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Atypical Relapse of Nephrotic Syndrome Without Edema in an Adolescent: A Case Report

[1]I Gusti Putu Ayu Susilawati Wida Lestari*, [2]Febriyanti Angghita Putri Duarsa, [3]Putu Pradnyanita Mustika
[1] Department of Pediatrics, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia*; email: ayususilawati.as@gmail.com
[2] Department of Pediatrics, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia; email: febriduarsa@gmail.com
[3] Department of Pediatrics, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia; email: pradnyamustika@gmail.com
*Correspondence

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Abstract
Introduction: *Relapse of nephrotic syndrome in children is typically characterized by the recurrence of edema accompanied by proteinuria. However, some patients may present with atypical clinical manifestations without edema, which can lead to delayed diagnosis and treatment. This case report aims to describe an atypical relapse of nephrotic syndrome without edema in an adolescent and to highlight the diagnostic approach, clinical course, and management during hospitalization.* ***Case Report:*** *A 16-year-8-month-old male adolescent with a previous diagnosis of nephrotic syndrome presented with acute left flank pain, brownish and foamy urine, and no peripheral or periorbital edema. Clinical findings, laboratory investigations, treatment, and follow-up data were collected and analyzed. Laboratory evaluation revealed massive proteinuria, mild hypocalcemia, and vitamin D deficiency, while renal function remained within normal limits.* ***Discussion:*** *The patient was diagnosed with atypical relapse of nephrotic syndrome without edema and was treated with full-dose prednisone, supportive therapy, and serial clinical and laboratory monitoring. Potential precipitating factors included chronic productive cough and temporary nonadherence to prednisone therapy. Significant clinical improvement was observed during five days of hospitalization. At outpatient follow-up, urinalysis showed negative urinary protein and blood findings without the development of edema, indicating complete remission.* ***Conclusion:*** *Relapse of nephrotic syndrome in adolescents can occur without edema and present with atypical manifestations. Careful evaluation of proteinuria, prompt initiation of appropriate therapy, and close clinical monitoring are essential to achieve favorable clinical outcomes.*

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Introduction

Nephrotic syndrome is the most common glomerular disorder in children and is characterized by massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia (Mbanefo & Sampson, 2022; Hilmanto *et al*., 2022; Jalanko *et al*., 2022; Lal & Perveen, 2026). The disease results from increased permeability of the glomerular filtration barrier, leading to significant urinary protein loss and systemic complications (Trautmann *et al*., 2023). The global incidence of childhood nephrotic syndrome ranges from 1.15 to 16.9 cases per 100,000 children annually, while the prevalence in Indonesia is estimated at approximately 6 cases per 100,000 children under 14 years of age (Mbanefo & Sampson, 2022; Trautmann *et al*., 2023; UKK Nefrologi Ikatan Dokter Anak Indonesia, 2021). The condition occurs more frequently in boys, and minimal change disease remains the predominant histopathological finding in pediatric patients (UKK Nefrologi Ikatan Dokter Anak Indonesia, 2021; Trautmann *et al*., 2023). Most pediatric patients are classified as having steroid-sensitive nephrotic syndrome, with approximately 85-90% achieving remission after corticosteroid therapy (Trautmann *et al*., 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). Despite favorable treatment response, nephrotic syndrome remains an important cause of morbidity in children and adolescents because of its chronic relapsing course and potential complications (Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025).

Relapse is a common feature of steroid-sensitive nephrotic syndrome and is defined as the recurrence of significant proteinuria after previous remission has been achieved (Trautmann *et al*., 2023; Yamanto *et al*., 2020). The International Pediatric Nephrology Association guideline reports that 70-80% of children with steroid-sensitive nephrotic syndrome experience at least one relapse, while up to 50% may develop frequently relapsing or steroid-dependent disease (Trautmann *et al*., 2023). Recurrent relapse is associated with prolonged corticosteroid exposure, increased risk of treatment-related adverse effects, and reduced quality of life (Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025; Vivarelli *et al*., 2023). Several precipitating factors have been identified, including upper respiratory tract infections, immunologic activation, and poor adherence to corticosteroid therapy (Vivarelli *et al*., 2023; Roy *et al*., 2021). Early recognition of these triggers is important to reduce disease-related complications and prevent delayed management (Trautmann *et al*., 2023). Therefore, careful clinical and laboratory monitoring remains essential during the long-term follow-up of pediatric nephrotic syndrome patients (Wang *et al*., 2023).

