CASE REPORT

Focal Segmental Glomerulosclerosis – A Report from Primary Care Perspective.

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Submitted: 28/11/2024. Revised edition: 08/01/2025. Accepted: 23/03/2025. Published online: 01/06/2025.

Abstract

Nephrotic syndrome is a prevalent condition characterized by heavy proteinuria, hypoalbuminemia, peripheral oedema, and hypercholesterolemia. It primarily affects the lower extremities and can arise from a variety of underlying causes. Focal segmental glomerulosclerosis (FSGS) is a leading cause of primary glomerular disease in adults, accounting for approximately 35% of cases and up to 80% in African American populations. Early diagnosis and appropriate management are essential to mitigate morbidity, mortality, and associated complications. We report the case of a young female presenting with bilateral lower limb swelling and symptoms of fluid overload, ultimately diagnosed with nephrotic syndrome. The diagnosis was confirmed through a simple urinalysis. Despite implementing dietary salt restriction and treatment with diuretic therapy, including daily administration of loop diuretics, the patient did not achieve a therapeutic response. Consequently, she required lifelong renal replacement therapy.

Keywords: *Focal segmental glomerulosclerosis, Primary care, Quality of life.*

Introduction

Nephrotic syndrome is a common condition characterized by heavy proteinuria, hypoalbuminemia, peripheral oedema, and hypercholesterolemia [1]. It has multifactorial etiology for peripheral oedema, including chronic venous insufficiency, pulmonary hypertension, and cardiac, renal, or hepatic disorders [2]. Early diagnosis and timely medical intervention are critical to reducing mortality, morbidity, and complications such as end-stage renal disease (ESRD), which can impose significant emotional, physiological, and financial burdens on patients, caregivers, and healthcare systems.

Focal segmental glomerulosclerosis (FSGS) is a leading cause of primary glomerular disease in adults, accounting for approximately 35% of all cases and up to 80% in African American patients. The diagnosis and evaluation of FSGS are guided by a combination of clinical history, laboratory findings, and renal histopathological analysis [3].

Case report

A 26-year-old woman presented with a two-week history of bilateral lower limb swelling and shortness of breath. The swelling, initially confined to the thighs for the preceding two months, had progressively worsened over the past two weeks, becoming extremely oedematous and extending to the sacral region. No redness or wounds were observed on either lower limb. The patient reported difficulty sleeping at night due to breathlessness, which was alleviated when she assumed a seated position. During the same period, she experienced fatigue, lethargy, and new-onset facial swelling.

Over the past month, her lower limb deterioration led to severe ambulatory limitations, rendering her unable to walk, even for basic tasks such as using the restroom. She required assistance and a wheelchair for mobility and reported significant pruritus over both lower limbs. In the last two weeks, she began wearing diapers to manage her bathroom needs. The patient also reported persistent vomiting over the past two weeks, resulting in poor oral intake and significant weight loss of 3 kg in one week. Her body exhibited noticeable disproportionality, with marked muscle wasting in the upper body contrasting with grossly swollen lower limbs, which she described as resembling "elephant legs." She denied experiencing any lower urinary tract symptoms, such as increased frequency, dysuria, or incontinence. No other significant complaints were noted.

Her symptoms began with bilateral lower limb swelling up to the knees, for which she sought treatment at a private clinic. A diagnosis of cellulitis was made, and she was prescribed antibiotics. Despite completing the course, the swelling worsened, extending up to her thighs. She sought a second opinion at another private clinic and was prescribed diuretics for two weeks, with minimal improvement in the swelling. Subsequently, she sought care at a government healthcare clinic.

On physical examination, the patient was alert but appeared lethargic and pale, with no jaundice. Peripheral examination revealed good pulse volume with a capillary refill time of less than two seconds. Respiratory examination revealed reduced breath sounds bilaterally at the lung bases. There was marked soft pitting oedema in both lower limbs, extending to the sacrum. All other systemic examinations were unremarkable. Urinalysis and blood investigations were performed for further evaluation (Table 1 – 2, Figure 1).

