Glomerulonephritis Associated with
Staphylococcus aureus Infection

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Glomerular lesions associated with staphylococcal infections arise in many different clinical situations, but are most commonly encountered in patients with infective endocarditis and bacteremia with ventriculoatrial (V-A) or ventriculoperitoneal (V-P) shunts (1). Infective endocarditis has been divided into subacute bacterial endocarditis (SBE) and acute bacterial endocarditis (2).

Renal lesions commonly seen in SBE include localized infarcts, abscesses, therapy-related interstitial nephritis, and glomerulonephritis (1–2). The incidence of glomerulonephritis associated with SBE has not been determined. The most common organisms leading to SBE are the streptococcus viridans group and coagulase-negative staphylococci, including Staphylococcus (Staph.) epidermidis (1). The renal manifestations are microscopic hematuria, which is occasionally macroscopic. Proteinuria may be detected in urine, but nephrotic syndrome is unusual. The extent of renal failure is frequently mild, but uremia was reported to be present in 5 to 10% of patients with SBE (2). In addition, non-specific evidence of inflammation, rheumatoid factor, cryoglobulinemia, and circulating immune complexes are present. Depressions of complement levels is typical but not always present. On histopathological examination, focal and segmental (occasionally diffuse) glomerular changes with fibrinoid necrosis or intracapillary thrombosis are seen in the acute stages (2). In addition, polymorphonuclear neutrophils or nuclear debris are present. Adhesions to Bowman’s capsule or cellular crescents are often seen. In the late stages, segmentally sclerotic glomerulonephritis with or without fibrocellular crescents is present. It is usually situated at the periphery of one or several lobules. Adhesions between the sclerotic lesion and Bowman’s capsule or cellular crescents are also seen. This segmentally sclerotic region is thought to represent a later lesion resulting from healing of the necrotic lesion (2). IgG, IgM, and C3 deposits in the mesangial regions and the glomerular capillaries are demonstrated by immunofluorescence study, and dense mesangial and subendothelial deposits are revealed by electron microscopy.

The frequency of acute bacterial endocarditis is increasing, particularly in intravenous drug abusers (3). Many causal organisms have been implicated, but the most common is Staph. aureus (3). Symptoms of severe infection and signs of cardiac involvement always precede the renal symptoms. The renal manifestations are microscopic hematuria, which is occasionally macroscopic, and proteinuria. Oliguria is sometimes present at the onset of renal involvement. The extent of the renal failure is frequently mild, but occasionally acute renal failure with a rapid deterioration in renal function is seen. Hypertension is unusual. Serological examination demonstrates non-specific evidence of inflammation, rheumatoid factor, cryoglobulinemia, and circulating immune complexes are present. Complement levels are decreased during the acute phase of this disease. Histopathological examination commonly reveals diffuse exudative proliferation with or without crescents, an expression which is similar to poststreptococcal acute glomerulonephritis (2). Polymorphonuclear neutrophils or mononuclear cells are present. IgG and C3 deposits along the capillary walls or in the mesangial regions are demonstrated on immunofluorescence study. Electron-dense subepithelial and intramembranous deposits are most commonly seen on electron microscopy, and subendothelial and mesangial deposits also occur.

Although infection of V-A or V-P shunts seems to be relatively common, the subsequent development of glomerulonephritis may occur in less than 5% of infected patients (1). The causal organism is Staph. epidermidis in approximately 70% of shunt nephritis and Staph. aureus in 20% (1). The renal manifestations that appear following symptoms of infection and signs of increasing intracranial pressure are microscopic hematuria, and occasionally macroscopic hematuria. Proteinuria is variable, but is sufficient to result in a nephrotic syndrome. There is non-specific evidence of inflammation in most patients, and in some cases, rheumatoid factor and cryoglobulinemia are detected. Complement studies indicate reduced C3, C4 and C1q levels. The most common glomerular lesion is type I mesangiocapillary glomerulonephritis, in some cases with crescent formation (2). On immunofluorescence microscopy, depositions of IgM and C3 in capillary walls are usually revealed. Ultrastructural examination commonly shows subendothelial electron-dense deposits.

Recently, we reported glomerulonephritis in association with methicillin-resistant Staph. aureus (MRSA) infection as a new type of staphylococcal infection-associated glomerulonephritis (4–7). The renal manifestations appeared within 10 weeks after MRSA infection. The most common renal manifestation was rapidly progressive glomerulonephritis (RPGN) with nephrotic syndrome in about 60% of patients. Henoch-Schönlein
Clinically, one case showed acute glomerulonephritis (11), one had acute interstitial nephritis (12), and three of these cases had developed RPGN (9, 10, 13). On renal histopathological examination, one of these RPGN cases revealed mesangial proliferative glomerulonephritis with IgG, IgA, and complement depositions similar to our cases (10), but others showed pauci-immune crescentic glomerulonephritis (13). Toth reported eight patients with infective endocarditis and crescentic glomerulonephritis (14). There were reportedly some similar cases of postinfectious glomerulonephritis without deposition of immunoglobulins in glomeruli (15–18). In addition, Angangco et al described a case of pauci-immune glomerulonephritis associated with staphylococcal infection, that did not show the presence of anti-neutrophil cytoplasmic antibody (19). As seen in the above reports, there are some cases of pauci-immune crescentic glomerulonephritis associated with staphylococcal infection. On the other hand, cases of glomerulonephritis with IgA deposition similar to our cases have been reported. In cases of glomerulonephritis associated with bacterial endocarditis, 18% reportedly demonstrated IgA deposition in glomeruli (3). A few cases of shunt nephritis with IgA deposition in glomeruli were described (20), and about one-half of the cases with shunt nephritis reportedly demonstrated IgA deposition in glomeruli (21). As shown by the above-mentioned reports, glomerulonephritis associated with staphylococcal infection may present a variety of types of histological features.

Glomerulonephritis with infective endocarditis and shunt nephritis might be immune complex-mediated glomerulonephritis, as evidenced by not only the existence of circulating immune complexes and hypocomplementemia and of glomerular immunoglobulin depositions, but also due to the detection of staphylococcal antigens within the involved glomeruli. On the other hand, in our cases, based on our observation, SEs produced by MRSA as superantigens may activate T cells, and activated T cells may cause polyclonal activation of B cells via production of circulating immune complexes, resulting in RPGN. In those cases of pauci-immune crescentic glomerulonephritis associated with MRSA infection, it may be difficult to clarify a pathogenesis that is immune complex-mediated, superantigen-associated, or undetermined mechanisms. The variety of types of glomerulonephritis associated with staphylococcal infection may be the result of differences in their pathogenesis. Therefore, it seems important to accumulate a number of cases of glomerulonephritis following MRSA infection in order to investigate the specific pathogenesis.

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Reference


See also p 424.


