Case Report

Collapsing Glomerulopathy and Thrombotic Microangiopathy in Postpartum Period: Two Case Reports

Abstract

Collapsing glomerulopathy (CG) is a distinct histopathologic pattern of glomerular injury characterized by global/segmental wrinkling of the glomerular basement membrane with podocyte hyperplasia and hypertrophy along with tubulointerstitial changes. There is no specific treatment for CG due to etiological heterogeneity, and newer insights into the pathogenesis may lead to the development of targeted therapy. The most common form of CG is the primary or idiopathic followed by secondary (due to viral infections, autoimmune disease, drugs, etc.) and genetic causes. Thrombotic microangiopathy (TMA) is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and organ failure of variable severity. We here present two young women with preeclampsia who presented with acute kidney injury, anemia, and schistocytes in peripheral smear suggestive of TMA. Renal biopsy showed interesting histopathology of CG in addition to TMA in the first patient and CG alone in the second. Both the patients received supportive therapy while the first patient also received plasmapheresis. One patient had complete recovery, and other had partial recovery of renal function at last follow-up. Combined histopathological lesion of CG with TMA has never been reported in postpartum period so far in literature.

Keywords: *Collapsing glomerulopathy, plasmapheresis, postpartum, thrombotic microangiopathy*

N. Gopalakrishnan, J. Dhanapriya, C. Padmakumar, T. Dineshkumar, A. A. Kurien[1], R. Sakthirajan, T. Balasubramaniyan

Institute of Nephrology, Madras Medical College, Rajiv Gandhi Government General Hospital, [1]Center for Renal and Urological Pathology Pvt Ltd, Renopath, Chennai, Tamil Nadu, India

Introduction

Collapsing glomerulopathy (CG) was described first in 1978 and named as malignant focal segmental glomerulosclerosis (FSGS). In the 1980s, CG was diagnosed in HIV patients and termed "HIV-associated nephropathy." In 1986, Weiss *et al*.[1] described six cases of this condition in young black non-HIV patients with severe proteinuria and rapidly progressive renal failure. Detwiler *et al*.[2] and Valeri *et al*.[3] observed the unique features of this variant of FSGS, and Columbia classification[4] classified CG as a distinct variant of FSGS. However, recently, studies suggest that sooner or later, CG may be designated as a separate entity. We present here two female patients with preeclampsia who developed acute kidney injury (AKI) and jaundice in the postpartum period. Renal biopsy revealed CG probably as a result of ischemia due to thrombotic microangiopathy (TMA).

Case Reports

Case 1

A 22-year-old female with 36 weeks of gestation presented with edema, oliguria, and eclamptic seizure. She had preeclampsia in her first pregnancy 3 years ago. A girl child was delivered by emergency cesarean section. She had jaundice, and her blood pressure was 160/100 mm of Hg. Laboratory investigations showed urinalysis: 3 + proteinuria with urine protein creatinine ratio (PCR): 6.4; blood hemoglobin: 8.6 g/dl; platelet count: 100,000/cu.mm; peripheral smear: schistocytes; blood urea: 87 mg/dl; serum creatinine: 4.7 mg/dl; serum uric acid: 6.7 mg/dl; serum lactate dehydrogenase (LDH): 3066 IU/L; serum total bilirubin: 3.2 mg/dl; alanine aminotransferase 41 IU/L; and aspartate aminotransferase: 45 IU/l. Renal biopsy revealed fibrin thrombi partially occluding the capillary tuft in one glomerulus with endothelial swelling [Figure 1a]. Two glomeruli showed segmental collapse of the capillary tuft with hyperplasia of the overlying podocytes [Figure 1b]. Hyaline droplets were noted in a few of the podocytes. Tubulointerstitium showed signs of acute injury. All stains for immunofluorescence were negative. A diagnosis of TMA with CG was made. The patient was treated with six sessions of

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Address for correspondence:
Dr. J. Dhanapriya, Institute of Nephrology, Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India.
E-mail: priyamdhana@gmail.com

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plasmapheresis along with hemodialytic support. Her serum creatinine normalized to 1 mg/dl with urine spot PCR of 0.3 at the end of 1 month. She is on follow-up maintaining normal renal function at the end of 20 months.

