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CASE REPORT

Collapsing Focal Segmental Glomerulosclerosis in a Kidney Transplant Patient due to Dengue Infection - Case Report

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ABSTRACT

This study reports a case of collapsing focal segmental glomerulosclerosis (FSGS) associated with dengue virus infection in a 20-year-old Afro-descendant patient with a history of kidney transplant due to Alport syndrome. The patient, who had experienced typical dengue symptoms for 3 weeks, developed nephrotic syndrome, worsening renal function, and required renal replacement therapy. Despite treatment with intravenous methylprednisolone, renal function did not improve. A renal biopsy confirmed collapsing FSGS. This case suggests a potential link between dengue and collapsing FSGS in kidney transplant patients, emphasizing the need for vigilance and prompt management in endemic areas.

Descriptors: Nephrotic Syndrome; Arbovirus; Dengue; Collapsing Focal Segmental Glomerulosclerosis; Kidney Transplant.

Glomerulosclerose Segmentar e Focal Colapsante em Paciente Transplantado Renal devido à Infecção por Dengue - Relato de Caso

RESUMO

Este estudo relata um caso de glomeruloesclerose segmentar e focal (GESF) colapsante associada à infecção pelo vírus da dengue em um paciente afrodescendente de 20 anos com histórico de transplante renal devido à síndrome de Alport. O paciente, que apresentou sintomas típicos de dengue por 3 semanas, desenvolveu síndrome nefrótica, piora da função renal e necessitou de terapia de substituição renal. Apesar do tratamento com metilprednisolona intravenosa, a função renal não melhorou. A biópsia renal confirmou GESF colapsante. Este caso sugere uma possível associação entre dengue e GESF colapsante em pacientes transplantados renais, destacando a necessidade de vigilância e manejo precoce em áreas endêmicas.

Descritores: Síndrome Nefrótica; Arbovírus; Dengue; Glomeruloesclerose Segmentar e Focal Colapsante; Transplante Renal.

INTRODUCTION

Dengue is an arboviral infection spread by *Aedes aegypti* mosquitoes, carrying four serotypes (DENV-1 to DENV-4).[1] It significantly impacts health in developing countries, with lifelong immunity to one serotype but only temporary immunity to others. The incubation period ranges from 3 to 14 days, during which the virus replicates in dendritic and endothelial cells, causing viremia and immune response activation.[2] Symptoms vary from mild fever and joint pain to severe forms like hemorrhagic fever.[3-5]

Dengue outbreaks are worsened by tropical climates, rapid urbanization, and poor waste management, leading to high medical costs and productivity losses. Brazil experienced major outbreaks in 2019 and 2022[6] and reports increased cases in 2023 and 2024.[7] Rapid urbanization and demographic changes, including rising diabetes and hypertension rates, complicate chronic kidney disease (CKD) and affect kidney transplant patients,[5] who are highly vulnerable to severe dengue.[2]

Dengue has been linked to various kidney disorders, including acute kidney injury (AKI), proteinuria, hematuria, and glomerulonephritis. AKI occurs in 3% of dengue cases and may result from shock, rhabdomyolysis, acute tubular necrosis,[8,9] or glomerulonephritis, notably collapsing focal segmental glomerulosclerosis (FSGS).[10] FSGS involves glomerular sclerosis and podocyte damage and can be primary or secondary to medications, genetics, or viruses.[10-16] The collapsing variant of FSGS is characterized by sclerotic, collapsed glomerular capillaries, and hyperplasia of glomerular epithelial cells.[17,18] In kidney transplant patients, dengue may impair renal function, which usually recovers after the infection resolves, though long-term outcomes remain uncertain.[5] This case is the first to report severe renal complications, including nephrotic syndrome and acute renal failure, in a transplant patient.

Ethics statement

The Research Ethics Committee of the Hospital Ana Nery, Universidade Federal da Bahia, approved the study protocol, with Certificate of Presentation of Ethical Appreciation (CAAE): 81097024.7.0000.0045 and case number 7.165.689. The patient has provided written informed consent for the publication of this case report, including any associated data and images. This research was conducted in accordance with the Declaration of Helsinki of the World Medical Association.

Case presentation

A 20-years-old Afro-descendant male patient with CKD secondary to Alport syndrome, started renal replacement therapy with peritoneal dialysis at age 12 and subsequently underwent kidney transplant in June 2016 from deceased donor, standard, immunological risk, with immunological induction using basiliximabe and methylprednisolone. Under regular follow-up with tacrolimus, azathioprine, prednisone and amlodipine, the patient maintained stable serum tacrolimus levels and post-transplant renal function.

In January 2024, tests showed creatinine at 0.9 mg/dL, without proteinuria. In April 2024, he presented with progressive edema of the lower extremities, abdominal distension, weight gain (9 kg) over the last week, and foamy urine. He denied decreased urine output and hematuria. Addittionally, he reported fever, general malaise and joint and muscle pain 7 days prior, which resolved spontaneously without medication.

On objective physical examination, the patient presented pallor of 1+/4+. Lung auscultation revealed the absence of vesicular sounds in the lower third of the left lung and crackles at the bases. The abdomen was distended with a positive piparote sign. The lower extremities showed poor perfusion with bilateral edema of 3+/4+.