Edema is widely recognized as the hallmark manifestation of nephrotic syndrome and often becomes the primary reason patients seek medical attention (Mbanefo & Sampson, 2022; UKK Nefrologi Ikatan Dokter Anak Indonesia, 2021). In routine clinical practice, recurrence of edema commonly serves as an early sign of relapse and prompts further evaluation (Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). However, according to the Kidney Disease: Improving Global Outcomes and International Pediatric Nephrology Association guidelines, relapse is established based on recurrent nephrotic-range proteinuria rather than the presence of edema itself (Trautmann *et al*., 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). The Ikatan Dokter Anak Indonesia also emphasizes the importance of routine urine protein monitoring in children with previous nephrotic syndrome (UKK Nefrologi Ikatan Dokter Anak Indonesia, 2021).

Consequently, the absence of edema does not exclude relapse and may create diagnostic challenges if clinicians rely solely on physical findings. This condition highlights the importance of maintaining a high index of suspicion and performing serial urinalysis in patients with a history of nephrotic syndrome (Trautmann *et al*., 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025).

Relapse of nephrotic syndrome without clinical edema is an uncommon presentation, particularly in adolescents (Rodriguez-Ballestas & Reid-Adam, 2022). Patients may present with nonspecific manifestations such as flank pain, foamy urine, or urine discoloration that can mimic urinary tract infection, acute glomerulonephritis, nephrolithiasis, or musculoskeletal disorders. Early relapse may occur before hypoalbuminemia becomes severe enough to reduce plasma oncotic pressure and produce clinically apparent edema, making massive proteinuria the only objective finding during initial evaluation (Trautmann *et al*., 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). Lack of awareness regarding this atypical presentation may delay diagnosis and appropriate corticosteroid treatment (Trautmann *et al*., 2023; Coondoo *et al*., 2014). The present case report describes an atypical relapse of steroid-sensitive nephrotic syndrome in a 16-year-old male adolescent who presented with acute left flank pain, brownish foamy urine, and massive proteinuria without peripheral or periorbital edema. This report aims to emphasize the diagnostic challenges and clinical importance of considering relapse in pediatric nephrotic syndrome patients who develop urinary abnormalities despite the absence of edema.

Case Report

A 16-year-8-month-old male adolescent presented to the Emergency Department with a complaint of left flank pain that had started one day prior to admission. The pain had a sudden onset, worsened with coughing and walking, and was accompanied by brownish and foamy urine. The patient denied other symptoms such as periorbital or peripheral edema. One day before the onset of symptoms, the patient had completed a long-distance car trip from Jember.

The patient had a history of nephrotic syndrome diagnosed in January 2026 and had been regularly followed at the pediatric outpatient clinic. At the time of initial diagnosis, he presented with periorbital edema, bilateral lower extremity edema extending to the scrotum, and progressive shortness of breath. He received initial prednisone therapy at a dose of 2 mg/kg/day (maximum 80 mg/day) for four weeks, followed by an alternating-dose regimen of 1.5 mg/kg every 48 hours starting in March 2026. The patient admitted that he had missed one day of prednisone during the Eid holiday because he forgot to take the medication. Since February 2026, reddish spots had appeared on the neck and chest after starting prednisone therapy, prompting the patient to self-administer topical betamethasone ointment. In addition, he reported chronic productive cough that had worsened four days before admission. A Mantoux test performed in January 2026 was negative.

The social history revealed that the patient had previously used electronic cigarettes (vaping) daily for approximately six months and smoked about five conventional cigarettes per day. He also admitted to occasionally sharing vaping devices with friends. His smoking habit had been reduced since January 2026 after the diagnosis of nephrotic syndrome. In addition, the patient had a history of alcohol consumption before the diagnosis and continued to consume alcohol occasionally afterward.

On physical examination, the patient appeared moderately ill and was fully conscious (Glasgow Coma Scale E4V5M6). Vital signs were as follows: blood pressure 107/58 mmHg, pulse rate 72 beats/minute, respiratory rate 20 breaths/minute, body temperature 37°C, and oxygen saturation 99% on room air. Body weight was 62 kg and height was 167 cm. Nutritional status was assessed as normal with a well-nourished appearance. No peripheral or periorbital edema was observed. Local examination showed tenderness over the left flank region without costovertebral angle tenderness.

Based on the previous history of nephrotic syndrome and the presence of massive proteinuria without peripheral or periorbital edema, the patient was diagnosed with atypical relapse of nephrotic syndrome without edema. He was admitted for inpatient management and received full-dose prednisone (maximum 60 mg/day), a low-salt diet, supportive therapy, and serial clinical and laboratory monitoring. The patient was hospitalized for five days and showed significant clinical improvement during the admission period.

