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DENGUE FEVER WITH NEPHROTIC RANGE PROTEINURIA- AN UNSUAL PRESENTATION—A CASE REPORT

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ABSTRACT

A 35 years male patient presented with fever and diagnosed as a case of dengue haemorrhagic fever (DHF). He subsequently developed nephrotic range of proteinuria. The patient did not have classical nephrotic syndrome. The proteinuria improved without specific treatment. A renal biopsy was not performed due to self-resolution of the proteinuria and as azotemia was absent. Heavy proteinuria is not a typical characteristic of dengue virus infection. Dengue fever with nephrotic range proteinuria is a rare presentation reported so far.

INTRODUCTION

Dengue virus infection is one of the most prevalent viral induced hemorrhagic disorders of public health significance, with millions of infections each year. The main dengue vector is the female of the *Aedes aegypti* mosquito. There are four serotypes of the dengue virus (DEN-1-DEN-4), a RNA flavivirus. Various clinical manifestations have been described during the viremic stage. Bleeding diathesis and vascular leakage are major complications. Renal problems may develop, including acute kidney injury (AKI) from dengue, shock syndrome (DSS) and IgA nephropathy, which are transient. Massive proteinuria is not a common finding in patients with dengue hemorrhagic fever (DHF). We report a case of DHF with nephrotic range proteinuria.

CASE REPORT

A 35-year-old male with no past medical illness, presented with fever, chills, myalgia. He was admitted to the hospital on the fourth day of illness. On admission temperature recorded 102...F. There were purpuric spots over extremities (Figure 1 & 2) and back. On second day of admission he developed gum bleeding. Although on third day he became afebrile but developed signs of right sided pleural effusion and ascites. His platelet counts on admission was 25,000 /uL, haematocrit 35%. Platelet count dropped to 22,000/uL the next day. He also had chest radiographic evidence of pleural effusion, suggesting plasma leakage. Ultrasonogram showed normal kidneys but moderate ascitis. The dengue virus IgM was positive on admission. A diagnosis of DHF was made. His liver function test showed raised ALT 100 U/l. Serum albumin 4.9 gm / dl (normal range 3.8 - 5.5 gm/ dl).

The patient did not have any haematuria, casts in his urine but have 3+ proteinuria and 24 hour urinary total protein was 0.68 gm. His serum creatinine level was normal throughout the admission. As nephrotic-level proteinuria is not usually associated with DHF, screening for other causes of proteinuria were done. Complement levels (C3, C4) was within normal limit. Post-infectious causes such as hepatitis B, hepatitis C and streptococcus-antistreptolysin O titre (ASOT) were negative. A repeat 24-hour urine total protein normalised to 0.06 g/day. We concluded this self-limiting nephrotic-range proteinuria is most likely due to the dengue viral infection.



Fig. shows purpuric spots over extremities

Key Words : Dengue haemorrhagic fever nephrotic-range proteinuria, plasma leakage.

DISCUSSION

DHF is a severe form of the disease characterized by fever, haemorrhagic phenomena, thrombocytopenia and evidence of plasma leakage (increased haematocrit, pleural effusion, ascites and hypoalbuminaemia)^{1,2}. All of these features were present in the described patient. Renal complications in dengue virus infection are mainly associated with severity of disease. Acute renal failure and hemolytic uremic syndrome have been reported in cases of DSS. Apart from acute kidney injury as a result of shock and renal hypoperfusion, different manifestations of dengue-virus-induced nephropathy have been reported including microscopic hematuria and albuminuria³. Heavy proteinuria in the nephrotic range is not common in dengue virus infection. In Southeast Asia, two patients from Singapore were reported as having self-limited heavy proteinuria secondary to DHF³.

To clarify the main pathophysiology of kidney involvement in DHF, Boonpucknavig et al performed a kidney biopsy in 20 patients with DHF and renal impairment using fluorescent antibody technique to localize IgG, IgM, and C3 in glomeruli⁵. Electron microscopy revealed focal thickening of the glomerular basement membrane and mesangial cell hypertrophy at immune complex lodging sites⁵. In vivo studies using preformed soluble dengue antigen-antibody complexes injection directed to glomerulonephritis and proteinuria with deposition of immune complexes in the glomeruli of mice. The differential diagnosis for DHF includes malaria, leptospirosis, hantavirus infection, typhoid fever, HIV, enteroviral infection, influenza and sepsis, as well as autoimmune disorders^{4,5}. Leptospirosis and hantavirus infection may mimic DHF in almost all aspects, including renal injury and renal histology. A correlation between dengue virus infection and nephrotic syndrome has not been well established due to insufficient numbers of patients diagnosed with these two co-morbidities^{3,4}. Pre-existing nephrotic syndrome or glomerulonephritis need to be excluded when systemic autoimmune disease or persistent proteinuria are seen. In our patient with self-limited nephrotic range proteinuria was not associated with hypoalbuminemia and hypercholesterolemia. The presence of proteinuria, haematuria, generalized oedema and hypertension associated with low C3 and C4 suggests an immune-mediated acute glomerular injury, which was

absent in reported case. Pleural effusions and ascites occur in DHF as a result of increased vascular permeability³. With excessive intravenous fluid infusion and plasma leakage, large pleural effusions may form causing respiratory distress. However, thoracentesis is rarely indicated due to spontaneous resolution of pleural fluid by reabsorption during the convalescent stage^{1,2,3}. A right pleural effusion was present in our patient and it did not resolved even after one week after the patient had recovered from DHF. Pleuracentesis was performed to relieve the effusion. Judicious fluid therapy and nutritional support are helpful in patients with multiple organ involvement. More evidence that the dengue virus can induce glomerulopathy comes from two studies where dengue virus type 2 was inoculated in mice^{4,5}. Finally, the autoimmune-mediated mechanisms possibly involved in the pathogenesis of DHF might also be related to the renal injury observed⁴.

Awareness of the possibility of proteinuria with DHF is needed for the optimal care for patients with DHF. Albumin replacement may be started early to minimize the sequelae of dengue-virus-associated nephropathy and hasten effusion fluid resorption. Further studies of proteinuria in DHF patients are needed for better understanding of the pathophysiology of proteinuria, nephrotic syndrome, and glomerulonephritis in DHF.

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