Role of the host response in Infective Endocarditis

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Infective endocarditis (IE) is a condition most often caused by bacterial infection of a native or prosthetic heart valve, but it can also involve infection of an implanted cardiac device or catheter. IE is more prevalent in lower socioeconomic groups and ethnic minorities, who also have higher rates of complication and lower overall survival. It is increasingly frequent and is associated with an extremely poor clinical outcome (with one-year mortality >30%) which exceeds that of than many common cancers. There are many risk factors described for the development of IE; nevertheless, up to 30–50% of patients with this diagnosis does not have any known risk factor. Therefore, it is likely that immunogenetic influences affect the risk of development and outcomes in IE. Our laboratory has discovered a subset of (cMet+) memory T-cells that are detectable in the peripheral blood of humans and mice and that specifically migrate to the heart during episodes of cardiac inflammation. Unexpectedly - we have detected very high levels of cMet+ memory T-cells in the peripheral blood of patients with IE (n=20), compared to healthy controls but also compared to inflammatory cardiomyopathies in which this subset is known to be significantly raised in the blood. Functionally, these T cells displayed a Th2-like phenotype. Crucially, cMet+ T cells were also found to infiltrate valves of IE patients undergoing surgery. We attempted to assess the specificity of these T cells, but found that, while all the patients examined responded to the recall antigen Tetanus Toxoid, only one patient responded to the cardiac autoantigens tested. The specificity of these T cells therefore remains to be established. In a novel model of periodontitis-induced IE, immunofluorescence microscopy and flow cytometric showed that cMet+ T cells infiltrate the valves of diseased animals, and they can be seen adhering to the endocardial endothelium and in the tissue. Echocardiography showed cardiac alteration consistent with valve damage and the cMet+ T cells produce Th2-type cytokines, like in human IE. Collectively, our data suggest that the host response plays an important role in the development of IE.