Case 2

A 27-year-old female with preeclampsia underwent cesarean section at 38 weeks of gestation for fetal distress. She had oliguria and severe hypertension. Evaluation revealed anemia (hemoglobin: 7.5 g/dl), thrombocytopenia (platelet count: 110,000/cu.mm), renal failure (serum creatinine: 7.7 mg/dl), nephrotic proteinuria (urine PCR: 3.9), schistocytes in peripheral smear, deranged liver function tests, and elevated serum LDH (1749 IU/L). Renal biopsy showed segmental collapse of capillary tuft in 2 glomeruli with hyperplasia of overlying podocytes. No platelet or fibrin thrombi was seen. All stains for immunofluorescence were negative. She was given supportive therapy and hemodialysis. Plasmapheresis was planned in view of laboratory evidence of TMA though there was no histological evidence. However, the patient was not willing and opted for conservative therapy. Ultrastructural examination of kidney biopsy revealed endothelial swelling and foot process effacement [Figure 1c]. She recovered partially with serum creatinine of 1.6 mg/dl at the end of 19 months.

Discussion

CG is not a specific disease, but rather, a unique pattern of glomerular and tubulointerstitial injury due to heterogeneous factors, namely, infections, environmental factors, autoimmune diseases, and ischemic insults probably with underlying genetic susceptibility.[5] The "hallmark" of CG is podocyte hyperplasia. Although the exact pathomechanism of CG is yet to be deciphered, disruption of mitochondrial functionality is thought to be the central trigger. Other proposed mechanisms include dysregulation of vascular endothelial growth factor (VEGF) expression and acute ischemia. Ischemic processes, such as TMA, can cause mitochondrial dysregulation.[6]

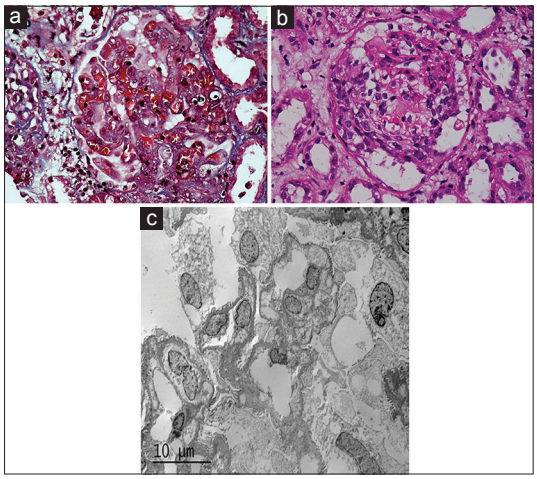

Figure 1: (a) Renal biopsy showing fibrin thrombi and swollen endothelial cells (trichrome stain). (b) Renal biopsy showing collapse of the capillary tuft with hyperplasia of the podocytes (H and E). (c) Electron micrograph showing endothelial swelling and foot process effacement (×12,000)

Both of our patients were pregnant females with a history of preeclampsia. The differential diagnosis included were HELLP syndrome, AKI due to sepsis, TMA, or underlying glomerular disease but both presented with AKI, jaundice, and fragmented red blood cells in peripheral smear more in favor of suggestive of TMA. Although the renal biopsy revealed TMA with CG, the cause of AKI in both the patients was multifactorial (preeclampsia/sepsis/TMA). Viral (hepatitis B surface antigen, anti-hepatitis C virus, HIV, cytomegalovirus qualitative PCR, parvovirus B19 DNA PCR) and autoimmune (serum antinuclear antibody, anti-double stranded DNA) serology were negative for both patients. Serum complements (C3, C4) were normal. There were no features of disseminated intravascular coagulation. Due to logistic reasons, we could not do genetic mutations of TMA. Renal biopsy showed features of CG in both but TMA only in the first patient. Both patients required dialysis support; first patient underwent plasmapheresis with complete recovery and second patient with partial recovery of renal function.

More recently, the direct causal relationship between patchy infarction and *de novo* CG in transplanted kidneys has been reported.[7] Demonstration of CG in the vicinity of acute cortical necrosis of obstetric origin by Kazi and Mubarak[8] and observation of three cases of CG in the proximity of patchy infarction secondary to severe accessory renal artery in renal allografts[9] indicate the role of ischemia in causing CG.

The placenta in preeclampsia increases the expression and secretion of soluble fms-like tyrosine kinase 1, which inhibits VEGF receptors (VEGFRs) with ensuing endothelial dysfunction and TMA. An analogous situation is TMA occurring in association with the use of bevacizumab, a VEGF inhibitor,[10,11] and sunitinib, a tyrosine kinase inhibitor used for metastatic renal cell carcinoma, which causes dysregulation of VEGFR and platelet-derived growth factor receptor pathways.[12]

In our patients, preeclampsia was the trigger for TMA. TMA results in glomerular ischemia due to endotheliosis and fibrin thrombi in the capillaries further causing CG. The sequential schema [Figure 2] would explain the pathomechanism of CG in our patients.

