleen and lung [2]. The study also suggested that TB often goes unrecognized in these patients, and can be accompanied by other infections or neoplasms [2].

Excisional biopsy of a clinically appropriate lymph node is traditionally favored as a diagnostic procedure for a multitude of infectious and neoplastic disorders. However, fine-needle

aspiration (FNA) is replacing it as a first line diagnostic procedure, reserving excisional biopsy for non-diagnostic FNA results that require further investigation [3–4].

We conducted a retrospective review of the lymph node pathology identified at CHBAH to contribute to medical knowledge of common causes of lymphadenopathy requiring biopsy in South Africa, and the role of FNA as an adjunct to excisional lymph node biopsy.

Methods

The study was a retrospective descriptive audit conducted at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa. The study population consisted of all patients over the age of 12 years who underwent lymph node biopsies at CHBAH between 1 January 2010 and 31 December 2012. Lymph node biopsy reports were extracted from the database of the National Health Laboratory Service (NHLS) Division of Anatomical Pathology.

Patient demographic details were obtained from the laboratory requisition forms submitted by attending clinicians and from pathology reports. There was no review of patient charts or files. Further information regarding HIV status (determined with antibody testing using 4th generation HIV enzyme-linked immunosorbent assay), CD4 count (cells/ul), if relevant, and FNAs performed (smears in our setting) were accessed through the NHLS DisaLab system, using the patients' name and hospital number. Consent was not obtained from participants for their records to be used as patient information was anonymized and de-identified prior to analysis.

All lymph node biopsy and FNA biopsy specimens were analyzed by pathologists employed by the NHLS at CHBAH, including one of the authors. Unfortunately, the authors reviewed not all the slides during this retrospective study. Histologic diagnoses were based on morphologic findings and, in the appropriate context, ancillary tests including Mycobacterial staining and culture, immunohistochemistry, FISH (fluorescent in-situ hybridization) techniques, and flow cytometry. The World Health Organization diagnostic criteria were applied to the histopathology demonstrated on lymph node biopsies. The diagnosis of tuberculous lymphadenitis was confirmed by Ziehl-Neelsen stain for acid fast bacilli and positive Mycobacterial culture. Mycobacterial culture and Mycobacterial PCR testing using Xpert MTB/RIF are performed in cases of clinically and histopathologically (granulomatous) suspected Mycobacterial lymphadenitis. Ziehl-Neelsen stains for acid fast bacilli were routinely performed on all lymph node biopsies and FNA biopsies that displayed granulomatous inflammation (necrotizing and non-necrotizing). HIV lymphadenitis was graded as follows: grade 1 if associated with hyperplastic features and enlargement of germinal centres with increased apoptosis and phagocytosis by macrophages; grade 2 if there was a reduction in lymphoid follicles and mature lymphocytes, but an increase in plasma cells and perifollicular blood vessels; and grade 3 if the germinal centres were sclerotic. HIV lymphadenitis was not used as a surrogate marker for HIV infection, as it describes a histological pattern not entirely specific to HIV.

There were no specific exclusion criteria. Specimens deemed unsuitable for histopathologic or cytologic analysis by the pathologist were excluded. Unsuitable samples were attributed to tissue samples not representative of lymphoid tissue or poor quality specimens that could not be evaluated. Non-diagnostic specimens were included in the analysis. In cases where a single patient had more than one lymph node biopsy during the period of the study, the repeat biopsies were evaluated as a subset. A total of 203 reports of FNAs preceding lymph node biopsy were evaluated. Findings of the FNA were analyzed in conjunction with adequacy of FNA samples submitted for cytology, prior to comparison with biopsy. Of the FNAs, 23% were inadequate for assessment, 76% were adequate and in 1% adequacy was not commented on.

Statistical analysis was performed using STATA version 12 for Windows (StataCorp LP, Texas; www.stata.com) and GraphPadQuickCalcs (GraphPad Software Inc, California; www.graphpad.com). A statistician was consulted. The Human Research Ethics committee at the University of the Witwatersrand granted ethical approval of this study (Clearance Certificate number M130626).

Results

The majority of patients (55%) who had lymph node biopsies were female (Table 1). Over 90% of patients were of the African/black racial group, in keeping with the racial demographic distribution in SA. The median age of patients was 40 years, with a minimum of 12 and a maximum of 94. The most common indication for biopsy was an uncertain diagnosis (more than two differential diagnoses entertained), followed by a suspicion for lymphoma, carcinoma and TB (Table 2).

