MPGN secondary to Lyme disease: the role of cryoglobulins

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We have read the interesting case of Lyme disease-related cryoglobulinaemic membranoproliferative glomerulonephritis (MPGN) reported by Schneider et al. [1]. After several scarce cases of MPGN secondary to Lyme disease reported to date [2–5], this case report is intriguing due to the concurrence of type II cryoglobulinaemia (CG). The authors support the view that MPGN ‘is to be seen as indirectly Borrelia-related through CG-mediated complement activation’, based on the characteristic finding of subendothelial deposits of crystalloid material as well as the ‘full-house’ histological pattern. The presence of CG in Lyme disease-associated MPGN might indeed be revealing of potential pathogenetic mechanisms not evident in the cases reported earlier. Type I MPGN is an IC-mediated glomerulonephritis caused by the deposition of IgG and C3, involving activation of the classical complement pathway, triggered by an inciting event, such as an infection or a neoplastic or autoimmune disease. In addition, type II CG is caused by the development of IgM–IgG immune complexes (ICs) and is associated with acute or chronic infections and neoplastic and autoimmune diseases. Lyme disease, on the other hand, is a chronic infection inciting by itself IC formation, as evidenced by its concurrence with other IC-mediated manifestations, such as Guillain–Barré syndrome, acoustic mononeuritis and serumitis and with increased levels of rheumatoid factor (anti-IgG Igm), etc. [2]. The specific IgM response peak in Borrelia burgdorferi infection, which leads to polyclonal activation of B cells and the formation of ICs, as well as cryoglobulins/IgM rheumatoid factor, takes place several weeks after the initiation of the infection. Later, the specific IgG response develops against an increasing array of spirochetal polypeptides and non-protein antigens, eventually leading to spirochete lysis by the classical complement pathway. Therefore, our understanding is that all three of these conditions are manifestations of the infection-induced immunostimulation and the resulting formation of ICs, which is why the optimal treatment seems to be the combined use of antibiotics and immunosuppressive drugs, such as corticosteroids [1–4, 6]. The prominent common denominator involved in the pathogenesis of this pathology is the activation of the classical complement pathway. In this constellation of manifestations, we think that the infectious as well as the autoimmune parts are closely intercalated and, therefore, indistinguishable. Regarding the ‘full-house’ histological pattern, despite the fact that an MPGN pattern associated with autoimmune diseases is indeed often characterized by the deposition of multiple immunoglobulins and complement proteins (IgG, IgM, IgA, C1q, C3, kappa and lambda light chains), the exact pathophysiological role of C1q immune deposits in propagating glomerulonephritis is yet to be elucidated, and it is questionable whether it represents a pathognomonic finding or just a manifestation of the activated classical complement pathway. To this context, the presence of C1q deposits does not reveal a causative relation of MPGN with CG and, therefore, we believe that such an association is actually speculative, an opinion which is further supported by the fact that the same diagnosis and histological findings were documented in the cases reported earlier even in the absence of CG.

Conflict of interest statement. None declared.

References