IgE and Immune Complex Glomerulonephritis

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ABSTRACT

A case is presented of immune complex proliferative glomerulonephritis associated with peripheral eosinophilia, renal deposits of IgE, and eosinophils in glomeruli and interstitial tissue. Two sequential renal specimens are described. This study also reviews prior reports of IgE in glomerulonephritis and discusses possible explanations for the presence of IgE.

Introduction

A case is presented of immune complex proliferative glomerulonephritis associated with peripheral eosinophilia, renal deposits of IgE, and eosinophils in glomeruli and interstitial tissue. The implications of these unusual findings are discussed.

Case Report

A 68-year-old male was admitted to the hospital because of a non-productive cough, muddy colored urine, and weakness of two weeks duration. The patient denied any history of atopy; he had not been on any medication other than tetracycline which was started several days prior to admission. Seven months prior to admission, he had undergone a left upper lobectomy for a poorly differentiated squamous cell carcinoma of the lung. At the time of discharge from the admission for the lobectomy, the blood urea nitrogen was 27 mg per dl; the urine had a specific gravity of 1.021 and was negative for both blood and protein. Liver, bone, and gallium scans were negative. Hemoglobin was 11.6 g per dl; hematocrit, 34 percent; PO₂, 92 mm Hg; PCO₂, 34 mm Hg, and pH 7.4.

Admission physical examination demonstrated blood pressure at 145/80 and temperature of 101°F. Rash and edema were absent. Urine output was 400 to 700 ml per 24 hours, and urinalysis revealed +3 protein, many red blood cells (RBC's) and white blood cells (WBC's), and four to six coarsely granular casts per high power field. Urine and throat cultures were negative. Blood urea nitrogen was 96 mg per dl; creatinine, 4.5 mg per dl; HB,Ag negative; antinuclear antibody negative; and antistreptolysin O titer 333. The sedimentation rate (Westergren) was 109 mm per hr. Differential white blood count revealed 0 percent eosinophils. A roentgenogram of the chest demonstrated pulmonary edema and a left lung infiltrate.

On the fifth hospital day, blood urea nitrogen was 107 mg per dl; creatinine, 4.5 mg per dl. An immunologic profile performed on the sixth hospital day...
showed an antiDNA titer of 17, negative cryoglobulin, C-3, 35 mg per dl (normal 123 to 167 mg per dl); and total complement 84 mg per dl (normal 30 to 100 mg per dl). On the tenth hospital day, a differential blood count disclosed 20 percent eosinophils. A 24 hour urine collection on the 21st hospital day showed a protein content of 2.3 g per 24 hours and a creatinine clearance of 28 ml per min.

An open renal biopsy, performed on the 23rd hospital day, was processed according to methods previously described. Three glomeruli were sclerosed. The 22 unhyalinized glomeruli showed hypercellularity and narrowing of urinary spaces (figure 1). Capillary lumens were compressed and contained eosinophils. Mesangial zones were wide, and there was a conspicuous infiltrate of mesangial eosinophils. The interstitium was diffusely edematous with patchy fibrosis and focal chronic inflammation. Immunofluorescent study (0 to 4+ scale) revealed 2+ (0 to 4+ scale) IgA staining in a focal, segmental, granular pattern; 2+ IgG in a diffuse granular pattern; 1+ IgM, sparsely; 4+ C-3 in a diffuse granular pattern; and 3+ IgE in granular segmental fashion (figure 2). Deposits of albumin (1+) and fibrinogen (2+) were seen within the tubules and interstitium. Deposits of IgE (3+) were detected in the interstitium. Electron microscopy confirmed the findings by light microscopy and also disclosed thickened glomerular basement membranes. Osmophilic deposits were present in the glomeruli, intramembranous, subendothelial and mesangial locations (figure 3). Greater than 90 percent of podocyte foot processes were effaced. Some tubular basement membranes contained osmophilic deposits. The final pathologic diagnosis was immune complex, proliferative glomerulonephritis.

On the 26th hospital day, the patient was placed on 80 mg per day prednisone. The serum creatinine stabilized at 2.5 to 3.5 mg per dl, and the sedimentation rate dropped to 50 mm per hr. Peripheral eosinophil count returned to 0. The patient also improved physically and by chest roentgenogram. He was discharged on the 31st hospital day on 60 mg per day prednisone.