The most frequent site of biopsy was cervical, followed by "other" which included laparoscopic biopsies (of intra-abdominal nodes), axillary and inguinal nodal biopsies. Laparoscopic biopsies were performed as part of a staging or curative process for patients known to have carcinoma. In other instances, lymph nodes were found incidentally at laparotomy or laparoscopy and sampled.

Interestingly, of the suspected lymphoma cases, 28% were diagnosed with non-Hodgkin lymphoma, and 23% with Hodgkin lymphoma. Of the suspected TB cases, 62% displayed necrotizing granulomatous inflammation on biopsy, while 53% of staging carcinoma had confirmed carcinoma on biopsy.

Overall, malignancy was the largest biopsy pathology group (39%), with 36% of this group having carcinoma and 27% non-Hodgkin lymphoma. 22% of the total sample comprised nodes that displayed necrotizing granulomatous inflammation (including histopathology demonstrating definite mycobacterial infection and suspicious for mycobacterial infection). 8% of the sample comprised HIV reactive nodes and in the remainder no specific pathology was identified (including nonspecific reactive lymphoid hyperplasia).

KS accounted for 2.5% of lymph node pathology in the sample. Concomitant lymph node pathology was diagnosed within four cases of nodal KS (29% of the subset). The co-existing pathologies were mycobacterial infection in one patient, Castleman disease in two patients, and a combination of mycobacterial infection and Castleman disease in the fourth patient.

HIV positive patients constituted 49% of the sample, with the majority of patients in this subset (64%) having a CD4 count below 350 cells/ul. 27% were HIV negative and in the remaining nodes, the HIV status of patients was unknown. The most common lymph node pathologies in HIV positive patients were mycobacterial infection (31%), HIV reactive nodes (15%), non-Hodgkin lymphoma (15%) and non-specific reactive lymphoid hyperplasia (15%) (Table 3). Only 8.7% were of Hodgkin lymphoma. In contrast, the most common lymph node pathologies in HIV negative patients were nonspecific reactive lymphoid hyperplasia (45%), carcinoma (25%) and Mycobacterial infection (11%). In this group, non-Hodgkin lymphoma and Hodgkin lymphoma constituted 9% and 8%, respectively.

Amongst the cases with non-Hodgkin lymphoma, 66% were HIV positive. Of the HIV positive subset, 50% were diagnosed with Diffuse Large B-Cell Lymphoma (DLBCL) and 17.5% with Burkitt lymphoma. Plasmablastic lymphoma, Intermediate Burkitt/ DLBCL and Anaplastic Large Cell Lymphoma each contributed a further 10% to the HIV positive group. In contrast, DLBCL was found in only 21% of the HIV negative group. Only one HIV negative case was classified as HIV lymphadenitis. This diagnosis was influenced by incorrectly specified clinical information regarding HIV status in the laboratory request form. As mentioned earlier,

Table 1. Incisional, Excisional and Core Biopsy Diagnosis in relation to Demographics.

Demographic		Malignancy, n = 219						Necrotizing nodes, n = 125	HIV[1] React nodes, n = 46	Not definitive, n = 170	TOTAL, n = 560 n(%)
		KS[2]	NHL[3]	CHL[4]	Car[5]	Other	Subtotal				
GENDER	Male	9	29	27	21	11	97	58	17	80	252(45)
	Female	5	31	22	58	6	122	67	29	90	308(55)
RACE	Asian				1		1	2			3(0.5)
	Black	14	58	46	69	16	203	116	44	160	523(93.3)
	White			2	9		11	3	1	9	24(4.2)
	Mixed Race		2	1		1	4	4	1	1	10(2)
AGE	Median 40										
	(12–94)										
AGE BAND	12-20yr		4	5	2		11	11	1	18	41(7.3)
	21-35yr	11	13	20	13	9	66	59	22	40	187(33.4)
	36-50yr	3	25	17	31	6	82	46	20	53	201(36)
	51-65yr		15	7	25	1	48	8	3	48	107(19)
	>65yr		3		8	1	12	1		11	24(4.3)

[1]HIV: Human Immunodeficiency Virus

[2]KS: Kaposi sarcoma

[3]NHL: non-Hodgkin Lymphoma

[4]CHL: Hodgkin Lymphoma

[5]Car: carcinoma.

