

**Patterns of lymph node biopsy pathology at
Chris Hani Baragwanath Academic Hospital
over a period of three years
2010-2012**

Denasha Lavanya Reddy

Student number: 742452

A research report submitted to the Faculty of Health Sciences, University of
Witwatersrand, in fulfillment of the requirements for the degree of Master of Medicine in
the branch of Internal Medicine

Johannesburg, 2015

Declaration

I, Denasha Lavanya Reddy, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the clinical discipline of Internal Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Signature: _____

_____ day of _____, 2015.

Dedication

Dedicated to my family, colleagues and patients who have inspired my research.

Publications and presentations arising from this study

Reddy DL, Venter WDF, Pather S. Patterns of lymph node biopsy pathology at Chris Hani Baragwanath Academic Hospital (CHBAH) over a period of three years 2010-2012. Poster presentation: Abstract number CS/TH-P-13. Faculty of Health Sciences, Biennial Research Day & Postgraduate Expo, 17 September 2014. (Abstract published in the *South African Journal of Infectious Diseases*:2015; 30(1):9.)

Addendum: Note that the data presented in this poster, regarding HIV reactive nodes and FNAs done, was reviewed and re-analyzed thereafter.

Reddy DL, Venter WDF, Pather S. Patterns of lymph node biopsy pathology at Chris Hani Baragwanath Academic Hospital (CHBAH) over a period of three years 2010-2012. Poster presentation (Poster 64). Southern African HIV Clinicians Society 2nd Biennial Conference, Cape Town International Convention Centre, Cape Town, South Africa, 24-27 September 2014.

Addendum: Note that the data presented in this poster, regarding HIV reactive nodes and FNAs done, was reviewed and re-analyzed thereafter.

Reddy DL, Venter WDF, Pather S (2015) 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. PLoS ONE 10(6): e0130148. doi:10.1371/journal.pone.0130148.

Published June 19, 2015. Article included as appendix.

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 (range 12-94). 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 mycobacterial infection), 8% comprised HIV reactive nodes; in the remainder no specific pathology was identified (nonspecific reactive lymphoid hyperplasia). Kaposi sarcoma (KS) accounted for 3% 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 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. 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 excellent agreement with regard to Hodgkin lymphoma (K 0.774, SE 0.07, 95% CI 0.606-0.882, p=0.001), and good agreement with regard 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).

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 differed 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.

Acknowledgements

I would like to thank my supervisors, Prof Francois Venter and Dr Sugeshnee Pather, for their patience, support, guidance and enthusiasm during this time. I would like to acknowledge the staff at the NHLS for their help during data collection, and the masters in epidemiology students who assisted me with data analysis. Dr Alison Bentley provided invaluable academic guidance. And finally, I would like to acknowledge my patients at Chris Hani Baragwanath Academic Hospital who inspire me daily.

Table of contents

	Page number
Title page	i
Declaration	ii
Dedication	iii
Publications and presentations arising	iv
Abstract	v-vi
Acknowledgements	vii
Table of contents	viii-xi
List of abbreviations	xii
List of figures	xiii
List of tables	xiv
1.0 Introduction	
1.1 Lymph node function and anatomy	1
1.2 Causes of lymphadenopathy	2-4
1.3 Malignancy in South Africa	5-6
1.4 HIV and TB in South Africa	6-7
1.5 Presentation of TB in our setting	8-9
1.6 Importance of a correct diagnosis for lymphadenopathy	9

	Page number
1.7 Diagnostic procedures for establishing a cause of lymphadenopathy	10-13
1.8 FNA and the history of the procedure	13-14
1.9 FNA: the procedure	14-15
1.10 Advantages and disadvantages of FNA and biopsy	16-19
1.11 Aim of the study	20
2.0 Materials and Methods	
2.1 Study design and site	20
2.2 Study population	20
2.3 Methods	21-22
2.4 Exclusion criteria	22
2.5 Separate Analysis	22
2.6 Statistical Analysis	22
2.7 Ethical Approval	23
3.0 Results	
3.1 Demographic characteristics	23
3.2 Indications for biopsy and topographic site of biopsies	25
3.3 Patterns of lymph node biopsy pathology	27

	Page number
3.4 Distribution of disease according to HIV status	31
3.5 Distribution of high-grade non-Hodgkin lymphoma according to HIV status	33
3.6 Correlation of FNA and lymph node biopsies	33
3.7 Analysis of patients with more than one lymph node biopsy	35
4.0 Discussion	
4.1 Study findings	35-41
4.2 Recommendations	41-42
4.3 Limitations of the study	42
5.0 Conclusion	42
6.0 Appendices	
6.1 Plagiarism Declaration form	43
6.2 Human Research Ethics Committee approval form	44
6.3 Protocol Approval form	45
6.4 Data	46-61
6.5 Turn it in Report	62-64

6.6 Published journal article (PLOS ONE)	65-74
6.7 Conference poster	75
7.0 References	76-80

List of abbreviations

1. CHBAH- Chris Hani Baragwanath Academic Hospital
2. SA- South Africa
3. HIV- Human Immunodeficiency Virus
4. TB- Tuberculosis
5. CD4- Cluster of differentiation 4
6. AIDS- Acquired Immunodeficiency Syndrome
7. FNA- Fine needle aspiration
8. KS- Kaposi sarcoma
9. WHO- World Health Organization
10. DALYs- Disability-adjusted life years
11. NHLS- National Health Laboratory Service
12. FISH- Fluorescent in-situ hybridization
13. PCR- Polymerase Chain Reaction
14. Xpert MTB/RIF (Genexpert MTB/Rif Cepheid): rapid PCR to detect
Mycobacterium tuberculosis DNA and resistance to rifampicin
15. NHL- non-Hodgkin lymphoma
16. CHL- classical Hodgkin lymphoma
17. HHV8- Human herpesvirus 8
18. DLBCL- Diffuse large B-cell lymphoma
19. LN- lymph node
20. CML- chronic myeloid leukaemia
21. SNOMED- Systematized Nomenclature of Medicine

List of figures

	Page number
1. Figure 1. Diffuse large B-cell lymphoma, H&E stain x400 magnification	28
2. Figure 2. Kaposi sarcoma (right side of image) and necrotizing granulomatous inflammation (left side of image), H&E stain x100 magnification	29
3. Figure 3. HHV8 immunohistochemistry demonstrating Castleman disease (left side of image) and Kaposi sarcoma lymphangiectatic variant (right side)	30

List of tables

	Page number
1. Table 1. Diseases associated with lymphadenopathy	4
2. Table 2. Advantages and disadvantages of FNA	18
3. Table 3. Advantages and disadvantages of biopsy	19
4. Table 4. Biopsy Diagnosis in relation to Demographics	24
5. Table 5. Biopsy Diagnosis in relation to Indications and site of biopsy	26
6. Table 6. Biopsy diagnosis in relation to HIV status	32
7. Table 7. Statistical Agreement between lymph node FNA and lymph node biopsy	34