The patient was readmitted with a diagnosis of congestive heart failure four days after discharge. Laboratory data showed erythrocyte sedimentation rate of 28 mm per hr; creatinine, 2.2 mg per dl; BUN, 60 mg per dl; and C-3 level 72 mg per dl. Urinalysis was normal. He responded well to diuretic therapy and was discharged seven days after admission on digoxin 0.125 mg per day, prednisone 40 mg per day, and Lasix 40 mg per day.

Five days after discharge and 17 days after the renal biopsy, the patient was brought to the emergency room after becoming increasingly short of breath. A chest roentgenogram showed increased congestive heart failure as compared to a study done six days earlier. During evaluation, the patient suddenly complained of severe chest pain, became diaphoretic, and suffered cardiopulmonary arrest. He died in the emergency room three hours after admission.

A restricted autopsy of chest and abdomen was performed 24 hours after death. The left lung weighed 575 gms and was dark red. The right lung weighed 1200 gms and was hemorrhagic, congested, and markedly edematous. The right kidney weighed 185 gms and the left kidney 150 gms. Examination of the epicardium revealed fibrinosis and adhesions to the lateral, inferior, and lower anterior walls of the left ventricle. The heart weighed 525 gms, and there was a ventricular aneurysm. Yellow discoloration was noted in the interventricular septum and posterior wall. The coronary arteries were calcified and markedly narrowed. Microscopical examination revealed acute and chronic congestion of the lungs. The liver was acutely congested, and the heart had large areas

Figure 1. Hematoxylin and eosin stain of renal biopsy shows glomerular hypercellularity, inflammatory cellular infiltration and mesangial widening (× 200).
FIGURE 2. Direct immunofluorescent stain for IgE shows granular deposits in glomerulus (×400).

FIGURE 3. Two mesangial eosinophils are seen in this electron micrograph. Also note subendothelial, intramembranous, epimembranous, and mesangial osmiophilic deposits (×6,500).
of acute necrosis. The kidneys displayed interstitial lymphocytes and plasma cells, but no eosinophils were seen. There was focal, mild glomerular mesangio­pathy (figure 4). Immunofluorescence on renal tissue was not performed. Electron microscopical examination showed renal autolysis, but glomeruli lacked osmiophilic deposits.

**Discussion**

The patient described herein suffered from immune complex glomerulonephritis, possibly poststreptococcal; however, a tumor antigen-antibody immune complex disease cannot be ruled out. In contrast to previous reports of IgE participation in immune-mediated glomerulonephritis, this patient had moderate peripheral eosinophilia, eosinophilic infiltration of glomeruli, and thick glomerular basement membranes. McPhaul et al,5 in examining 146 renal biopsy specimens for the presence of IgE, described only one case of prominent glomerular IgE staining accompanied by significant glomerular exudation and peripheral eosinophilia of 20 to 30 percent. This was a 13-year-old male with chronic glomerulonephritis with no history of streptococcal infection or significant antistreptolysin titer. None of the biopsies reviewed showed significant thickening of glomerular basement membranes. Robertson et al6 studied 373 renal biopsies, 17 of which were diagnosed as diffuse proliferative glomerulonephritis. Of these 17 samples, nine were streptococcal-associated lesions. Four of those nine poststreptococcal lesions exhibited glomerular deposits of IgE by immunofluorescent techniques. However, there was no mention of infiltration of eosinophils into the glomeruli.

The presence of both glomerular and interstitial eosinophils in this case is not readily explained. Neither tissue nor blood eosinophilia is considered characteristic of any type of glomerulonephritis.1 Immune complexes have been shown to be chemotactic for and phagocytosed by eosinophils;4,7 however, in most immune-complex diseases, eosinophils are not found in elevated levels in either tissue or blood.1 As mentioned previously, the presence of IgE in glomerulonephritis has been described. Camussi et al2 further implicated the IgE-basophil-mastocyte system in the pathogenesis of poststreptococcal glo-

![Figure 4. Hematoxylin and eosin stain of postmortem sections of kidney discloses mild glomerular mesangio­pathy (X 250).](image-url)
merulonephritis by demonstrating a transient reduction in circulating basophils in the acute phase of the disease. Moreover, it was shown that the number of mastocytes in poststreptococcal glomerulonephritis is decreased with evidence of mastocyte degranulation.

A possible explanation for the phenomena seen in this case is the appearance of a peculiar immune complex strongly chemotactic for eosinophils or the presence of an antigen from either tumor or a bacterium with an unusual affinity for IgE. The activation of the IgE-basophil-mastocyte system and production of eosinophilic chemotactic factor would then account for the presence of eosinophils in the renal tissue.

References