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Primary focal segmental glomerulosclerosis in second trimester pregnancy presenting as rapidly progressive renal failure: diagnostic and therapeutic challenges: a case report

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Abstract

Background Proteinuria in pregnancy is often attributed to preeclampsia, but primary glomerular diseases such as focal segmental glomerulosclerosis can also present during pregnancy, complicating diagnosis and management.

Case presentation A 29-year-old gravida 2, para 1 African woman presented at 25 weeks of gestation with generalized edema and turbid urine. Initial investigations revealed nephrotic-range proteinuria (7.2 g/24 hours), hematuria with red blood cell casts, and deteriorating renal function, with serum creatinine rising from 1.8 to 5 mg/dL within 3 days. Due to worsening renal impairment, pregnancy termination was performed, leading to partial renal recovery, though nephrotic-range proteinuria persisted. Renal biopsy at 4 months postpartum confirmed primary focal segmental glomerulosclerosis.

Conclusions Early recognition and prompt treatment of pregnancy-associated glomerular disease are vital for renal recovery. Differentiating focal segmental glomerulosclerosis from preeclampsia is essential, and targeted immunosuppressive therapy can achieve sustained remission, highlighting the need for a multidisciplinary approach.

Keywords Primary focal segmental glomerulosclerosis, Second trimester pregnancy, Renal failure, Immunosuppressive therapy, Case report

Introduction

Physiological proteinuria, defined as urinary protein excretion of less than 300 mg per 24 hours, is common during pregnancy. However, pathological proteinuria, often associated with preeclampsia, can also occur [1]. While preeclampsia is a frequent cause of proteinuria in pregnancy, primary and secondary renal disorders may also present with proteinuria as an initial manifestation [2]. Among these rare causes of proteinuria and renal dysfunction during pregnancy is focal segmental glomerulosclerosis (FSGS), a leading cause of nephrotic syndrome and end-stage renal disease (ESRD), which has an incidence of 1.7 per 100,000 in the general population with rates up to 3–7 times higher in Black individuals than in White individuals [3, 4]. This disparity is largely due to *APOL1* risk alleles, which are absent in Europeans and Asians but increase FSGS risk 17-fold when two are present [5, 6]. The interplay between glomerular disease and pregnancy is complex, as pregnancy can influence maternal disease progression and accelerate the onset of end-stage renal disease (ESRD) [7]. Pregnancies complicated by renal disease carry a high risk of adverse

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maternal and fetal outcomes [8–10] (Table 1). Therefore, prompt, etiology-based management of primary and secondary renal disorders is essential to optimize clinical outcomes [8, 9]. Only few case reports of primary FSGS presenting as nephrotic-range proteinuria during pregnancy have been reported so far. Here, we present a rare case of primary FSGS in pregnancy, characterized by nephrotic-range proteinuria and rapidly progressive renal dysfunction. To the best of our knowledge, this is the first reported case of primary focal segmental glomerulosclerosis in pregnancy in Africa.

Case presentation

A 29-year-old gravida 2, para 1 African mother presented at 25 weeks of gestation with generalized body swelling for 2 weeks, accompanied by turbid urine. She had no known history of chronic hypertension or renal disease, and her previous pregnancy had been uneventful. On examination, she was clinically stable with a pulse rate of 72 beats per minute, respiratory rate of 18 breaths per minute, blood pressure of 134/90 mmHg, and temperature of 36.7 °C. Abdominal examination revealed a gravid uterus consistent with 24 weeks of gestation. Notable findings included bilateral pitting edema up to the knees and periorbital edema. Other physical examination findings were unremarkable.

Initial laboratory investigations, including complete blood count, serum electrolytes, liver function tests, and coagulation profile, were within normal limits. Viral serologies for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C were negative. Autoimmune workup, including anti-nuclear antibody (ANA) and anti-double-stranded DNA (dsDNA), was negative, with normal complement (C3 and C4) levels. Serum creatinine at presentation was 1.8 mg/dL, and urinalysis revealed red blood cell (RBC) casts, 3+ hematuria, and nephrotic-range proteinuria with a 24-hour urinary protein excretion of 7.2 g. Serum albumin was found to be low (1.8 g/dL). An echocardiogram was also performed to evaluate for possible cardiac causes of edema and showed normal structure and function, with a left ventricular ejection fraction of 65%.

Within 3 days of admission, her renal function deteriorated rapidly, with serum creatinine rising to 5 mg/dL, and she became oliguric. Given the worsening renal function, pregnancy termination was discussed and subsequently performed. No immunosuppressive or antihypertensive therapy was initiated prior to pregnancy termination, as the patient remained normotensive and her case was managed conservatively with close monitoring and supportive measures.

