Necrotizing arteritis and crescentic glomerulonephritis in an ANCA-negative lupus nephritis patient

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INTRODUCTION

Small vessel vasculitis, inflammation which predominantly affects microvasculature such as capillaries, arterioles, and venules, is divided into two groups based on whether or not immune complex deposition is present. Small vessel vasculitis without immune complex deposition is generally accompanied by the presence of anti-neutrophil cytoplasmic antibody (ANCA) accumulation in the vessel wall. Small vessel vasculitis with immune complexes present more commonly occurs in diseases such as systemic lupus erythematous (SLE).[1]

Lupus vasculitis is a secondary vasculitis that can occur in over half of patients with SLE.[2] Lupus nephritis, a form of glomerulonephritis, is a common and severe example of renal disease in SLE, developing in as many as 50% of adult SLE patients.[3] Lupus nephritis is most often characterized by immune complex deposition in the microvasculature, causing a diffuse, proliferative glomerulonephritis; in this presentation, crescent formation is rare.[4] Lupus nephritis is further divided into six classes, based on the extent and pattern of inflammation and immune complex deposition.[2] Apart from immune complex deposition, lupus nephritis can be associated with anti-neutrophil cytoplasmic antibody (ANCA) positivity in about 15% of lupus patients.[2] When small vessel vasculitis in the kidneys is associated with anti-neutrophil cytoplasmic antibody (ANCA) positivity, it typically manifests as a rapidly progressive glomerulonephritis. Histologically, this presentation corresponds to necrotizing, crescentic glomerulonephritis.[4]

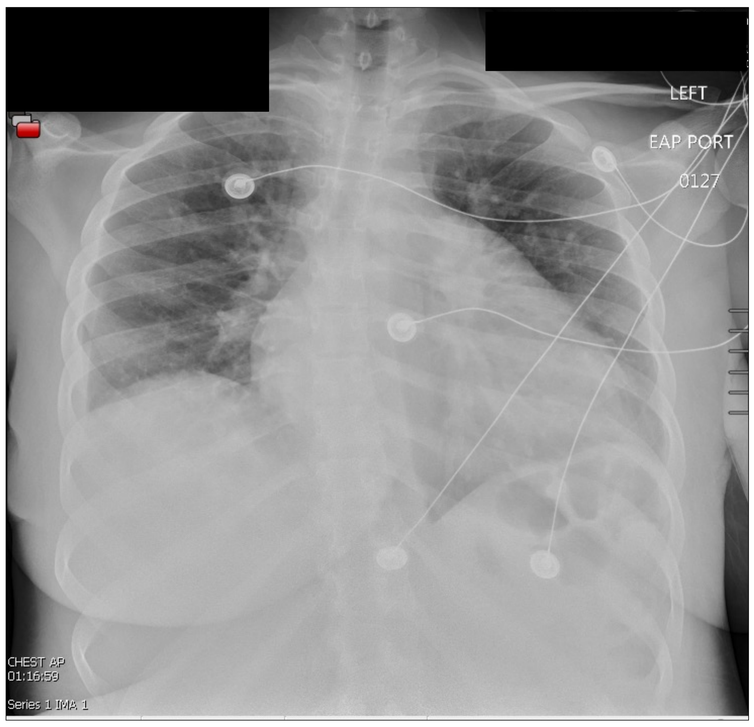

Figure 1. Chest x-ray on admission showing newly enlarged cardiac silhouette.

CASE PRESENTATION

A 24-year-old woman with a past medical history of SLE, hypertension, obesity, and medication non-adherence presented to the rheumatology clinic with complaints of fatigue and dyspnea for the past month. At the recommendation of rheumatology, the patient presented to the hospital for pulse-dose steroid administration in the setting of a suspected lupus flare. Chest x-rays obtained outpatient and upon admission showed evidence of newly enlarged cardiac silhouette. An echocardiogram obtained showed new-onset severe mitral and tricuspid regurgitation and right ventricular systolic pressure >90 mmHg consistent with pulmonary hypertension. There was no evidence of left ventricular systolic function or diminished ejection fraction.

Nephrology was consulted due to increasing sub-nephrotic range proteinuria. Kidney function continued to decline over the course of her hospital stay, progressing to a Stage III AKI. Urinalysis showed no active sediment.

Five days into hospitalization, the patient began experiencing severe LUQ abdominal and left lumbar pain accompanied by sudden-onset nausea and vomiting. Renal biopsy showed severe interstitial fibrosis and tubular atrophy, segmental sclerosis, crescent formation, and necrotizing arteritis, superimposed on lupus nephritis classes IV and V. Anti-MPO, Anti-PR3, P-ANCA, and C-ANCA were negative. Following biopsy results, the patient began a 3-month course of biweekly low-dose cyclophosphamide infusions per the Euro-Lupus protocol.[5]

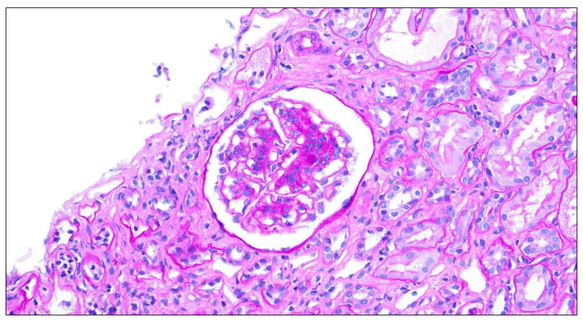

Figure 2. H&E stain: Mesangial hypercellularity and C1q deposition.