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Table 2. Incisional, Excisional and Core Biopsy Diagnosis in relation to Indications and site of biopsy.

		Malignancy, n = 219						Necrotizing nodes, n = 125	HIV[1] React nodes, n = 46	Not definitive, n = 170	TOTAL, n = 560
		KS[2]	NHL[3]	CHL[4]	Car[5]	Other	Subtotal				n(%)
INDICATION FOR BIOPSY	Suspect TB[6]	1	5	2	2	1	11	46	9	8	74(13)
	Suspect lymphoma	2	33	28	4	4	71	17	13	19	120(22)
	Staging Car[5]				60		60			54	114(20)
	Uncertain Diagnosis	9	16	14	12	9	60	45	20	77	202(36)
	Unknown	2	6	5	1	3	17	17	4	12	50(9)
SITE OF LYMPH NODE BIOPSY	Cervical	8	26	37	18	9	98	73	16	31	218(40)
	Inguinal	2	10	2	10	1	25	5	9	19	58(10)
	Axilla	2	11	7	35	6	61	18	12	38	129(23)
	Other	2	13	3	16	1	35	29	9	82	155(27)

[1]HIV: Human Immunodeficiency Virus

[2]KS: Kaposi sarcoma

[3]NHL: non-Hodgkin Lymphoma

[4]CHL: Hodgkin Lymphoma

[5]Car: carcinoma

[6]TB: Tuberculosis.

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Table 3. Incisional, Excisional and Core Biopsy diagnosis in relation to HIV status.

HIV Status		Malignancy, n = 219						Necrotizing nodes, n = 125	HIV[1] React nodes, n = 46	Not definitive, n = 170	TOTAL, n = 560 n(%)
		KS[2]	NHL[3]	CHL[4]	Car[5]	Other	Subtotal				
	Subtotals	14	60	49	79	17	219	125	46	170	560(100)
HIV[1] NEGATIVE			14	12	37	1	64	17	1	68	150(27)
HIV[1] UNKNOWN		1	6	13	28	1	49	23	4	60	136(24)
HIV[1] POSITIVE		13	40	24	14	15	106	85	41	42	274(49)
CD4[6] BAND (cells/ul)	<100		7	4		3	14	35	2	6	57(10)
	100–200	3	13	5	5	2	28	19	5	6	58(10.4)
	201–350	5	8	8	1	6	28	10	12	11	61(11)
	351–500	2	2	5	1		10	1	7	4	22(4)
	>500	1	3		3	4	11	2	5	6	24(4.3)
	Nil/ Unknown	2	7	2	4		15	18	10	9	52(9.3)

[1]HIV: Human Immunodeficiency Virus

[2]KS: Kaposi sarcoma

[3]NHL: non-Hodgkin Lymphoma

[4]CHL: Hodgkin Lymphoma

[5]Car: carcinoma

[6]CD4: Cluster of Differentiation 4 T-cells.

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HIV lymphadenitis is a histological pattern not entirely specific to HIV and therefore, cannot be used as a surrogate marker for HIV infection.

There were 203 (36%) patients in our study sample who also underwent FNAs prior to biopsy. Of the FNAs, 23% were inadequate for assessment, 76% were adequate and in 1% adequacy was not commented on. When compared with the histopathology diagnosis as per lymph node biopsies, FNA was found to have statistically significant good agreement/reliability with regards to Hodgkin lymphoma (K 0.774, SE 0.07, 95% CI 0.606–0.882, p = 0.001), non-Hodgkin lymphoma (K 0.640, SE 0.07, 95% CI 0.472–0.807, p = 0.001), carcinoma (K 0.723, SE 0.069, 95% CI 0.528–0.918, p = 0.001), and mycobacterial infection (K 0.726, SE 0.07, 95% CI 0.618–0.833, p = 0.001) (Table 4).

Table 4. Statistical Agreement between LN FNA and LN Biopsy.

