Post-Dengue Collapsing Focal Segmental Glomerulosclerosis: A Case Series of Viral Podocytopathy

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Abstract
Introduction: Dengue virus infection typically causes Acute Kidney Injury (AKI) via Acute Tubular Necrosis (ATN). However, severe glomerular involvement is rare. We report a case series of Collapsing Focal Segmental Glomerulosclerosis (FSGS) presenting as a "viral podocytopathy" following severe Dengue infection.
Materials & Methods: We analyzed the clinical data, laboratory profiles, and renal biopsy findings of three patients who presented with renal dysfunction and nephrotic range proteinuria following serologically confirmed severe Dengue infection at a tertiary care center.
Results: Case 1 (19-year-old female) presented 9 months post-infection with delayed-onset nephrotic syndrome and renal insufficiency (Serum Creatinine 3.1 mg/dL). Biopsy revealed collapsing glomerulopathy with 30% fibrosis, resulting in CKD Stage 4. Case 2 (24-year-old male) presented 2 weeks post-infection with massive proteinuria (10.2 g/day) and AKI (Creatinine 2.1 mg/ dL). Biopsy showed acute collapsing FSGS without fibrosis; he achieved partial remission with corticosteroids. Case 3 (35-year-old female) developed dialysis-dependent AKI (Creatinine 6.5 mg/ dL) during the critical phase. Biopsy distinguished Collapsing FSGS from ATN, guiding prognosis.
Conclusions: Dengue virus can act as a trigger for Collapsing FSGS, likely via cytokine-mediated podocyte injury. Early renal biopsy is essential in Dengue survivors with persistent proteinuria to distinguish this aggressive pathology from reversible ATN and to initiate timely management before irreversible fibrosis occurs.

Keywords: Dengue Virus; Collapsing Glomerulopathy; FSGS; Podocytopathy; Nephrotic Syndrome; Pseudocrescents.

Introduction

The renal spectrum of Dengue Viral Infection is expanding. While Acute Tubular Necrosis (ATN) resulting from capillary leak and hypotension remains the most common presentation [1], emerging evidence suggests Dengue can trigger glomerular disease [2].

Similar to Human Immunodeficiency Virus (HIVAN) and SARS-CoV-2 (COVAN), the Dengue virus may induce a specific "viral podocytopathy" characterized by the rapid onset of nephrotic syndrome and renal insufficiency [3]. The histological hallmark is the "collapsing" variant of FSGS, defined by global glomerular tuft collapse and podocyte hypertrophy. We present a case series of three patients with biopsy-proven Collapsing FSGS, temporally linked to severe Dengue episodes, to illustrate the clinical spectrum and importance of timing in diagnosis.

Case Presentations

Case 1: The Delayed Presentation (Chronic Sequelae) A 19-year-old female presented with an 8- month history of pedal edema and facial puffiness, which began approximately one month after a documented severe Dengue infection (NS1 Antigen Positive). She had been managed conservatively elsewhere but presented to us with worsening fluid overload.

Investigations:

- **Renal Function:** Serum Creatinine 3.1 mg/dL (eGFR 19 mL/min).
- **Urinalysis:** Nephrotic range proteinuria (8 g/24h).
- **Serology:** ANA, ANCA, C3/C4, HIV, HBsAg, and HCV were negative.

Renal Biopsy: Light microscopy showed 12 glomeruli four glomerulus exhibited global tuft sclerosis with circumferential proliferation of podocytes ("pseudocrescents"). There was significant chronicity, with tubular atrophy involving 30% of the core and interstitial fibrosis involving 25%. Immunofluorescence was negative for immune deposits.

Outcome: The diagnosis was Post-Dengue Collapsing FSGS. Due to the significant chronicity (interstitial fibrosis), immunosuppression was deemed unlikely to benefit. She was managed conservatively for CKD Stage 4.