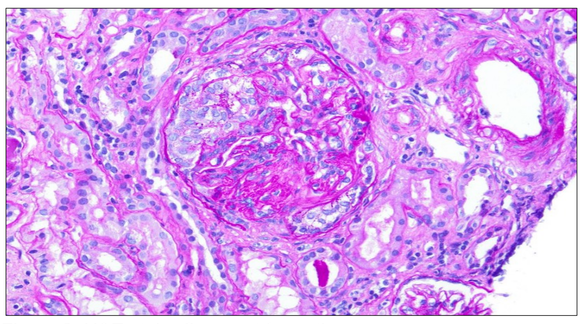

Figure 3. H&E stain: Crescent formation.

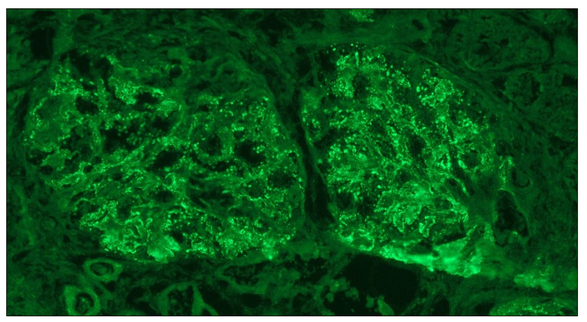

Figure 4. Immunofluorescence: C3 deposition.

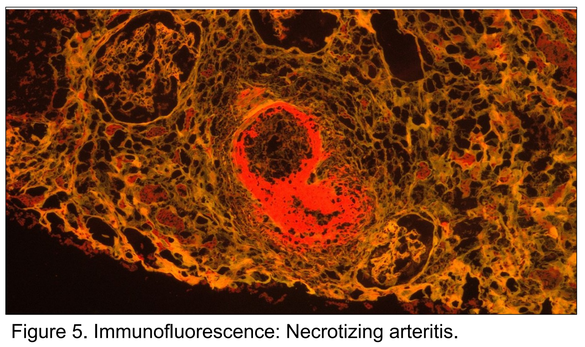

Figure 5. Immunofluorescence: Necrotizing arteritis.

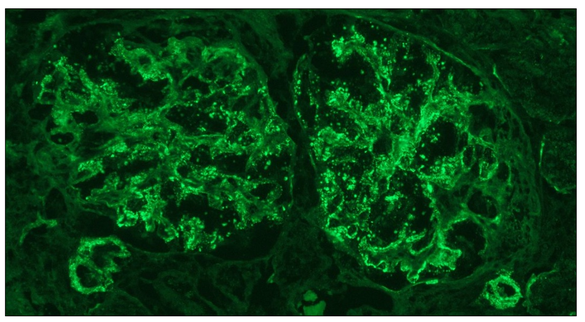

Figure 6. Immunofluorescence. C1q deposition.

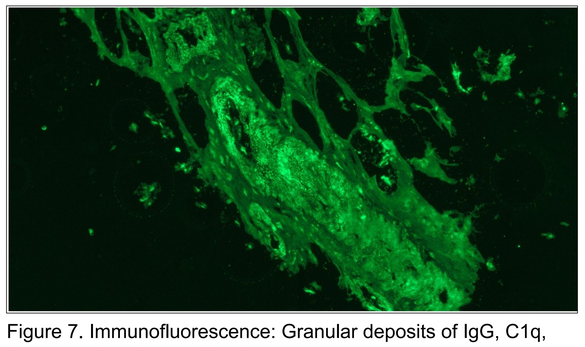

Figure 7. Immunofluorescence: Granular deposits of IgG, C1q, kappa, and lambda within the vasculature.

DISCUSSION

Studies have suggested that patients with lupus nephritis and positive ANCA serology are more likely to have necrotizing and segmental patterns of glomerulonephritis compared with those that are ANCA negative.[6] In addition, the patient's glomerular crescent formation and necrotizing arteritis consistent with rapidly progressive glomerulonephritis is more commonly seen in ANCA-positive small vessel vasculitis.[7] The patient's renal biopsy is more consistent with rapidly progressive glomerulonephritis, so we would expect an ANCA-positive serology. However, instead of a diffuse proliferative glomerulonephritis, there is a unique presentation of necrotizing, crescentic glomerulonephritis in addition to lupus nephritis in the absence of anti-neutrophil cytoplasmic antibodies.

References:

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