

Acute Kidney Injury and Massive Proteinuria Secondary to Epstein -Barr Virus -Associated Nephrotic Syndrome

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7 Abstract

8 The case is that of 69 year old female who went on vacation and fell on her knees. She noticed
9 progressive swelling of both legs over 2 weeks duration. During this period she gained 44
10 pounds in weight. She presented with sudden onset of edema of the lower extremity and weigh
11 gain. She had 16 g/day of proteinuria. Past medical history is significant of hypertension of
12 unknown duration. She had never seen a doctor in the last year. Her laboratory data showed
13 30 grams protein in 24 hrs urine, and her serum creatinine was 1.7 mg/dl. The baseline serum
14 creatinine was not known.

Index terms— epstein virus infection, interstitial nephritis, minimal change disease, nephrotic syndrome, proteinuria, acute renal failure.

I. The Case he case is that of 69 year old female who went on vacation and fell on her knees. She noticed progressive swelling of both legs over 2 weeks duration. During this period she gained 44 pounds in weight. She presented with sudden onset of edema of the lower extremity and weigh gain. She had 16 g/day of proteinuria. Past medical history is significant of hypertension of unknown duration. She had never seen a doctor in the last year. Her laboratory data showed 30 grams protein in 24 hrs urine, and her serum creatinine was 1.7 mg/dl. The baseline serum creatinine was not known.

24 Her laboratory showed negative ANA, ANCA, and normal complement levels. No monoclonal gammopathy
25 were detected on serum protein electrophoresis (SPEP) or urine protein electrophoresis (UPEP). EBV titers
26 came back IgM consistent with the high level of proteinuria possibly secondary to minimal change disease/tip
27 lesion FSGS.

28 1 II. Case Discussion

29 Infection with Epstein-Barr virus is ubiquitous in adults and it is estimated that over 95% of adults worldwide
30 is infected with the virus (1). It causes infectious mononucleosis (IM) in the acute phase. Most patients recover
31 without sequelae, however, acute complications are associated with EBV infection.

Sub-clinical renal involvement is not uncommon in EBV infection; 16% of patients with IM infection have abnormalities in urinary sediment (2). Immune complex glomerulonephritis in the form of minimal change disease or membranous glomerulopathies are the most common renal presentation of EBV infection. Acute renal failure and cholemic nephrosis are rare but can also occur (2,3).

Acute kidney injury in adults with minimal change disease has been reported in approximately 25-35% of adults. It is mainly presented at the time of nephrotic syndrome (4-9). However, Patients who develop AKI are more likely to be older, male, hypertensive, and have severe proteinuria. These features are present in our patient except for the gender. AKI occurred in 25% (24/95) patients with MCD in the United States (6). In 7 patients, it occurred in a relapse of MCD. However, in 17/95 the AKI occurred concurrently with the onset of MCD. Patients with AKI are older with hypertension. In these patients proteinuria was higher, and hypoalbuminemia and edema were severe (4). AKI was relentless in these patients; and most patients were oliguric at the time of presentation. It is noteworthy, that 20% of these patients required renal replacement therapy. Acute tubular necrosis was the underlying cause of AKI in these patients ??4-6, 7,9).

45 Meyer et al and others (10) reported that 18% of patients with AKI associated with MCD are due to
46 rhabdomyolysis and myoglobinuria. Two of his patients had MCD and 10/27 patients had acute interstitial
47 nephritis. However, Mayer et al failed to identify EBV RNA in the renal biopsy tissue and instead suggested
48 that the EBV antigens in infiltrating lymphocytes activated a massive T-cell mediated immune response. In
49 contrast, Bao (11) reported detection of the EBV genome using polymerase chain reaction (PCR) technique in
50 renal samples. EBV DNA has since been found in biopsies of patients with IgA nephropathy and membranous
51 nephropathy as well.

52 The pathogenesis of AKI in EBV infection remains unclear but activation of the T-lymphocytes may be
53 directly involved in EBV renal injury (2). Bao et al (11) demonstrated a predominance of cytotoxic T-cells in the
54 interstitium with evidence of EBV DNA detected with PCR in renal tissue in patients with interstitial nephritis.
55 EBV receptors (CD21) were detected in the proximal tubular cells and were up-regulated in the EBV infected
56 tissues (12).

57 Okada et al, in 2002 (??3) reported a case of chronic active EBV infection who developed both acute
58 interstitial nephritis and MCD. Renal biopsy of this case showed tubular epithelial atypia and lymphocytic
59 interstitial infiltrates. EBV DNA was also detected with PCR in some infiltrating lymphocytes.

60 There is no strong current literature on the use of steroids in IM. However, Mikhalkova et al treated a case of
61 MCD associated with EBV infection with steroids with rapid and complete response of the MCD (??4), however,
62 anecdotal reports claim its effectiveness in MCD.

63 In conclusion, MCD is rarely reported renal complication of EBV infection with few cases reported in the
64 literature. It is exquisitely response to steroids. EBV infection should be considered in all cases of heavy
65 proteinuria with LM, IF, EM features of MCD especially if the onset of MCD is preceded by viral prodromal
66 illness.

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