On admission, the patient's blood tests revealed microcytic anemia. Biochemical analysis showed renal function abnormalities and metabolic acidosis. These findings, combined with a urinalysis that showed proteinuria, hemoglobinuria, and numerous granular casts, suggested nephrotic syndrome, which was corroborated by 24-hour proteinuria of 12.3 g, hypoalbuminemia, and hypercholesterolemia (Table 1).

Atelectasis was noted in the right lower lobe and left lung, along with scattered small opacities, possibly due to inflammatory bronchopathy. The renal graft was of normal size, and a moderate amount of intraperitoneal free fluid was noted, without lymphadenopathy. Diagnostic thoracentesis of the pleural fluid was performed, which was characterized as a transudate according to biochemical studies. Polymerase chain reaction (PCR) for polyomavirus and cytomegalovirus was negative, as were viral serologies for HIV 1-2, hepatitis B, hepatitis C, HTLV I and II, *chikungunya*, and *zika*.

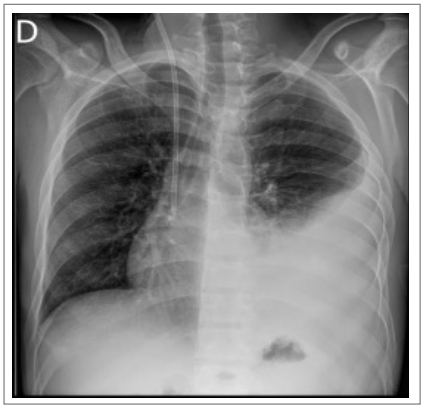
Due to the sudden deterioration of renal function, renal biopsy was performed. The patient received pulse therapy with methylprednisolone 1 g/day for 3 days, along with a single dose of ivermectin. The third immunosuppressive drug was replaced with mycophenolate mofetil and oral prednisone was continued after pulse therapy. However, IgM serology for DENV-2 was detected and confirmed by PCR, leading to the discontinuation of mycophenolate mofetil.

Table 1. Laboratory results.

Variables	Reference values	Before internment	Internally	1 month later
Complete blood count				
Red blood cells	4.0-5.5 million	4.4	3.7	2.91
Hemoglobin	12.5-17.5 g/dL	12.9	10.5	8.4
Hematocrit	40.0-50.0%	38.1	30.4	24.6
Red cell distribution width	11.5-15.9%	12.6	13.2	14.6
White blood cells	4,500-1,000 mm^3	8,570	4,810	5,030
Platelets	150,000-450,000/mm^3	430,000	241,000	170,000
Electrolytes				
Potassium	3.5-5.5 mEq/L	4.1	3.7	4.0
Calcium	8.8-11.0 mg/dL	10.8	-	9.4
Sodium	135-145 mmol/L	144	134	135
Renal function				
Creatinine	0.6-1.2 mg/dL	0.9	7.1	4.7
Urea	16.0-110.0 mg/dL	24.0	156.0	19.0
eGFR (CKD-EPI)	≥ 90 mL/min/1.73m^2	125	10.0	170
Total proteins	6.4-8.3 g/dL	7.9	3.5	4.1
Albumin	3.5-5.0 g/dL	4.9	1.6	1.9
Globulin	2.0-4.0 g/dL	3.0	1.9	2.2
Urinalysis				
pH	5.0-7.0	6.0	6.0	6.0
Density	1,015-1,025	1,015	1,010	1,010
Proteinuria	Absent	Absent	500.0 mg/dL	Present 2+
Glucose	Absent	Absent	50.0 mg/dL	Absent
Hemoglobin	Absent	Absent	Present 50/µl (+)	Absent
Nitrite	Absent	Absent	Negative	Absent
Cylinders	Absent	Absent	Granular	Absent
Red blood cells	Absent	Absent	12 per field	13 per field
24-h UP	< 150 mg/24h	-	12,264	20,800

Source: Elaborated by the authors. 24-h UP = 24-h urine proteinuria; CKD/EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR= estimate of glomerular renal function.

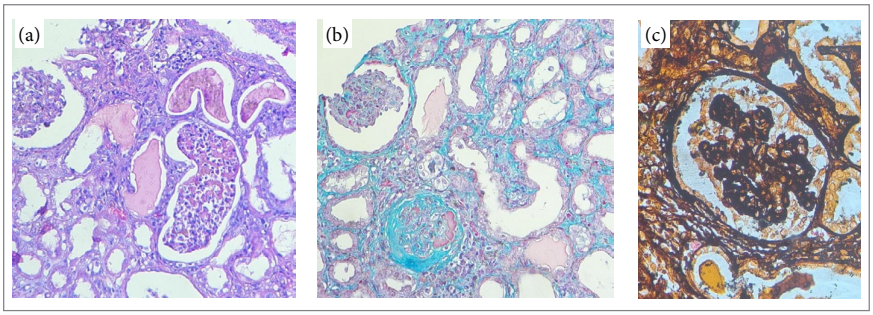
Imaging studies revealed a left pleural effusion and a moderate to large left pleural effusion without loculation (Fig. 1).



