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Letter to the Editor

LETTER TO THE EDITOR

The immunohistological profile of membranous nephropathy associated with syphilis infection

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Syphilis is a sexually transmitted infection caused by *Treponema pallidum*. Proteinuria in congenital and acquired latent (secondary or tertiary) syphilis has been mostly associated with membranous nephropathy (MN) [1]. The 10 MN patients in the present study had venereal disease research laboratory positivity confirmed with fluorescent treponemal antibody absorbed after the biopsy diagnosis. The clinical condition improved, proteinuria disappeared and serum albumin normalized within 1.9 ± 0.72 months of treatment with benzathine benzylpenicillin. Mean ± SD age was 31.2 ± 7.44 years, 60% were male, median proteinuria was 10.36 g/24 h (range 3.2–18.7 g/24 h) and mean serum creatinine 1.02 ± 0.23 mg/dL.

Immunopathologic data were gathered from Brazilian academic institutions (Universidade de São Paulo and Instituto de Nefropatologia). Four patients (40%) had positivity for phospholipase A2 receptor 1 (PLA2R1) antigen, eight (80%) for immunoglobulin G1 (IgG1) and two (20%) for IgG4. IgG2, IgG3, thrombospondin type 1 domain containing 7A (THSD7A) and C5b9 staining were negative in all cases. C4d stained in six (60%) cases. The immunofluorescence findings revealed classical aspects with staining with IgG, C3, Kappa and Lambda. Three (30%) patients showed a 'full house pattern', revealing positivity for all researched immunglobulins (IgG, IgA and IgM), fractions of complement (C3 and C1q) and light chains (Kappa and Lambda), within fine, uniform, granular deposits all along the glomerular basement membrane, and two (20%) positivity for C1q (Figure 1). Circulating anti-PLA2R antibody assays were not available.

The immunohistochemical PLA2R1 positivity was not expected. These histological findings support that PLA2R1 positivity alone is specific for primary MN, as it is also observed, besides syphilis, in chronic *Schistosoma mansoni* [2] infection, membranous lupus nephritis [3] and cancer [4]. In this regard, PLA2R1 expression can be increased in podocytes by non-specific inflammatory mediators such as tumour necrosis factor-like weak inducer of apoptosis (TWEAK) [5]. Also, PLA2R1 is found only in MN, with 100% specificity for this nephropathy. IgG1 is more associated with secondary forms of MN [6]. C4d positivity is associated with interstitial fibrosis, indicating complement activation of the classical and lectin pathway [7].

Knowledge of the morphological presentation of syphilis-associated MN may help in the diagnosis of this re-emerging disease.

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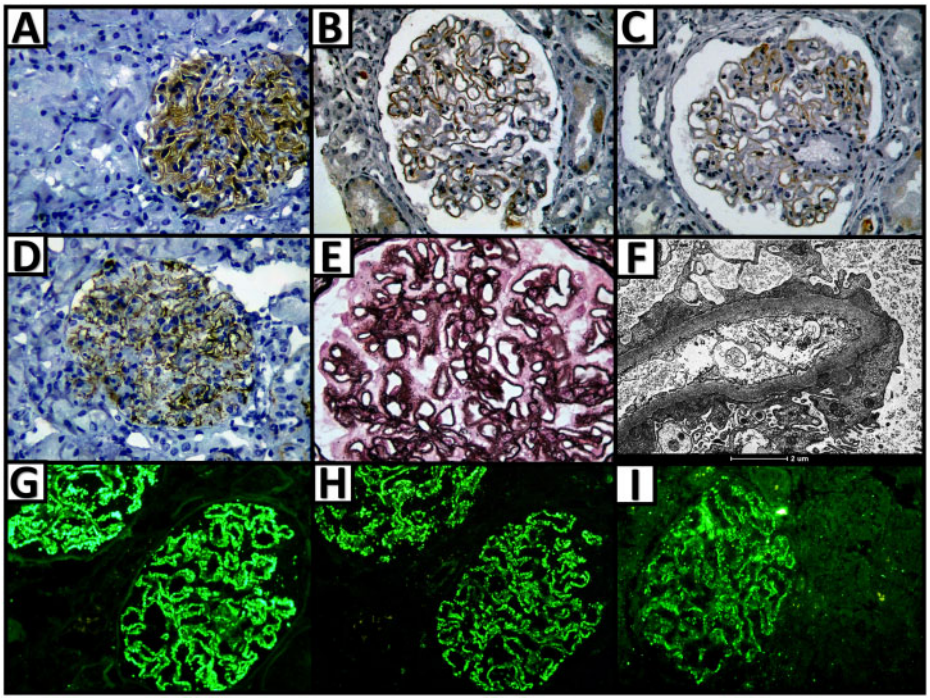

FIGURE 1: (A–D) Immunohistochemical staining—strong global granular staining of the GBM for PLA2R, IgG1, IgG4 and C4d, respectively. (E) Light microscopy with Jone's Methenamine Silver—diffuse thickening of GBM with subepithelial 'spikes'. (F) Electron microscopy—subepithelial deposits with basement membrane material ('spikes'). (G–I) IgG4 immunofluorescence staining—strong global granular staining of the GBM IgG, C3 and C1q, respectively. GBM, glomerular basement membrane.

CONFLICT OF INTEREST STATEMENT

None declared.

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