Case 2: The Early Presenter (Acute Podocytopathy) A 24-year-old male presented with sudden onset frothy urine and anasarca only 14 days after discharge for Dengue Fever (Dengue IgM Positive). Unlike Case 1, he presented immediately upon symptom onset.

Investigations:

- **Renal Function:** Serum Creatinine elevated at 2.1 mg/dL from a baseline of 0.9 mg/dL.
- **Biochemistry:** Severe hypoalbuminemia (1.8 g/dL) and hyperlipidemia.
- **Urinalysis:** Massive proteinuria (10.2 g/24h).
- **Serology:** ANA, ANCA, C3/C4, HIV, HBsAg, and HCV were negative.

Renal Biopsy: Performed on Day 5 of admission. Histology revealed classic collapsing glomerulopathy: wrinkling of the glomerular basement membrane and implosive tuft collapse with epithelial cell hypertrophy. Crucially, tubular atrophy was minimal (<5%), indicating acute injury without chronicity. Immunofluorescence was negative.

Outcome: Given the acute presentation and lack of fibrosis, he was treated with oral Prednisolone (1 mg/kg). At 12 weeks follow-up, creatinine normalized to 1.1 mg/dL, and proteinuria decreased to sub-nephrotic range (1.5 g/day), achieving partial remission.

Case 3: The Dialysis-Dependent Presentation A 35-year-old female was admitted to the ICU with Dengue Shock Syndrome. She developed oliguric AKI requiring Hemodialysis (HD). While her platelet count and hemodynamics stabilized over 3 weeks, she remained dialysis-dependent, prompting a nephrology referral.

Investigations:

- **Renal Function:** Pre-dialysis Serum Creatinine 6.5 mg/dL. Urine output <400 mL/day.
- **Urinalysis:** Spot Urine Protein-to-Creatinine Ratio (UPCR) 6.5 g/g.

- **Serology:** ANA, ANCA, C3/C4, HIV, HBsAg, and HCV were negative.

Renal Biopsy: Biopsy was performed to rule out cortical necrosis. It showed severe Collapsing FSGS with extensive acute tubular injury. Immunofluorescence was negative for immunoglobulins and complements, ruling out immune-complex mediated glomerulonephritis.

Outcome: The biopsy ruled out simple ATN and confirmed severe glomerular injury. She was weaned off dialysis after 6 weeks but remained with CKD Stage 5 (eGFR 12 mL/min), highlighting the aggressive nature of the disease in susceptible individuals.

Feature	Case 1	Case 2	Case 3
Age / Sex	19 / Female	24 / Male	35 / Female
Dengue Severity	ere Dengue (NS1+)	Dengue Fever (IgM+)	engue Shock Syndrome
Latency	1 Month (Presented at 9 months)	14 Days	ng Critical Phase
tatio n	dema, Chronic Renal Failure	Anasarca, Acute Nephrotic Syndrome	liguric AKI (Dialysis Dependent)
Serum Creatinine	3.1 mg/dL	2.1 mg/dL	6.5 mg/dL
Proteinuria	8 g/24h	10.2 g/24h	g/g (Spot UPCR)
Biopsy Findings	Collapsing FSGS + **30% Fibrosis**	Collapsing FSGS + **<5% Fibrosis**	Collapsing FSGS + **Severe ATN**
Treatment	Conservative (CKD management)	Prednisolone (1 mg/kg/day)	emodialysis + Supportive

Outcome	CKD Stage 4 (Irreversible)	artial Remission (Cr 1.1 mg/dL)	KD Stage 5 (Dialysis Independent)