Laboratory Investigations

The patient underwent laboratory investigations including complete blood count, blood chemistry, complete urinalysis, serum electrolytes, calcium level, and vitamin D level to establish the diagnosis and evaluate his clinical condition.

Table 1
Complete Blood Count

Parameter	04/04/2026	08/04/2026	Reference Range
Leukocytes (×10³/µL)	19.20	17.16	4.0-10.0
Hemoglobin (g/dL)	15.3	16.1	13.0-18.0
Hematocrit (%)	43.7	47.0	40.0-54.0
Platelets (×10³/µL)	402	491	150-400

Table 2
Complete Urinalysis

Parameter	04/04/2026	08/04/2026	Reference Range
Color	Yellow	Yellow	Yellow
Clarity	Slightly cloudy	Clear	Clear
Specific gravity	>1.030	1.020	1.000-1.030
pH	6.5	7.5	4.5-8.0
Protein	4+	3+	Negative
Blood	1+	Negative	Negative
Red blood cells	1-3/HPF	Negative	0-2/HPF
White blood cells	0-2/HPF	0-1/HPF	0-1/HPF
Bacteria	Positive	Negative	Negative

Table 3
Blood Chemistry (04/04/2026)

Parameter	Result	Reference Range
Blood urea nitrogen	17 mg/dL	10-50
Serum creatinine	0.7 mg/dL	0.3-1.2
Random blood glucose	111 mg/dL	80-200
Estimated glomerular filtration rate	131 mL/min/1.73 m²	-

Table 4
Serum Electrolytes (04/04/2026)

Parameter	Result	Reference Range
Sodium	138 mmol/L	130-145
Potassium	3.9 mmol/L	3.5-5.5
Chloride	101 mmol/L	95-108

Table 5
Calcium and Vitamin D Levels (07/04/2026)

Parameter	Result	Reference Range
Serum calcium	9.1 mg/dL	9.3-10.7
Total 25-OH vitamin D	10.40 ng/mL	30-100

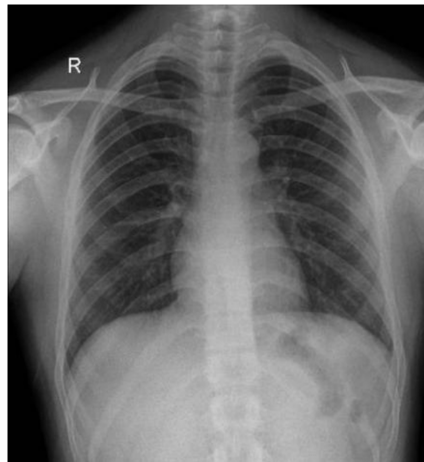

Figure 1. Chest X-Ray (Anteroposterior View, 22/01/2026)

No abnormalities were observed in the cardiac silhouette or pulmonary fields.

