International Journal of Research in Medical Sciences
Thomas J et al. Int J Res Med Sci. 2023 Dec;11(12):4580-4582
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20233739

Case Report

When you least expect it: nephrotic syndrome following dengue fever

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Received: 18 October 2023
Revised: 14 November 2023
Accepted: 16 November 2023

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ABSTRACT

This case report highlights a rare occurrence of nephrotic syndrome in a previously healthy 20-year-old gentleman. The patient exhibited bilateral lower limb swelling, facial puffiness, and abdominal distension. Notably, he had been hospitalized two weeks prior with dengue fever, characterized by a transient reduction in platelet counts. Routine examinations revealed proteinuria, with creatinine at 0.97 and albumin at 2.2. A renal biopsy confirmed focal segmental glomerulosclerosis (FSGS)- NOS type. This case underscores the significance of considering renal complications in individuals with recent dengue fever, especially when presented with atypical symptoms. The scarcity of reported cases depicting nephrotic syndrome as a sequelae to dengue fever further emphasizes the uniqueness of this scenario.

Keywords: Dengue, Nephrotic, FSGS

INTRODUCTION

Nephrotic syndrome as an aftermath of dengue fever.[1] Dengue fever is commonly associated with thrombocytopenia and other hematological abnormalities, but its link to nephrotic syndrome is infrequently reported.[1] This case report delves into the clinical presentation, diagnostic journey, and subsequent management of a 20-year-old gentleman who developed nephrotic syndrome following an episode of dengue fever.

CASE REPORT

A 20-year-old gentleman, with no significant past medical history, presented to the nephrology OPD with complaints of swelling in both lower limbs, abdominal distension and facial puffiness persisting for one week. There was no reported frothing of urine or hematuria prior to this episode. The patient denied any history of similar illnesses during childhood, and there was no record of alternate medicine intake, NSAID use, urinary tract infections, allergies or recent vaccinations. Approximately two weeks prior to the onset of current symptoms, the patient was admitted to the hospital due to high-grade fever and generalized body pain. The diagnosis at that time was confirmed as dengue fever based on a positive dengue IgM and NS1 antigen report, with a platelet count dropping to around 92,000. However, he did not require platelet transfusions and was discharged on the fifth day after being managed conservatively. No complications of dengue were reported, and his platelet count on discharge was 1.3 lakhs. There is no family history of nephrotic syndrome.

During examination, bilateral pitting pedal edema was observed, along with ascites. In response to the reported complaints, routine tests were conducted, revealing 2+ proteinuria in urine with no active sediments. A 24-hour urine protein analysis revealed 4500 mg/day. His creatinine measured at 0.97 mg/dl, and albumin at 2.2 g/dl. A provisional diagnosis of nephrotic syndrome was established, leading to the decision for a renal biopsy to further evaluate the condition.

The biopsy results indicated FSGS- NOS (Figure 1). The patient was initiated on steroid therapy at a dose of 1 mg/kg/day which was gradually tapered over 6 months and is currently under regular follow-up, showing resolution of nephrotic state, improvement in his albumin to 4 g/dl and resolution of proteinuria.

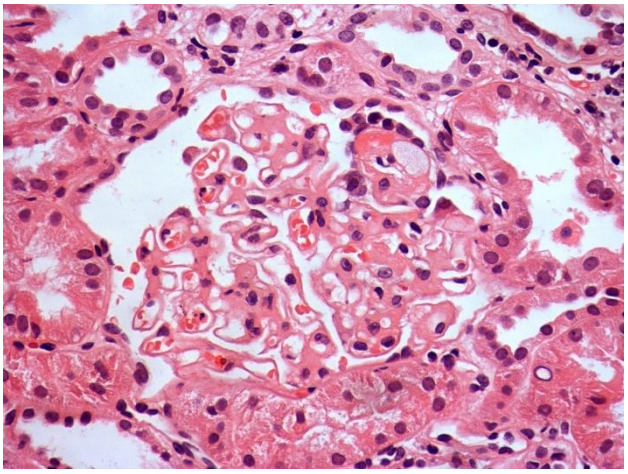

Figure 1: Light microscopy (at 200X) reveals glomerulus with focal and segmental sclerosis.