The patient presented with drastically worse blood test results at the time of diagnosis. A complete blood analysis verified normochromic normocytic anemia, indicative of chronic kidney disease (CKD). Due to her pronounced oedema, a renal function assessment was conducted, revealing significant renal dysfunction with elevated creatinine levels (246.8 µmol/L) and raised urea concentrations (11.6 mmol/L). Her eGFR was 14 ml/min/1.73m² (CKD-EPI

equation), categorizing her as Stage 5 CKD (End-Stage Renal Disease) using the KDIGO 2018 guidelines. Liver function tests indicated hypoalbuminemia, consistent with nephrotic syndrome and glomerular disease. Urinalysis showed 4+ proteinuria, confirming nephrotic-range proteinuria (>3g/day). Given the worsening blood investigations and persistent proteinuria, a kidney biopsy was performed, revealing global sclerosis, with 15 glomeruli exhibiting segmental glomerulosclerosis and focal hyalinosis. The tubules displayed widespread early interstitial fibrosis, with 50% of them atrophied, and some tubules contained hyaline casts. Immunofluorescence was negative for IgG, IgA, IgM, C3, C1q, and fibrinogen. She was diagnosed with focal segmental glomerulosclerosis (FSGS) associated with acute tubular necrosis/injury. Had these urine and laboratory tests been conducted earlier, the results might not have been as bad, potentially facilitating an earlier diagnosis and management before the patient progressed to end-stage renal disease.

Discussion

Chronic kidney disease (CKD) has emerged as a global public health challenge due to its rising prevalence, risk of progression to end-stage renal disease (ESRD), and associated morbidity and mortality. In Malaysia, CKD is particularly concerning due to its increasing prevalence and low public awareness. According to the Malaysian National Health and Morbidity Survey (NHMS) 2011, the prevalence of CKD in West Malaysia was 9.07%, which rose to 15.5% by 2018 [1]. A more recent study that included populations from East Malaysia confirmed a similar prevalence of 15.5%, with 6.81% of cases classified as stages 3 to 5 CKD [4]. CKD is often asymptomatic and irreversible, and its progression to ESRD necessitates dialysis, reflecting a significant public health burden [4]. In 2020, over 51,000 individuals in Malaysia required dialysis, with 9,592 new cases reported. The healthcare costs associated with CKD and ESRD in Malaysia are estimated at RM3.2 billion for dialysis and RM1.5 billion for indirect expenses [5]. Chronic kidney disease (CKD) has become a global public health issue due to the rising prevalence of CKD patients, the risk of advancement to end-stage renal disease (ESRD), and increased morbidity and mortality rates.

The management of CKD relies primarily on early detection and intervention to prevent disease progression, as no definitive cure exists. Delayed diagnosis or mismanagement of nephrotic syndrome, a common precursor to CKD, can accelerate the development of chronic kidney failure. Focal segmental glomerulosclerosis (FSGS) and membranous nephropathy are the most frequent primary causes of nephrotic syndrome, contributing to approximately 2% of the 52% of new dialysis cases reported in Malaysia in 2022 [6]. FSGS accounts for 29.8% of primary glomerulonephritis cases in Malaysia, with an estimated 2,320 reported cases. It predominantly affects younger individuals, with a mean age of 35.8 ± 14.9 years, and males (57.2%) are more commonly affected [7].

Nephrotic syndrome typically presents with marked oedema, proteinuria, hypoalbuminemia, and often hyperlipidemia. The most common initial symptom is the sudden onset of oedema, particularly in the lower extremities, which may extend to the proximal lower limbs, abdomen, or genitalia in severe cases [2]. Other symptoms include exertional dyspnea, fatigue, foamy urine, and significant fluid-associated weight gain. Diagnostic criteria include clinical evidence of peripheral edema, heavy proteinuria (spot urine protein-to-creatinine ratio >3.5 g/24 hours or >300 mg/mmol), and hypoalbuminemia [8]. In this case, the patient presented with extensive oedema extending to the sacral region, consistent with nephrotic syndrome.

