EARLY IMMUNE RESPONSES IN ACUTE PANCREATITIS AND THEIR ROLE IN PREDICTING DISEASE SEVERITY

ABSTRACT

The 2012 Atlanta classification of acute pancreatitis (AP), which stratifies the severity as one of three risk categories, namely mild (MAP), moderately severe (MSAP), and severe (SAP), does not predict severity. Identifying immune parameters for use as prognostic markers that may be more accurate in stratifying patients' risk profiles at the early phase of acute pancreatitis is likely to improve treatment strategies. This study aimed to identify and assess the potential of early immune markers that could be used to stratify the three patient groups of AP. Forty patients diagnosed with AP (21 MAP, 14 MSAP, and 5 SAP) were recruited from the Chris Hani Baragwanath and the Charlotte Maxeke Johannesburg Academic Hospitals in Johannesburg, South Africa. Twelve millilitres of blood was sampled from the patients at Day (D) 1, 3, 5, and 7 post-epigastric pain and assayed together with a once-off sample from six age and sex-matched healthy controls (HC). For cytokine analysis, multiplex assay kits were used. An RT2 profiler array and real-time polymerase chain reaction, as well as multiparametric flow cytometry assays, were used to profile innate and adaptive immune response-related genes and leucocytes, respectively. Of the 40 patients, biliary and alcohol-induced pancreatitis were equally common (n=18, 45% each) and were the most prevalent aetiologies. The IL-6 cytokine increased with AP severity and over time, peaking on Day 7 with significant differences between Day 3 and 7 in MAP ($p=0.001$) and MSAP group ($p=0.013$). Genes that were highly expressed included (C-C motif) receptor 8 (CCR8) and myeloperoxidase (MPO). These two genes were identified as potential severity markers with a fold change of 1172.45 and 91.77, respectively. While IL-6 increases with severity are not novel, the link to CCR8 and MPO gene expression was established. Further linkages were made with increasing frequency of classical monocytes (CD14+CD16-) and the depletion of CD14+HLADR- monocyte subset to severity. In conclusion, differences in CCR8 and MPO gene expression and elevation of IL-6 and their linkage to different innate and adaptive immune cell frequencies suggest that these markers have a role in disease severity and should be explored further.

Keywords: *acute pancreatitis, prognostic markers, chemokine (C-C motif) receptor 8, myeloperoxidase, adaptive immune response, innate immune response, classical monocytes.*