DISCUSSION

Dengue virus serotypes 1 to 4 (DENV-1-4) are arboviruses belonging to the genus Flavivirus of the family Flaviviridae.[1] Dengue symptoms range from a mild flu-like syndrome to severe, and sometimes fatal, disease, classified by the WHO as severe dengue (SD), which may affect multiple organ systems.[2] Although the liver is the most commonly affected organ, gastrointestinal, hepatic, respiratory, cardiac, neurological, and renal manifestations during DENV infection have already been reported.[3]

The presence of DENV in the kidney has been demonstrated through the detection of viral antigens in tissue cells and in macrophages and monocytes circulating in kidney blood vessels.[4] Furthermore, the observation of microtubule reticular structures and dilation of the endoplasmic reticulum in necrotic cells, along with dense virus-like particles in glomeruli in a transmission electron microscope (TEM), suggests viral infection.[5]

Analysis of kidney samples from DENV-infected human cases revealed parenchymal and circulatory damage.[6] Tubular necrosis, evidenced by the presence of pyknotic nuclei of epithelial cells, thickening of the glomerular basement membrane, mesangial proliferation, glomerular congestion and hyalinosis, interstitial areas with focal fibrosis, diffuse mononuclear infiltrate, and hemorrhage foci in the cortical and medullary regions, and the increase in populations of CD68+ and CD4+ cells have been reported.[6]

Recent studies have illuminated the multifaceted mechanisms through which dengue can impact renal function. Direct invasion of renal cells by the dengue virus, coupled with the dysregulation of the immune response, may contribute to the development of glomerular diseases.[7] While the exact pathway remains a subject of ongoing research, several potential mechanisms have been proposed.

Firstly, the immune response triggered by dengue infection is a key player in the development of FSGS especially collapsing variety of FSGS. Dengue virus, known for its ability to evade the immune system, can lead to the formation of immune complexes. These complexes may deposit in the glomeruli, initiating an inflammatory response. The subsequent release of pro-inflammatory cytokines and chemokines can contribute to glomerular damage, potentially progressing to FSGS.[7] Secondly, studies suggest that the Dengue virus can directly invade renal cells. The viral particles may gain access to the renal tissue, leading to direct injury to glomerular cells. This invasion can disrupt the delicate balance of glomerular function, contributing to the development of FSGS lesions in specific segments of the glomeruli.[7]

In addition, dengue infection is known to cause endothelial dysfunction, affecting the lining of blood vessels. This dysfunction extends to the renal vasculature, potentially disrupting the normal filtration function of the glomeruli. The compromised endothelial integrity may lead to increased permeability, proteinuria, and, over time, scarring characteristic of FSGS.[8]

Another mechanism suggested is damage to podocytes, specialized cells crucial for maintaining the filtration barrier in the glomeruli, which may be directly targeted by dengue infection. Podocyte injury, whether through viral invasion or immune-mediated mechanisms, can compromise the structural integrity of the glomeruli, contributing to the development of FSGS lesions.[9] In 2018, Araújo et al described 13 patients with a diagnosis of arboviruses (dengue or Zika) and FSGS on kidney biopsy. The collapsing variant was identified in 11 patients, and DENV was identified by PCR technique in seven of them.[10]

Lastly, the release of inflammatory mediators in response to dengue infection can contribute to a pro-inflammatory microenvironment in the kidneys. This sustained inflammatory state may promote the development and progression of FSGS lesions.[9]

CONCLUSION

Dengue-induced FSGS is likely a result of the complex interplay between direct viral effects, immune responses, and the susceptibility of renal cells. This multifaceted mechanism underscores the need for a comprehensive understanding of the pathophysiology to develop targeted therapeutic interventions for individuals at risk of Dengue-induced FSGS. Further research in this area will undoubtedly unveil additional layers of complexity and

provide novel insights into the prevention and treatment of this intricate renal complication.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Thomas J, Khan MF, Siddini V, Vankalakunti M, Ballal HS. When you least expect it: nephrotic syndrome following dengue fever. Int J Res Med Sci 2023;11:4580-2.