The 24-hour urine protein collection test remains the gold standard for quantitative protein assessment. However, it is often impractical in

outpatient settings or when patients undergo concurrent laboratory testing. A urine dipstick test, showing proteinuria of 3+ (≥300 mg/dL), provides an accessible screening tool for identifying nephrotic-range proteinuria. Initial laboratory investigations, including a urine dipstick test, played a crucial role in detecting nephrotic syndrome in this patient during her third visit to the government health clinic [1,8].

Primary care serves as the initial point of contact for patients, playing a pivotal role in the early detection and management of nephrotic syndrome. Accurate history-taking, thorough physical examination, and basic laboratory investigations are essential for identifying systemic causes of peripheral edema. In this case, the patient's recurrent complaints of significant lower limb oedema, extending to the sacrum, necessitated renal evaluation through simple yet effective diagnostic tools like urine dipstick tests. These initial findings guided subsequent confirmatory laboratory investigations and timely referral for specialist care [9]. Figure 2 reflects the algorithm of nephrotic syndrome approach in terms of assessment and management [9].

Without early diagnosis and treatment, nephrotic syndrome can progress to ESRD. In this patient, a urine study revealed proteinuria exceeding 3+, consistent with heavy proteinuria. Follow-up tests, including a 24-hour urine protein collection, confirmed the diagnosis. Data from the Malaysian Renal Registry indicate that approximately 15% of nephrotic syndrome patients progress to ESRD within a 72-month follow-up period. The 5 and 10-year survival rates for patients with FSGS are 87.4% and 80.6%, respectively, with hypertension present in 41.3% of cases at diagnosis [7]. In this case, glucocorticoid resistance and high-dose diuretics failed to alleviate the patient's severe edema. She required continuous ambulatory peritoneal dialysis to manage her symptoms and improve her quality of life. Complications such as bacterial infections, including cellulitis, peritonitis, and sepsis, can exacerbate the patient's condition by inducing further edema and thrombosis [1,9].

The patient received her diagnosis of nephrotic syndrome at 26 years old, profoundly affecting her physical, emotional, and social well-being. She required frequent dialysis sessions, which imposed significant emotional and physical burdens on both the patient and her caregiver. This case highlights the critical role of primary care in early diagnosis and the need for comprehensive support systems for young patients facing chronic conditions like ESRD [10].

Conclusion

This case underscores the critical importance of early detection and effective management of nephrotic syndrome, particularly in the context of Focal Segmental Glomerulosclerosis (FSGS). The delayed diagnosis in this patient, despite hallmark symptoms such as severe oedema and proteinuria, highlights the diagnostic challenges often encountered in primary care settings, where FSGS may not be immediately recognized. Timely recognition of nephrotic syndrome, supported by a comprehensive diagnostic evaluation, is essential to prevent progression to end-stage renal disease (ESRD) and the subsequent requirement for renal replacement therapy. This case emphasizes the pivotal role of primary care providers in identifying early clinical signs, initiating appropriate investigations, and ensuring timely referral to specialists. Such proactive approaches are integral to improving patient outcomes and enhancing quality of life. Given the complex and chronic nature of nephrotic syndrome, a multidisciplinary approach to long-term management is imperative. This strategy should focus on optimizing care delivery, preventing complications, and addressing the ongoing physical, emotional, and social needs of patients.

Acknowledgement

The authors would like to sincerely acknowledge the support and guidance of the Head of the Department of Family Medicine at International Islamic University Malaysia (Kuantan) and the Prince Court Medical Centre. Their invaluable assistance in the preparation of this case report is greatly appreciated.

Authors contribution

KI and MSES contributed to the conceptualization and refinement of the case report, and improving the overall quality of the manuscript.