Pathological Diagnosis	% observed agreements	% agreements expected by chance	Kappa	SE	95% Confidence Interval	P-value
CHL[1]	94.09	76.92	0.744	0.07	0.606–0.882	0.001
NHL[2]	92.61	79.50	0.640	0.07	0.472–0.807	0.001
Car[3]	96.55	87.55	0.723	0.069	0.528–0.918	0.001
Granulom inflam NOS[4]	97.04	95.20	0.385	0.07	-0.005–0.775	0.001
MI[5]	89.16	60.49	0.726	0.07	0.618–0.833	0.001
Non-specific reactive LNH[6]	80.30	67.28	0.398	0.067	0.249–0.547	0.001

[1]CHL: Hodgkin Lymphoma

[2]NHL: non Hodgkin Lymphoma

[3]Car: carcinoma

[4]Granulom inflam NOS: Granulomatous Inflammation not otherwise specified

[5]MI: Mycobacterial Infection

[6]Non-specific reactive LNH: non-specific reactive lymph node hyperplasia.

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There were two cases where a single patient had more than one lymph node biopsy during the period of the study. Both patients were HIV positive with CD4 counts below 200 cells/ul. FNAs were performed prior to biopsy in both cases and were not definitive. The sites of the biopsies were, respectively, axillary and cervical in the first patient, and cervical both times, in the second patient. The definitive biopsies were both repeated due to a high index of clinical suspicion, and subsequently confirmed to be non-Hodgkin lymphoma.

Discussion

Our study affirmed local demographic patterns, in that the majority of patients who underwent lymph node biopsy at CHBAH were middle-aged African/black females. We have demonstrated that nodal pathology diagnoses at CHBAH are inclusive of malignancy, necrotizing granulomatous inflammation and reactive nodes (due to HIV or other). The most common lymph node pathologies at CHBAH as per biopsy are in keeping with local African literature [5–7]. However, our data is unique in that it also describes differences in pathology between HIV positive and negative patients, the former further stratified by CD4 count.

Our study highlights the known significant correlation between HIV incidence and incidence of aggressive B-cell lymphomas and Hodgkin lymphoma [8–9]. Associated risk factors for the development of these malignancies are high HIV viral loads and low CD4 counts, although malignancies may occur at any CD4 count. The pathogenesis is thought to be immune dysregulation with loss of T-cell immunity against onco-viruses like Epstein-Barr Virus and human herpesvirus 8 [8].

The most common indications for requesting a lymph node biopsy in our setting were an uncertain diagnosis and the suspicion of malignancy or TB, which reflects the relative dominance of the latter two diseases in Southern Africa. The global prevalence and death rates from TB are on the decline. However, in contrast, Africa is showing an increase in the tuberculous burden [10].

In a study performed at CHBAH, TB was diagnosed in 1291 patients over a period of two months [1]. The association between HIV infection and TB is well described in South Africa. The high prevalence of TB is also reflected by HIV statistics for SA [11]. South Africa carries the highest global burden of HIV with an estimated 5.6 million people infected, with TB being the most common serious opportunistic infection [11–13].

The previous CHBAH study showed that of the patients diagnosed with TB, 74% had pulmonary TB and of the patients with extrapulmonary TB, pleural and miliary were the most common forms [1]. However, more recent publications suggest that TB lymphadenitis is the most common form of extrapulmonary TB [3–4,14]. The high prevalence of TB and TB suspicious lymphadenitis at CHBAH has been described, notably in the age band 25–44 years [15]. In our study, 22% of lymph node biopsies and 27% of FNAs comprised nodes that displayed necrotizing granulomatous inflammation (including histopathology and cytology demonstrating definite mycobacterial infection and suspicious for mycobacterial infection), confirming the high prevalence of TB in CHBAH.

The study by Martinson et al stated that the risk of TB increases at lower CD4 counts, and suggested that early antiretroviral therapy reduced the population prevalence of TB in HIV infected patients [12]. This suggestion may also be evident in our study as the majority of HIV positive patients in our sample had CD4 counts less than 350 cells/ul and the commonest lymph node pathology in this group was confirmed and suspected TB.

There is a wide differential diagnosis for peripheral TB lymphadenitis. Patients with lymphoma in rural KwaZulu Natal were misdiagnosed based on clinical similarities to TB and were placed on empiric TB treatment, delaying the lymphoma diagnosis by a median of five

months [16]. The dangers of misdiagnosing TB, and subsequent empiric TB treatment, are progression of underlying disease (malignancy or other infection); toxicity of TB therapy; and development of drug-resistant therapy [11, 17].

A Zambian study suggested that primary HIV lymphadenopathy was a significant cause of superficial lymphadenopathy [18]. This finding is also highlighted in our study, as HIV reactive nodes comprised 8% of the total sample, and was amongst the largest nodal pathology group in HIV positive patients (15%).