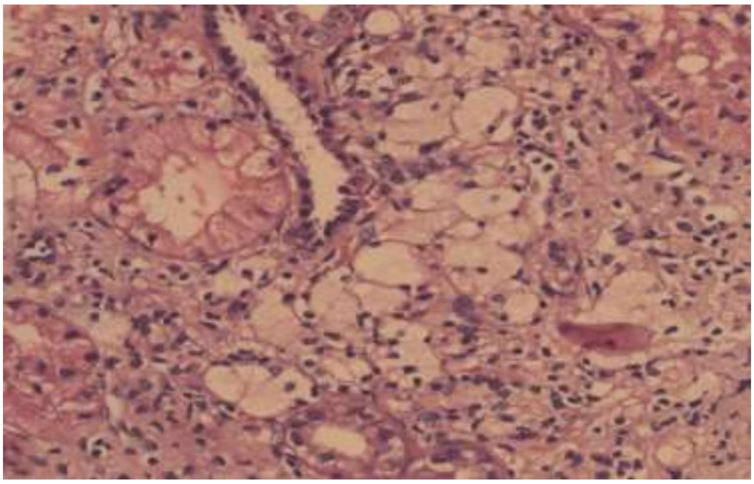
Discussion
This case series illustrates that Dengue-induced Collapsing FSGS is a distinct clinical entity that ranges from steroid-responsive acute disease to irreversible renal failure.

The Pathophysiology: Cytokine-Mediated Injury The temporal sequence in all three cases— Dengue infection followed immediately by Nephrotic Syndrome—suggests a viral trigger. Dengue infection is known to trigger a "cytokine storm," characterized by high levels of TNF-α and IL-6. These cytokines have been shown to directly downregulate nephrin and podocin expression, leading to cytoskeletal collapse and podocyte effacement [2, 3]. This mechanism mirrors the pathogenesis seen in other viral podocytopathies, suggesting that the systemic inflammatory milieu of severe Dengue can directly target the glomerular filtration barrier.

The Diagnostic Significance of "Pseudocrescents" In our series, the biopsy finding of "circumferential proliferation of podocytes" was the histological hallmark. Unlike the "true crescents" seen in RPGN (which consist of parietal epithelial cells and immune cells), these are hyperplastic podocytes filling the urinary space [4]. This distinction confirms a primary podocytopathy rather than an immune-complex glomerulonephritis.

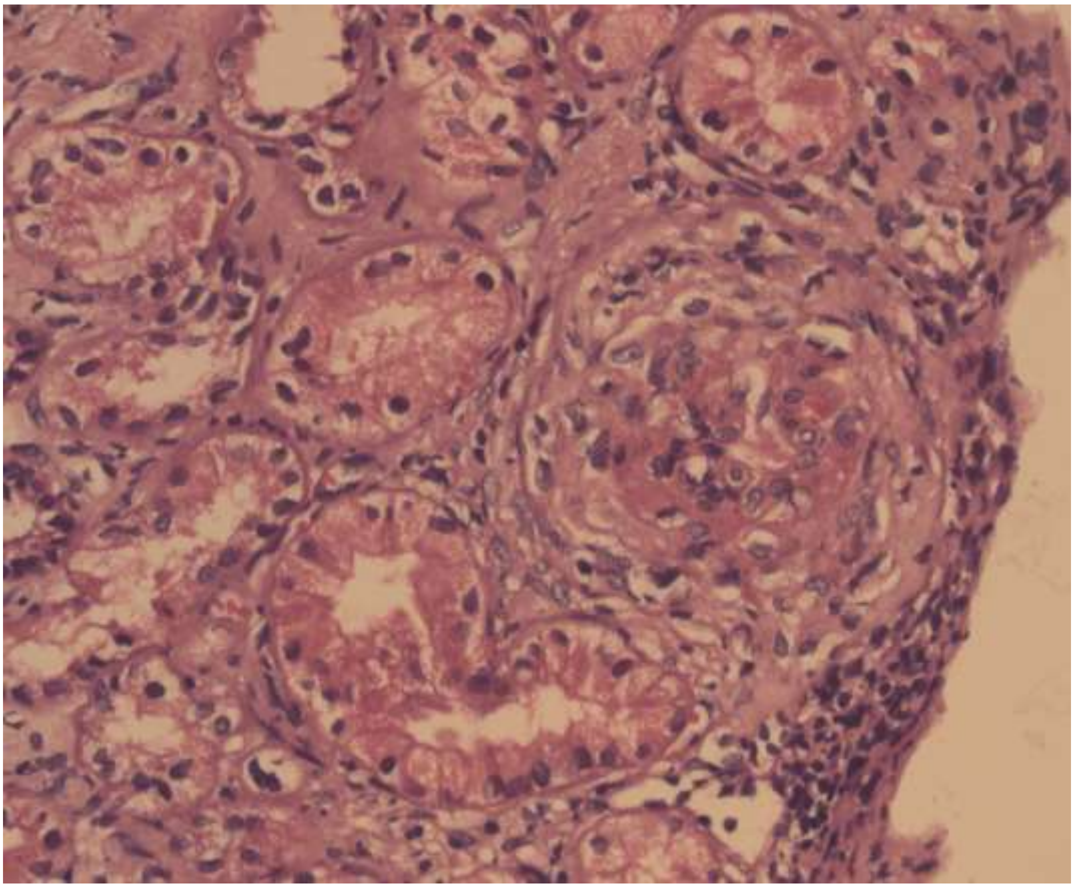
Impact of Delayed Diagnosis The contrast between Case 1 and Case 2 is clinically significant. Case 2, biopsied early (2 weeks post-infection), had minimal fibrosis and responded to steroids. Case 1, presenting 9 months post-infection, had established fibrosis and irreversible CKD. This underscores the need for quantifying proteinuria in all Dengue patients at discharge.