Following termination, her glomerular filtration rate (GFR) improved, with serum creatinine decreasing to 1.6 mg/dL within 4 weeks. However, nephrotic-range proteinuria persisted, prompting initiation of high-dose prednisolone (1 mg/kg/day) and enalapril, an angiotensin-converting-enzyme (ACE) inhibitor. The corticosteroid regimen was continued for 8 weeks, during which she achieved partial remission, with proteinuria decreasing to 255 mg/24 hours. However, she developed adverse effects, including weight gain, insomnia, and mood disturbances, necessitating discontinuation. Steroid tapering was performed gradually over 2 weeks. A total of 4 weeks after discontinuation, she experienced a relapse of nephrotic-range proteinuria (6.3 g/day).

A renal biopsy was done at 4 months postpartum, by which time her serum creatinine was 1.6 mg/dL and proteinuria had recurred. Light microscopy showed focal glomerular sclerosis in 2 of 16 glomeruli with capsule adhesion, and electron microscopy demonstrated segmental podocyte foot process effacement without electron-dense deposits, confirming a diagnosis of primary focal segmental glomerulosclerosis (FSGS).

Following steroid intolerance, cyclosporine (250 mg daily) was initiated and continued for 18 months before being tapered and discontinued. However, she relapsed within 1 month, necessitating a switch to tacrolimus (4 mg daily), which she has been taking for the past 18 months. Her most recent 24-hour urine protein measurements have been negative for three consecutive tests, indicating sustained remission.

Discussion

Focal segmental glomerulosclerosis (FSGS) is a form of glomerulonephritis characterized by segmental mesangial matrix expansion, capillary obliteration, sclerosis, hyalinosis, foam cell accumulation, and adhesion between the glomerular tuft and Bowman's capsule [11]. Podocyte injury, triggered by various factors, is considered a key mechanism underlying segmental glomerular sclerosis [12]. The term "FSGS" describes both a primary disease caused by direct podocyte injury and a secondary lesion that can develop in any form of chronic kidney disease (CKD) [13]. Its etiology includes genetic mutations, circulating permeability factors, infections, drug exposure, and maladaptive responses to renal injury [7].

Pregnancy has been identified as a potential trigger for FSGS, with several reports documenting new-onset or worsening disease during gestation, highlighting its complex and potentially harmful effects on renal function [10]. Although the exact pathogenesis remains unclear, proposed mechanisms include hyperfiltration-induced podocyte injury in susceptible individuals, leading to segmental sclerosis and the development of secondary FSGS [14]. Furthermore, elevated levels of estrogen and progesterone during pregnancy may impair the integrity

Table 1 Summary of previously reported cases of primary focal segmental glomerulosclerosis in pregnancy

Title	Author (year)	Country of origin	Age/sex	Gestational age at presentation	Presentation	Diagnosis	Management	Outcome
"Nephrotic syndrome due to focal segmental glomerulosclerosis occurring in early pregnancy"	Smyth and Wall [30]	Ireland	32/F	14 weeks	Shortness of breath, edema, nephrotic-range proteinuria (9 g/day), hypoalbuminemia	Renal biopsy confirmed primary FSGS (cellular variant)	Prednisolone 40 mg, azathioprine 100 mg, diuretics	Persistent nephrotic progression to ESRD, dialysis-dependent
"Focal segmental glomerulosclerosis (FSGS) in pregnancy: The case of a 27-year-old woman with nephrotic syndrome at 22 weeks of gestation"	Wang *et al.* [19]	China	27/F	22 weeks	Severe proteinuria (9.79 g/day), hypoalbuminemia (14 g/L), no hematuria	Postpartum renal biopsy confirmed primary FSGS	Prednisolone 60 mg, tacrolimus, LMWH, C-section at 31 weeks	Persistent nephrotic syndrome, progressed to ESRD at 16 months postpartum
"Collapsing Lesions and Focal Segmental Glomerulosclerosis in Pregnancy: A Report of 3 Cases"	Orozco-Guillén *et al.* [10]	Mexico	23/F	16–18 weeks	Severe proteinuria (> 10 g/L), anasarca, normal BP	Renal biopsy postpartum confirmed FSGS with collapsing lesions	Methylprednisolone, prednisolone, rituximab	Full remission within 1 month
"Collapsing Lesions and Focal Segmental Glomerulosclerosis in Pregnancy: A Report of 3 Cases"	Orozco-Guillén *et al.* [10]	Mexico	27/F	14 weeks	Hypertension, proteinuria (2.3 g/day)	Renal biopsy at 26 weeks confirmed FSGS with collapsing lesions	Methylprednisolone, prednisone, rituximab, tacrolimus	Partial remission postpartum
"Collapsing Lesions and Focal Segmental Glomerulosclerosis in Pregnancy: A Report of 3 Cases"	Orozco-Guillén *et al.* [10]	Mexico	27/F	35 weeks	Hypertension, proteinuria (11 g/day), normal fetal growth	Renal biopsy postpartum confirmed FSGS with collapsing lesions	Methylprednisolone, plasmapheresis, cyclophosphamide, prednisone, tacrolimus	Partial renal recovery, no dialysis dependence

C-section, cesarean section; F, female; LMWH, low molecular weight heparin

of the glomerular filtration barrier, increasing glomerular permeability and proteinuria, and thereby contributing to disease progression [15].