NHNY contributed to the histopathological examination (HPE) slides and authored the HPE report.

Table 1. Blood parameter in primary care

Test	Result	Reference range
Haemoglobin	7.0	(8.0-17)
White blood cells $10^{\wedge 3}$	10.3	(3.0-15.0)
Platelet $10^{\wedge 3}$	247	(150-300)
HCT	24%	(33-42)
MCV(fL)	91	(78-97)
MCH(pG)	29	(27-33)
MCHC (g/dL)	31	(31-35)
Iron (umol/L)	9.1	(5.83-34.80)
UIBC (umol/L)	16	(24-70)
TIBC (umol/L)	25	
TSAT (%)	36	(16-45%)
Serum ferritin (ug/L)	77	(13-68)
Sodium (mmol/L)	141	(129-156)
Potassium (mmol/L)	3.5	(3.0-4.5)
Chloride (mmol/L)	113	(92-115)
Creatinine (umol/L)	246.8	(26-90)
Urea (mmol/L)	11.6	(2.5-7.1)
Albumin (g/L)	21	(35-50)
Calcium (mmol/L)	1.8	(2.0-2.6)
Phosphate (mmol/L)	1.1	(0.8-1.5)

UIBC Unsaturated iron binding capacity, ***TIBC*** Total iron binding, ***TSAT*** transferrin saturation , ***MCH*** Mean corpuscular hemoglobin. ***MCHC*** Mean corpuscular hemoglobin concentration**,** ***MCV*** Mean corpuscular volume

Table 2. Urine analysis in primary care

Test	Result	Reference range
Urine analysis		
Glucose	Negative	
Protein	4+	
Bilirubin	1+	
Urobilinogen	Normal	
pH	6	
Ketone	1+	
Leucocyte	Negative	
Colour	Yellow	
Blood	Trace	
24H Urine Protein	8.93	(g/day)

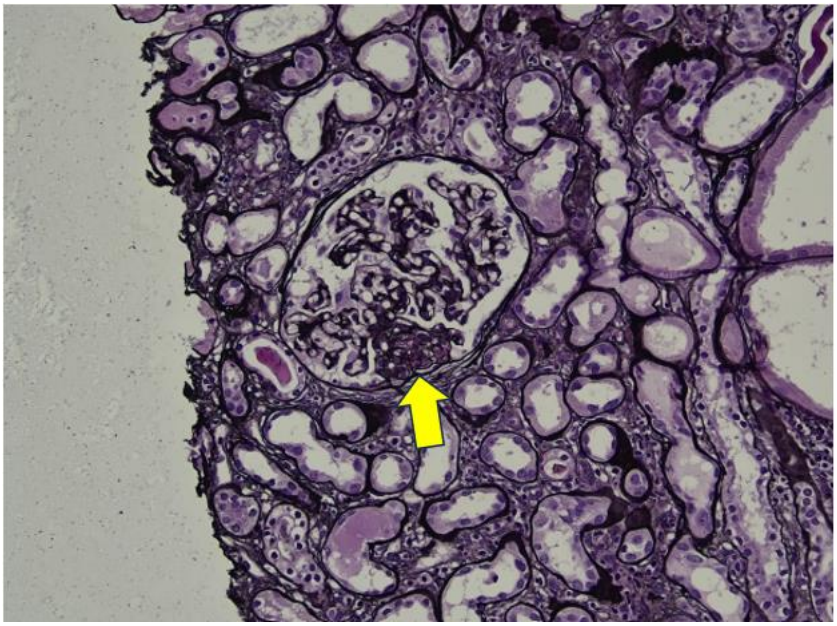

Figure 1. Glomerulus with segmental glomerulosclerosis. Inferior area. There are segments with preserved architecture. (Methenamine silver x200.)