HIV-associated lymphadenitis (reported in our setting as HIV reactive nodes) is a well-characterized pattern of histological findings in lymph nodes of many HIV-infected individuals. It is likely due to the lymphotropism of the HI virus. Grade 1 is associated with hyperplastic features, enlargement of germinal centres with increased apoptosis and phagocytosis by macrophages. In Grade 2 there is a reduction in lymphoid follicles and mature lymphocytes, but an increase in plasma cells and perifollicular blood vessels. In Grade 3, the germinal centres become sclerotic [19].

Rare causes of lymphadenopathy in our study included one case of Cryptococcosis (microbiologically confirmed) in an HIV positive male patient who had profound immunosuppression (CD4 count of 8 cells/ul). In addition, there was a case of myeloid sarcoma (extramedullary counterpart of chronic myeloid leukaemia) in an HIV positive female who had a CD4 count of 1626 cells/ul.

The association between KS and multicentric Castleman disease due to the common causal agent human herpesvirus 8 (HHV8) is well described in the literature [20]. This association has been demonstrated by the co-existence of both these pathologies in lymph nodes in our study. Interestingly, two patients in our study with coexisting KS and Castleman disease had CD4 counts above 350 cells/ul. CD4 counts were not available for the remaining two patients who had concomitant lymph node pathology. A possible explanation for the relatively high CD4 counts may be immune reconstitution inflammatory syndrome.

We then evaluated the outcomes of fine needle aspiration biopsy in our setting. FNA is widely regarded as the diagnostic modality of choice in diagnosing TB lymphadenitis [10, 21]. Our study affirms a good correlation between FNA diagnosis and biopsy diagnosis on lymph node specimens. In the event of inadequate FNA samples, the result should be treated with reserve. If there is a clinical concern for nodal-based mycobacterial disease or malignancy despite a non-contributory FNA, a clinically appropriate lymph node should be submitted for histopathologic assessment.

In the event of a persistent clinical concern, despite a negative histopathology result, the nodal biopsy should be repeated with emphasis on selection of a clinically appropriate node. The importance of a repeat biopsy where there is a high clinical suspicion for disease, particularly in HIV positive patients, was highlighted in the two patients from our study subsequently diagnosed with non-Hodgkin lymphoma [16]. Our findings suggest that negative biopsy findings in HIV positive patients should be treated with reserve if there is a high index of clinical suspicion for lymphoma.

Limitations of the study include its selection bias, retrospective nature, and possible information bias as data was extracted from a database in which variable SNOMED codes for nodes at different topographic sites may be used. However, our findings correlate well with both local and international literature on the subject. In correlating FNA with excisional lymph node biopsy, there is scope for prospective studies to directly compare the two modalities and develop clinical algorithms taking into account the clinical and demographic profile of patients who should proceed directly to lymph node biopsy in order to expedite diagnosis and treatment.

Conclusions

Our study showed that the most common lymph node pathologies occurring in patients who underwent biopsies at CHBAH are malignancies, nonspecific reactive lymphoid hyperplasia, necrotizing granulomatous inflammation due to mycobacterial infection, and HIV reactive nodes. The distribution of disease differs in HIV positive patients. FNA was found to have good overall correlation with histopathology biopsy diagnoses in our setting. The diagnosis specified in an FNA report should be interpreted in conjunction with the comment/s about adequacy of the aspirated specimen for assessment. Due to the coexistence of nodal KS with other pathologies, patients who have suspected nodal KS would benefit from proceeding directly to have biopsies for histopathological assessment.

Supporting Information

S1 Dataset. FNA Stratification.
(XLS)

Acknowledgments

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Author Contributions

Conceived and designed the experiments: DLR WDFV SP. Performed the experiments: DLR. Analyzed the data: DLR SP. Contributed reagents/materials/analysis tools: DLR WDFV SP. Wrote the paper: DLR WDFV SP.

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6.7 Conference Poster (Ammended)

PATTERNS OF LYMPH NODE BIOPSY PATHOLOGY AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL (CHBAH) OVER A PERIOD OF THREE YEARS (2010-2012)

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INTRODUCTION

Lymphadenopathy is a common presentation of disease in South Africa (SA), particularly in the era of Human Immunodeficiency Virus (HIV) and tuberculosis (TB) co-infection. This study is a retrospective analysis of lymph node biopsies performed on adolescent and adult patients at the largest hospital in Africa, Chris Hani Baragwanath Academic.