Initially classified as a single disease, FSGS is now recognized as a spectrum of disorders with distinct subtypes primarily affecting the glomerulus but can extend to involve the tubulointerstitium and renal vasculature over time [16]. Histologically, FSGS is defined by the segmental obliteration of glomerular capillaries due to extracellular matrix deposition [17].

Proteinuria in pregnancy presents significant diagnostic challenges, especially in resource-limited settings where distinguishing between preeclampsia and primary renal disorders, such as focal segmental glomerulosclerosis (FSGS), can be difficult. Preeclampsia should be considered in all cases of new-onset proteinuria and hypertension occurring after 20 weeks of gestation [18]. However, its likelihood decreases in the absence of classic features, such as hypertension, or when proteinuria begins before 20 weeks [19]. In diagnostically uncertain situations, measuring the ratio of soluble fms-like tyrosine kinase-1 (sFlt-1) to placental growth factor (PlGF) can aid in distinguishing preeclampsia from other causes of nephrotic syndrome [19].

In our case, the patient was a 29-year-old African woman who presented at 25 weeks of gestation with nephrotic-range proteinuria, hematuria, and cellular casts on urinalysis, along with a rapid rise in serum creatinine from 1.8 to 5 mg/dL within 3 days. Although RBC casts and hematuria are not typical of primary FSGS and are more often associated with secondary glomerulonephritis, a study from Bangladesh involving 100 patients found RBC casts in 10.5% of FSGS cases, indicating that these findings, while uncommon, can occasionally occur in primary FSGS [20]. The presence of cellular casts and the rapid deterioration in renal function further reduced the likelihood of preeclampsia. Given the severity of renal impairment and the low probability of a successful pregnancy with favorable maternal and fetal outcomes, pregnancy termination was discussed. A definitive diagnosis of FSGS was confirmed by renal biopsy 4 months after termination.

High-dose corticosteroids are the cornerstone of FSGS treatment, with steroid resistance defined as the persistence of nephrotic syndrome despite 4–6 months of therapy [21, 22]. Standard regimens typically include oral prednisolone at 0.5–2.0 mg/kg/day (minimum 60 mg/day) for 2–6 months, followed by a gradual taper over 1–4 months [23–25]. To reduce cumulative steroid exposure, alternate-day dosing regimens have also been explored [26, 27]. Steroid-sparing agents used in FSGS management include calcineurin inhibitors (CNIs), rituximab, and cytotoxic drugs such as mycophenolate mofetil (MMF), chlorambucil, and cyclophosphamide [25, 28–30] (Table 1). Among these, CNIs are considered relatively safe for use during pregnancy [31]. Data from pediatric studies suggest that tacrolimus may have a more favorable safety profile than cyclosporine, with lower nephrotoxicity, cholesterol levels, and cosmetic side effects, along with a reduced risk of relapse [32]. Rituximab is generally not recommended in pregnancy when alternative treatments are available, due to the risk of neonatal B-cell depletion and immunosuppression [33]. In our case, given the patient's rapid decline in glomerular filtration rate (GFR) at presentation, treatment priority was focused on preserving renal function. Complete remission of primary FSGS was initially achieved with corticosteroids. However, due to steroid dependency and recurrence of nephrotic-range proteinuria during tapering, therapy was transitioned to a calcineurin-inhibitor-based regimen. The patient is currently receiving tacrolimus and has achieved complete remission. A gradual taper and discontinuation of tacrolimus are planned, with salvage therapy using rituximab as a contingency in case of relapse following withdrawal.

Conclusions

Evaluation of proteinuria in pregnancy presents significant diagnostic and therapeutic challenges, particularly in resource-limited settings where distinguishing primary glomerular disease from preeclampsia is difficult. This case highlights that, despite the high risk of adverse renal outcomes in pregnancy-associated glomerular disease, early recognition and timely initiation of disease-modifying therapy can lead to favorable renal recovery, even in patients with severely impaired glomerular filtration.

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Data availability
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Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare no conflicts of interest regarding the research, authorship, and/or publication of this article.

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