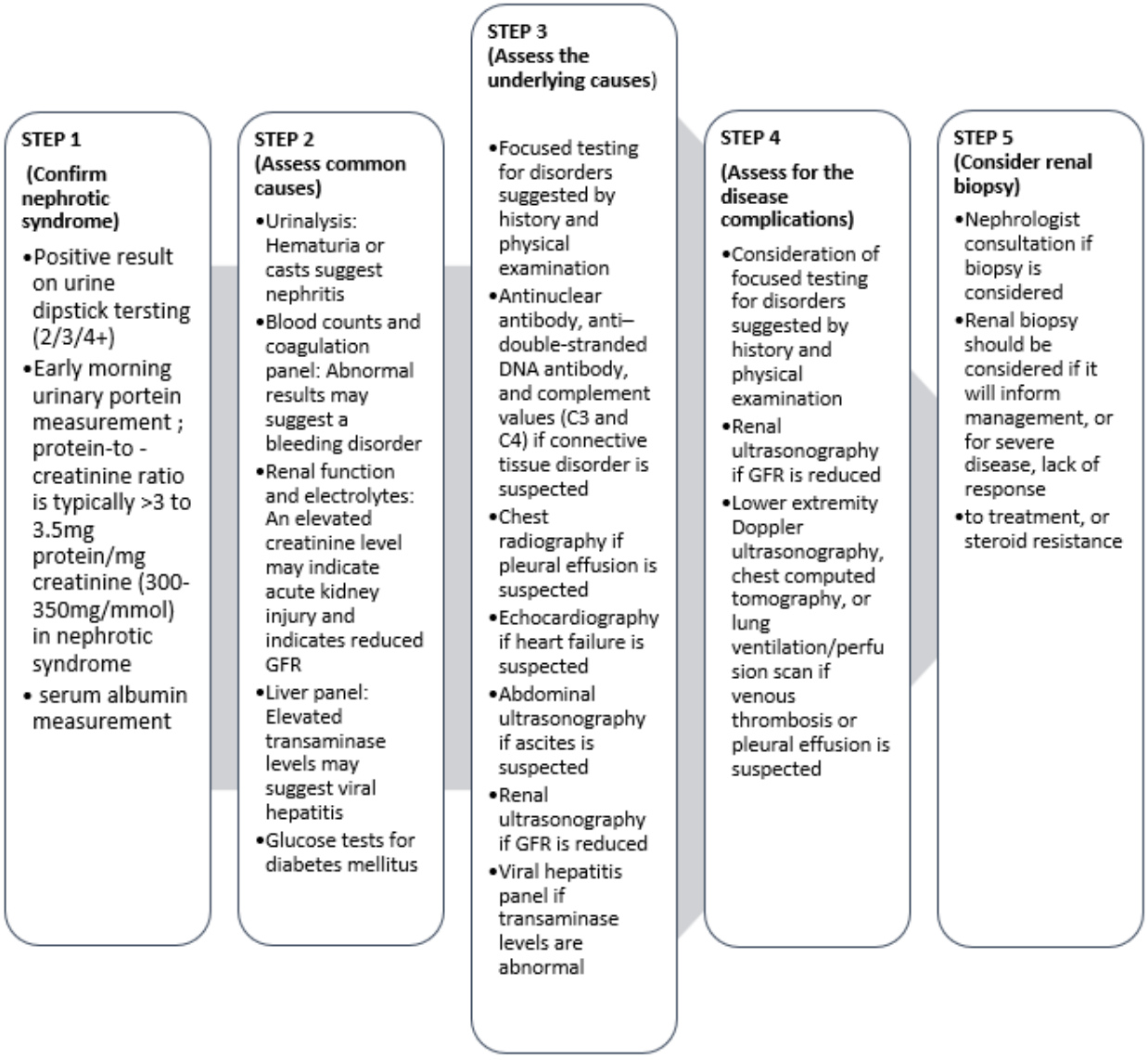

Figure 2. Algorithm for the diagnosis of nephrotic syndrome in adults, adapted from Hull et al, 2008(9)

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