Conclusion
We report a rare case series of Collapsing FSGS presenting post-Dengue infection. The presence of pseudocrescents on biopsy confirms a severe podocytopathy. Nephrologists should remain vigilant for glomerular disease in Dengue survivors. Persistent proteinuria after Dengue fever warrants an early biopsy to distinguish ATN from FSGS, potentially allowing for earlier intervention before fibrosis sets in.



Figures : renal biopsy : Tubulointerstitial Findings (Image 1)

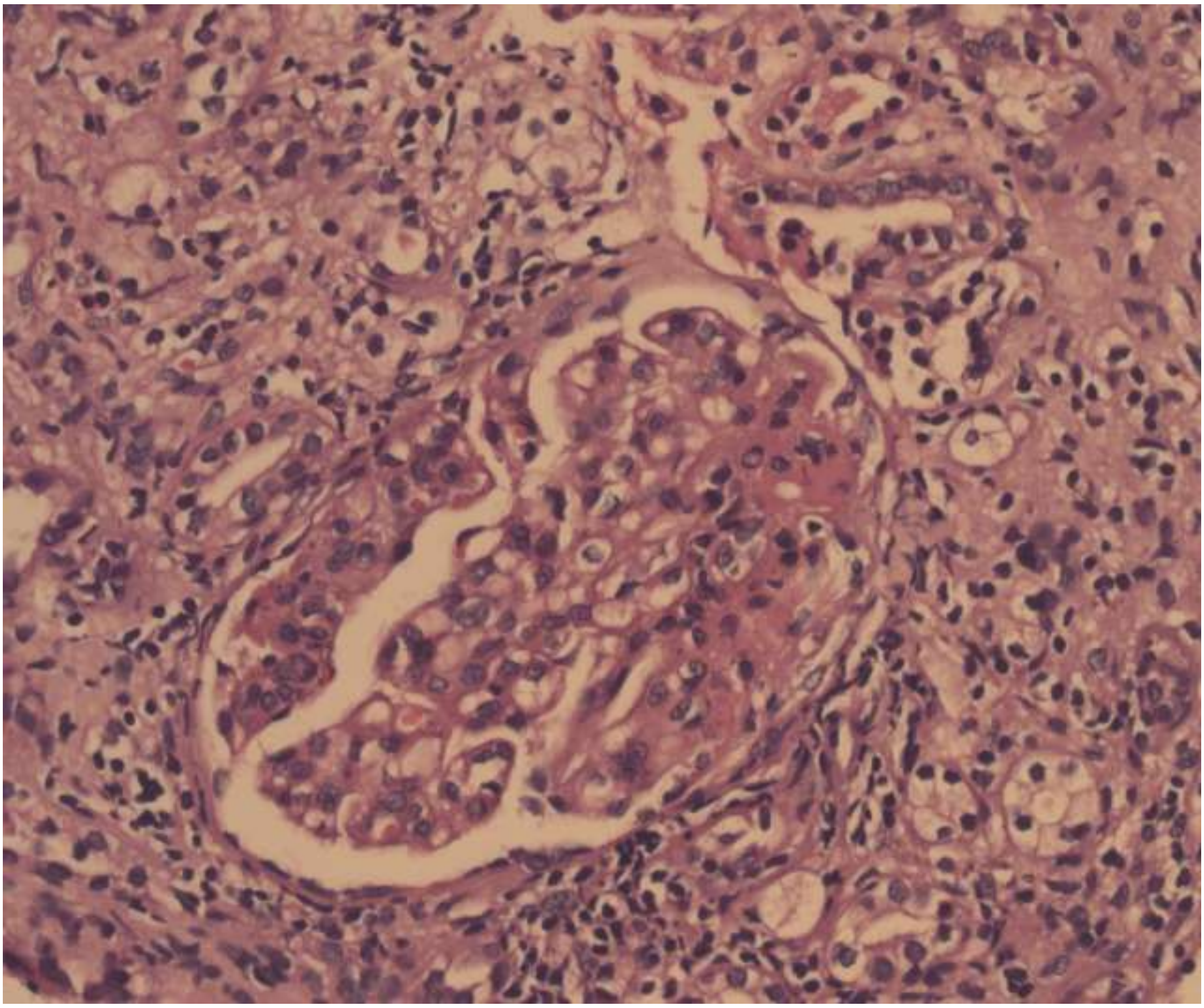
- **Suggested Title:** Severe Tubulointerstitial Injury & Microcystic Changes
- **Microcystic Tubular Dilation:** The renal tubules exhibit marked dilation with flattening of the lining epithelium, creating a "thyroid-like" or microcystic appearance.
- **Acute Tubular Injury (ATI):** There is evidence of severe tubular epithelial damage, including cytoplasmic vacuolization and luminal widening.
- **Interstitial Inflammation:** A diffuse mononuclear inflammatory infiltrate is visible within the widened interstitial spaces, consistent with the reactive inflammation seen in collapsing glomerulopathy.



Glomerular Findings - High Power (Image 2)

: The "Collapsing" Phenotype

- **Global Tuft Collapse:** The glomerular capillary tuft shows segmental to global collapse ("implosion"), characterized by wrinkling and retraction of the glomerular basement membrane.
- **Luminal Obliteration:** The capillary lumens are largely obliterated due to the collapse of the tuft architecture.
- **Podocyte Hypertrophy:** The visceral epithelial cells (podocytes) surrounding the collapsed tuft are prominent, hypertrophied, and hyperplastic. This "capping" of the collapsed tuft is a hallmark of Collapsing



: Collapsing Glomerulopathy: Glomerular and Tubular Correlation

- Bowman's Space Dilation: The urinary space is patent and markedly dilated, occupied by the retracted and collapsed glomerular tuft.
- Correlative Injury: This field demonstrates the characteristic association between the collapsing glomerular lesion and the surrounding severe tubulointerstitial damage.
- Differentiation: The presence of severe tubular injury and microcysts distinguishes this entity from other variants of FSGS (e.g., tip lesion or perihilar), where tubular damage is often less florid relative to the glomerular scar.

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