Source: Elaborated by the authors.

Figure 1. Chest x-ray view shows pleural effusion in the left hemithorax.

Renal biopsy revealed collapsing glomerulopathy, an acute diffuse tubular lesion with neutrophils in the lumen of rare tubules, interstitial fibrosis and tubular atrophy (grade I), and CD4 staining negative (Fig. 2).



Source: Elaborated by the authors.

Figure 2. a) Stain: periodic acid-Schiff (PAS), 40x. b) Stain: Masson's trichrome, 40x. c) Stain: Jones' methenamine silver, 100x. Renal parenchyma showing glomeruli, two of them globally sclerotic. Renal parenchyma represented by cortical and medullary regions, two of them globally sclerotic, with areas of hyalinosis. Hypertrophic and hyperplastic podocytes around collapsed capillary loops. The basement membrane is diffusely wrinkled, and Bowman's capsules are slightly thickened. The interstitium is dissociated by fibrotic cords (~ 20%) and contains a slight lymphocytic inflammatory infiltrate. The tubules are diffusely dilated, with partial desquamation, vacuolization, and attenuation of the epithelium. The basement membrane tends to remain intact. Interlobular arteries and arterioles are preserved. Peritubular capillaries are barely visible. Images courtesy of Dra. Denise Maria Avancini C. Malheiros and Dr. Felipe Lourenço Ledesma.

The patient did not respond to the established therapy and progressed with worsening renal function, requiring hemodialysis, which was initiated in May 2024. There have been no signs of renal function recovery, and the patient has remained on hemodialysis since then.

DISCUSSION

The relationship between dengue and renal lesions ranges from AKI to nephrotic syndrome, with AKI being a serious complication linked to high morbidity and mortality. The underlying mechanisms are not fully understood, affecting prevention and treatment.[19] Limited data are available on chronic glomerular, epithelial, and podocyte lesions, though some studies suggest a connection with *APOL1* gene variants G1 and G2.[10] Severe dengue involves immune-mediated mechanisms, which may be less apparent in transplant recipients with weakened immune responses in endemic areas.[1]

In 2016, Araújo et al.[20] reviewed 700 biopsies during a peak of the dengue epidemic, identifying 68 cases of FSGS, 13 positive for dengue IgM. Of these 11 had collapsing FSGS, and eight of them were positive for Flaviviridae. Among these eight patients, one carried the *APOL1* risk allele. The patients developed CKD stage 4 (< 30 mL/min), and one underwent a kidney transplant.[20]

In this case, a renal transplant patient with CKD developed dengue, leading to AKI and nephrotic syndrome, necessitating renal replacement therapy. Dengue was confirmed by serology, and a renal biopsy revealed collapsing FSGS. A PubMed search identified two cases linking collapsing FSGS to dengue, both showing partial recovery of renal function after treatment with methylprednisolone and diuretics.[10]

All cited reports, including this one, were from Brazil. Unlike previous cases, this case involved a renal transplant with a previously well-functioning graft that became compromised. Other causes of graft loss were ruled out. Managing these patients is challenging because immunosuppressive therapy complicates dengue infection, and abrupt discontinuation increases the risk of graft rejection. In this case, methylprednisolone therapy did not restore renal function, and the patient had to return to hemodialysis.

This case report highlights DENV's potential to infect renal tissue and contribute to the development of collapsing FSGS. While literature on this association is limited and mainly involves native kidneys, this is the first documented case of DENV-related collapsing FSGS in a transplanted kidney. It underscores the need for vigilance and monitoring in dengue-infected transplant patients. Collapsing FSGS related to dengue is rare but severe, requiring prompt clinical intervention. Further research is needed to understand dengue-related renal injury mechanisms and develop effective management strategies for transplant patients.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTIONS

Substantive scientific and intellectual contributions to the study: Guedes SA, Gutiérrez-Peredo GB, Durando CR, Mota IS, Costa FPM, Codes JJG, Machado MSB, Vieira NA, Pereira MLLC, Mattoso RJC; **Conception and design:** Guedes SA, Gutiérrez-Peredo GB, Durando CR, Mota IS, Costa FPM, Codes JJG, Machado MSB, Vieira NA, Pereira MLLC, Mattoso RJC; **Data analysis and interpretation:** Guedes SA, Gutiérrez-Peredo GB, Durando CR, Mota IS, Costa FPM, Codes JJG, Aires MAM, Machado MSB, Vieira NA, Pereira MLLC, Tapioca FPM, Mattoso RJC; **Article writing:** Guedes SA, Gutiérrez-Peredo GB, Durando CR, Mota IS, Mattoso RJC; **Critical revision:** Guedes SA, Gutiérrez-Peredo GB, Durando CR, Mota IS, Costa FPM, Codes JJG, Aires MAM, Machado MSB, Vieira NA, Pereira MLLC, Tapioca FPM, Mattoso RJC; **Final approval:** Gutiérrez-Peredo GB.

AVAILABILITY STATEMENT

All data generated or analyzed during this study is included in this article.

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