AIM

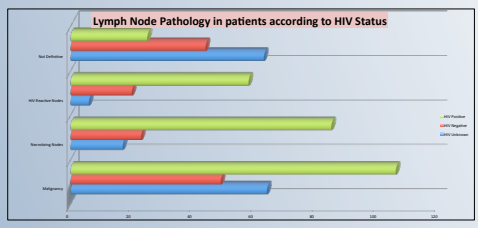
To outline the causes of lymph node pathology in our setting and to describe diagnostic correlation between fine needle aspiration biopsy (FNAB) and lymph node biopsy.

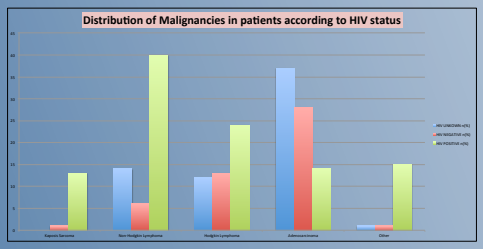
METHODS

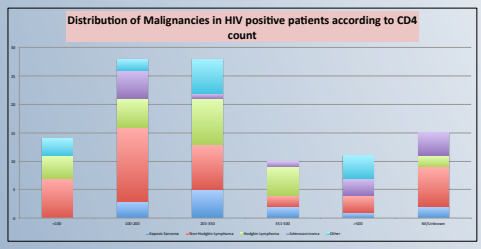
A sample of 600 lymph node biopsy reports of specimens from patients older than 12 years at Chris Hani Baragwanath Academic Hospital between 1 January 2010 and 31 December 2012 was extracted from the database of the National Health Laboratory Service (NHLS) Department of Histopathology and analyzed.
These reports also contained demographic information. Further information regarding HIV status, CD4 count and FNAs done were accessed through the NHLS DisaLab system. Biopsy specimens that were deemed unsuitable for histopathologic analysis were excluded. Ethical approval was obtained.

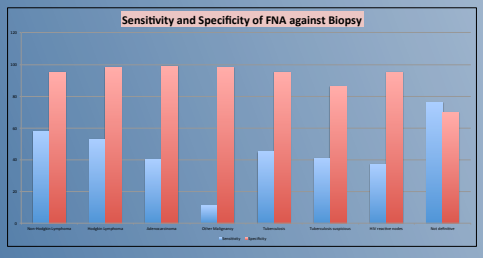
RESULTS

Of the 560 lymph node biopsies analyzed, the majority of patients were female (55%).
Over 90% of patients were black, followed by white, coloured and Asian groups. These findings are in keeping with the demographics of South Africa.
The median age of patients was 40, with a minimum of 12 and a maximum of 94. The largest age band was 36-50 and the smallest >65.
The commonest indication for biopsy was an uncertain diagnosis, followed by a suspicion of lymphoma, adenocarcinoma and TB.
The most frequent site of biopsy was cervical, followed by "other" (mostly laparoscopic biopsy), axillary and inguinal.









RESULTS

Overall, malignancy was the largest biopsy pathology group (39%), with 36% of this group being adenocarcinoma and 27% Non-Hodgkin lymphoma. 22% of the total sample were necrotizing nodes (including TB and TB suspicious), 15% of the sample were HIV reactive nodes and in the remainder a diagnosis was not definitive.
HIV positive patients constituted 49% of the sample, with the commonest CD4 band being 201-350 (22%). 24% were HIV negative and the rest HIV unknown.
The commonest lymph node pathologies in HIV positive patients were TB (24%), HIV reactive nodes (21%) and Non-Hodgkin lymphoma (14.5%).
Sensitivity of FNA was poor overall. However specificity was >95% for Non-Hodgkin and Hodgkin lymphomas, adenocarcinoma, TB and HIV reactive nodes.
There were two cases where a single patient had more than one lymph node biopsy during the period of the study. The definitive biopsies were both repeated due to a high index of clinical suspicion, and confirmed as Non-Hodgkin lymphoma.

CONCLUSIONS

Overall, the commonest lymph node pathologies in CHBAH are malignancies, necrotizing nodes and HIV reactive nodes.
The distribution of disease differs in HIV positive patients.
FNA has a high specificity but a low sensitivity compared to biopsy in our setting.

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