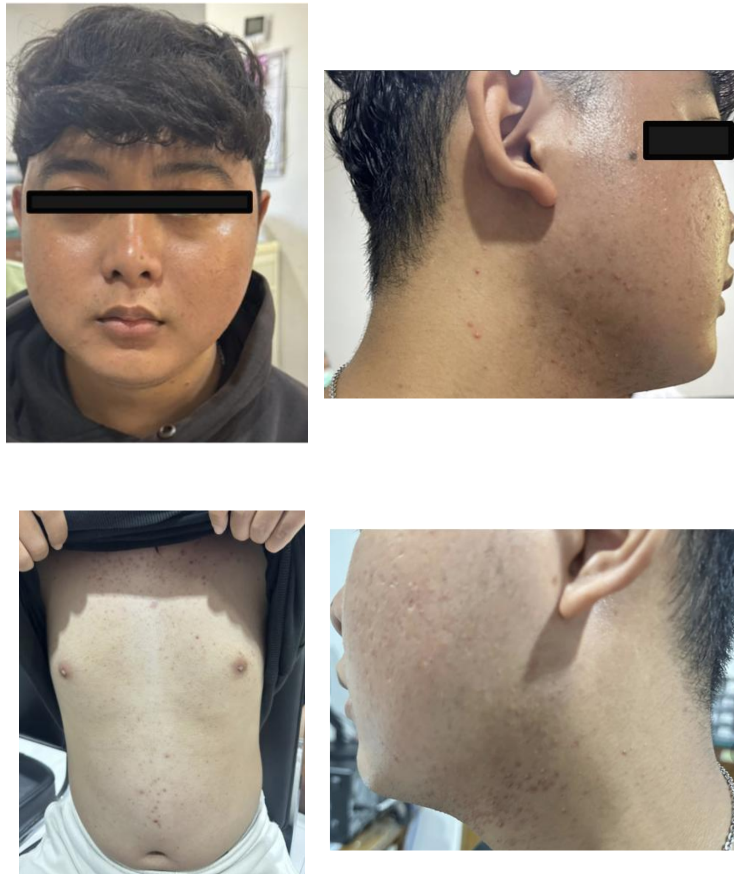

Figure 2. Clinical Photographs

Diagnosis

Based on the previous history of nephrotic syndrome and the finding of massive proteinuria without peripheral or periorbital edema, the patient was diagnosed with relapse of nephrotic syndrome without edema. In addition, mild hypocalcemia, vitamin D deficiency, and dermatitis suspected to be related to corticosteroid use were identified.

Management

The patient was treated with oral full-dose prednisone at a maximum dose of 60 mg/day, a low-salt diet, and supportive therapy consisting of oral paracetamol 500 mg three times daily and topical betamethasone ointment. During hospitalization, serial clinical and laboratory monitoring was performed, including assessment of general condition, vital signs, urine output, fluid balance, and repeated laboratory evaluation.
Because the productive cough persisted during hospitalization and was accompanied by sputum mixed with reddish-brown streaks, empirical antibiotic therapy with intravenous ceftriaxone 1 g every 12 hours was initiated on the third day of hospitalization.

Clinical Course

On the first day of hospitalization, the patient continued to complain of left flank pain, particularly when coughing and changing position, accompanied by brownish and foamy urine. He also reported productive cough and the appearance of brownish patches on the neck and back without itching. Laboratory evaluation showed leukocytosis (19.20 $\times 10^3/\mu L$), while urinalysis revealed 4+ proteinuria and 1+ hematuria. Renal function remained within normal limits, with blood urea nitrogen of 17 mg/dL and an estimated glomerular filtration rate of 131 mL/min/1.73 m^2.

On the second day, the left flank pain was still present but had begun to improve. The patient reported that the urine appeared dark yellow and remained foamy, without dysuria. On the third day, the left flank pain improved further and was only slightly noticeable during coughing. The urine became clearer, although still foamy. The productive cough persisted and was accompanied by sputum mixed with brownish blood streaks; therefore, empirical intravenous ceftriaxone 1 g every 12 hours was initiated. Additional investigations including chest radiography and serum calcium and vitamin D measurements were performed on the same day.

On the fourth day, both the flank pain and productive cough had decreased, and there was no longer any blood-streaked sputum. Chest radiography was unremarkable, while laboratory testing revealed vitamin D deficiency (10.40 ng/mL) and mild hypocalcemia (9.1 mg/dL).

On the fifth day, the patient no longer complained of flank pain, and the urine appeared clear yellow, although still foamy. The cough had also improved. Follow-up laboratory results showed improvement compared with previous tests, with leukocyte count of 17.16 $\times 10^3/\mu L$, proteinuria reduced to 3+, and negative urinary blood. The patient was discharged in improved clinical condition with continuation therapy consisting of full-dose prednisone (maximum 60 mg/day), vitamin D3 5000 IU once daily, cefixime 200 mg twice daily, and Tremenza 30 mg three times daily. Outpatient follow-up was scheduled for clinical evaluation and serial urinalysis. At outpatient follow-up, the patient had no peripheral or periorbital edema. Urinalysis showed negative urinary protein and negative urinary blood, indicating complete remission.

1. Discussion

Nephrotic syndrome is the most common glomerular disease in children and is characterized by massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia (Mbanefo & Sampson, 2022). Relapse in nephrotic syndrome is defined as the recurrence of significant proteinuria after a previous remission has been achieved (Trautmann *et al.*, 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). Most relapses in pediatric nephrotic syndrome are accompanied by peripheral and/or periorbital edema, making edema one of the principal clinical clues to disease recurrence (Trautmann *et al.*, 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). In the present case, however, relapse occurred in the absence of clinical edema despite the presence of massive proteinuria. This atypical presentation resulted in nonspecific manifestations and had the potential to delay diagnosis and treatment.

The diagnosis of relapse in this patient was established based on the prior history of nephrotic syndrome and the reappearance of nephrotic-range proteinuria, with urine dipstick protein of 4+ on urinalysis. According to the Kidney Disease: Improving Global Outcomes and International Pediatric Nephrology Association guidelines, relapse in childhood nephrotic syndrome is defined by urine protein of ≥3+ for three consecutive days or a urine protein-to-creatinine ratio ≥2 mg/mg after previous remission (Trautmann *et al*., 2023; Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group, 2025). In this case, although no peripheral or periorbital edema was observed during hospitalization, the presence of foamy urine and massive proteinuria strongly supported the diagnosis of relapse.