There is no specific treatment for CG. Inhibitors of cyclin-dependent kinases, retinoic acid derivatives and inhibitors of nuclear factor-κB and cyclooxygenase-2 have been shown to prevent the development and retard the progression of CG in experimental models.[13] Patients with CG are at high risk of progressing to end-stage renal disease (ESRD) (50%–100%) in most series.[14] Male gender, high serum creatinine at the time of biopsy, lack of remission of proteinuria, and severity of tubular

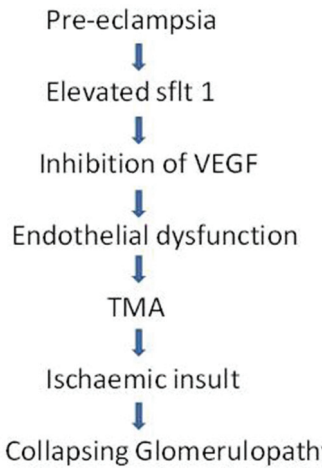

Figure 2: Proposed pathomechanism of collapsing glomerulopathy in preeclampsia

degenerative and regenerative changes were predictors of progression to ESRD.[3,14] It is worthwhile to note that natural history and prognosis of these lesions are primarily governed by the etiological condition as evidenced by complete recovery in the first patient after delivery and timely plasmapheresis.

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Conflicts of interest

There are no conflicts of interest.

References

1. Weiss MA, Daquioag E, Margolin EG, Pollak VE. Nephrotic syndrome, progressive irreversible renal failure, and glomerular "collapse": A new clinicopathologic entity? Am J Kidney Dis 1986;7:20-8.
2. Detwiler RK, Falk RJ, Hogan SL, Jennette JC. Collapsing glomerulopathy: A clinically and pathologically distinct variant of focal segmental glomerulosclerosis. Kidney Int 1994;45:1416-24.
3. Valeri A, Barisoni L, Appel GB, Seigle R, D'Agati V. Idiopathic collapsing focal segmental glomerulosclerosis: A clinicopathologic study. Kidney Int 1996;50:1734-46.
4. D'Agati VD, Fogo AB, Bruijn JA, Jennette JC. Pathologic classification of focal segmental glomerulosclerosis: A working proposal. Am J Kidney Dis 2004;43:368-82.
5. Mubarak M. Collapsing focal segmental glomerulosclerosis: Current concepts. World J Nephrol 2012;1:35-42.
6. Albaqumi M, Barisoni L. Current views on collapsing glomerulopathy. J Am Soc Nephrol 2008;19:1276-81.
7. Kazi JI, Mubarak M. Glomerular collapse in association with acute cortical necrosis in native kidneys: All that collapses is not idiopathic collapsing glomerulopathy. Nephrol Rev 2012;4:23.
8. Kazi J, Mubarak M. Collapsing glomerulopathy with patchy acute cortical necrosis secondary to postpartum hemorrhage. Clin Kidney J 2012;5:78-9.
9. Canaud G, Bruneval P, Noël LH, Correas JM, Audard V, Zafrani L, *et al.* Glomerular collapse associated with subtotal renal infarction in kidney transplant recipients with multiple renal arteries. Am J Kidney Dis 2010;55:558-65.
10. Patel TV, Morgan JA, Demetri GD, George S, Maki RG, Quigley M, *et al.* A preeclampsia-like syndrome characterized by reversible hypertension and proteinuria induced by the multitargeted kinase inhibitors sunitinib and sorafenib. J Natl Cancer Inst 2008;100:282-4.
11. Obhrai JS, Patel TV, Humphreys BD. The case progressive hypertension and proteinuria on anti-angiogenic therapy. Kidney Int 2008;74:685-6.
12. Costero O, Picazo ML, Zamora P, Romero S, Martinez-Ara J, Selgas R. Inhibition of tyrosine kinases by sunitinib associated with focal segmental glomerulosclerosis lesion in addition to thrombotic microangiopathy. Nephrol Dial Transplant 2010;25:1001-3.
13. Mubarak M, Kazi JI. Collapsing focal segmental glomerulosclerosis: A morphological lesion in search of nosologic identity. Nephrol Urol Mon 2011;3:240-6.
14. Schwimmer JA, Markowitz GS, Valeri A, Appel GB. Collapsing glomerulopathy. Semin Nephrol 2003;23:209-18.