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Review

Post-infectious group A streptococcal autoimmune syndromes and the heart

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ABSTRACT

There is a pressing need to reduce the high global disease burden of rheumatic heart disease (RHD) and its harbinger, acute rheumatic fever (ARF). ARF is a classical example of an autoimmune syndrome and is of particular immunological interest because it follows a known antecedent infection with group A streptococcus (GAS). However, the poorly understood immunopathology of these post-infectious diseases means that, compared to much progress in other immune-mediated diseases, we still lack useful biomarkers, new therapies or an effective vaccine in ARF and RHD. Here, we summarise recent literature on the complex interaction between GAS and the human host that culminates in ARF and the subsequent development of RHD. We contrast ARF with other post-infectious streptococcal immune syndromes — post-streptococcal glomerulonephritis (PSGN) and the still controversial paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), in order to highlight the potential significance of variations in the host immune response to GAS. We discuss a model for the pathogenesis of ARF and RHD in terms of current immunological concepts and the potential for application of in depth "omics" technologies to these ancient scourges.

Contents

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1. Introduction

Human infections with *Streptococcus pyogenes* (group A streptococcus, GAS) constitute a major, worldwide health problem, with up to 700 million cases annually [1]. GAS is an anaerobic, Gram-positive coccus and its only known reservoir is in humans. The oropharynx and skin are the primary colonization sites for GAS and around 12% of apparently normal individuals harbour GAS as a commensal organism in these locations [2].

GAS has a long history with human disease. Intriguingly, it can cause both infectious and post-infectious, immune-mediated diseases. The former includes non-invasive infections, such as pharyngitis and impetigo; invasive infections, such as pneumonia, septic arthritis and necrotising fasciitis; and toxin-mediated syndromes, such as toxic shock syndrome and scarlet fever. Immune syndromes following GAS infection include acute rheumatic fever (ARF), rheumatic heart disease (RHD), post-streptococcal glomerulonephritis (PSGN) and possibly, paediatric autoimmune neuropsychiatric disorders associated with

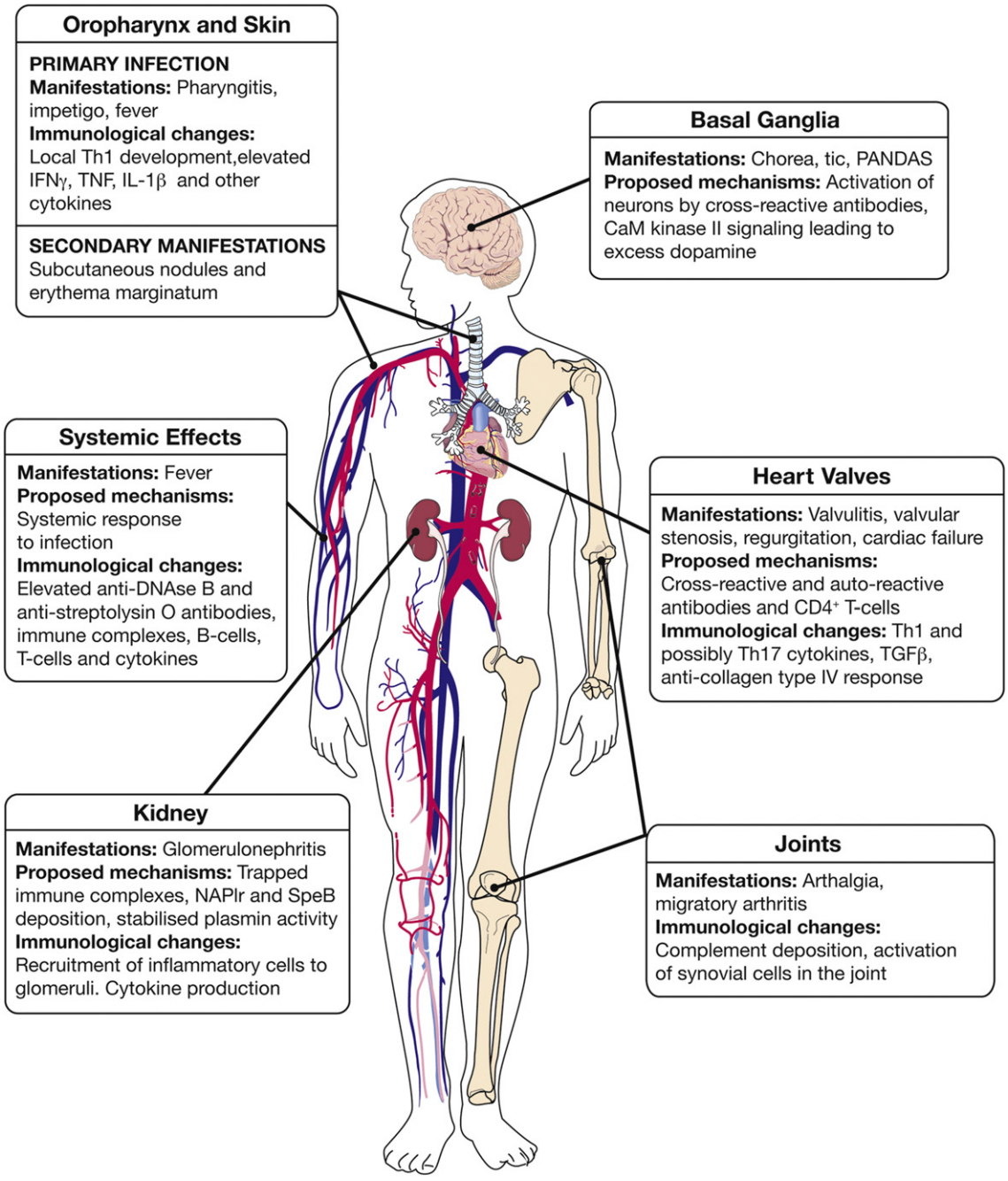

Fig. 1. Target organs of post-streptococcal immune syndromes.