The absence of edema in this case may be explained by the early phase of relapse, in which proteinuria has already recurred but plasma oncotic pressure has not yet declined sufficiently to produce fluid transudation into the interstitial space. Early detection in a patient with known nephrotic syndrome may also allow diagnosis to be established before edema becomes clinically evident. This phenomenon shows that relapse does not invariably present with edema and that urinary abnormalities may precede overt physical findings (Trautmann *et al*., 2023). Therefore, regular urine protein monitoring remains essential in all patients with a history of nephrotic syndrome, regardless of the presence or absence of edema.

The initial presentation of left flank pain and brownish urine created a diagnostic challenge because these symptoms may mimic urinary tract infection, acute glomerulonephritis, nephrolithiasis, or musculoskeletal disorders. However, renal function was preserved, blood pressure remained normal, and no edema was present, making alternative diagnoses such as acute nephritic syndrome less likely. In addition, the rapid clinical and laboratory improvement following full-dose prednisone therapy further supported the diagnosis of nephrotic syndrome relapse. This case shows the importance of maintaining a broad differential diagnosis while considering relapse in any patient with a history of nephrotic syndrome who presents with urinary abnormalities (Coondoo *et al*., 2014).

The course of childhood nephrotic syndrome is often influenced by identifiable relapse triggers, particularly infections and poor adherence to corticosteroid therapy (Trautmann *et al*., 2023; Vivarelli *et al*., 2023; Roy *et al*., 2021). In this patient, persistent productive cough before symptom worsening and omission of prednisone for one day were both plausible precipitating factors. Upper respiratory tract infections are among the most common triggers of relapse in steroid-sensitive nephrotic syndrome through immune activation and increased glomerular permeability (Trautmann *et al*., 2023). Likewise, nonadherence to corticosteroid treatment has been associated with a significantly increased risk of recurrence (Roy *et al*., 2021).

This patient was also found to have vitamin D deficiency accompanied by mild hypocalcemia. Mineral metabolism abnormalities are common in nephrotic syndrome due to urinary loss of vitamin D-binding protein and prolonged corticosteroid exposure (Vivarelli *et al*., 2023). These mechanisms may contribute to reduced serum concentrations of both vitamin D and calcium. Correction of these abnormalities is important because vitamin D deficiency may adversely affect bone health, particularly in adolescents receiving repeated or prolonged corticosteroid therapy.

In addition, the patient developed hyperpigmented lesions over the neck and back during corticosteroid treatment. Cutaneous adverse effects of long-term corticosteroid use include pigmentary changes, steroid acne, skin atrophy, and steroid-related dermatitis (Coondoo *et al*., 2014). In the present case, dermatologic consultation was not performed; therefore, a definitive diagnosis of the skin lesions could not be established. Nevertheless, clinicians should remain vigilant for dermatologic complications during prolonged steroid therapy.

During hospitalization, the patient showed progressive clinical improvement, including resolution of flank pain and normalization of urine color. Serial laboratory evaluations showed disappearance of hematuria and a reduction in proteinuria from 4+ to 3+ by the time of discharge. At outpatient follow-up, urinalysis revealed negative urine protein and negative urine blood without the development of edema, indicating complete remission. These findings show an excellent response to full-dose prednisone therapy and support the diagnosis of steroid-sensitive nephrotic syndrome relapse.

This case underscores that relapse of nephrotic syndrome may occur without clinical edema, and clinicians should not rely solely on the presence of edema to recognize disease recurrence. Periodic urine protein evaluation remains essential in patients with a history of nephrotic syndrome, particularly when atypical symptoms or known precipitating factors such as infection and medication nonadherence are present. Early recognition and prompt treatment are critical to achieving favorable clinical outcomes and preventing unnecessary diagnostic delays.

Conclusion

Relapse of nephrotic syndrome in children is typically accompanied by edema; however, this case shows that relapse may occur without clinical edema, resulting in atypical manifestations that can delay diagnosis. In patients with a history of nephrotic syndrome, evaluation of proteinuria remains essential even in the absence of edema, particularly when potential relapse triggers such as infection and medication nonadherence are present. This case shows the importance of maintaining a high index of clinical suspicion for atypical presentations of nephrotic syndrome relapse in adolescents to facilitate timely diagnosis, prompt initiation of appropriate therapy, and favorable clinical outcomes.

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