

CLINICAL CASE REPORTS

Syphilis as a rare cause of nephrotic syndrome in Paediatrics: a case report

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ABSTRACT

Syphilis is a rare but recognised cause of renal involvement, including nephrotic syndrome. Membranous nephropathy is the glomerulopathy most commonly associated with *Treponema pallidum* infection, typically mediated by immune complexes containing bacterial antigens. We report the case of a previously healthy 15-year-old female who presented with nephrotic syndrome, characterised by periorbital and lower limb oedema, accompanied by nonspecific respiratory symptoms. Laboratory evaluation revealed nephrotic-range proteinuria, hypoalbuminaemia, and preserved renal function. As part of the aetiological work-up, serological testing for syphilis (VDRL and TPHA) was positive. A kidney biopsy confirmed membranous nephropathy. The patient was treated with benzathine penicillin G and prednisolone, resulting in resolution of oedema, proteinuria and hypoalbuminemia. This case underscores the importance of taking a thorough sexual history and screening for sexually transmitted infections in adolescents presenting with nephrotic syndrome. Syphilis should be considered a relevant differential diagnosis, particularly given the rising prevalence of sexually transmitted diseases among young people.

Keywords: adolescent; membranous nephropathy; nephrotic syndrome; sexually transmitted diseases; syphilis

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INTRODUCTION

Syphilis is a sexually transmitted infection (STI) caused by the spirochaete *Treponema pallidum*. It remains a significant global public health concern, with approximately eight million new infections reported annually among adolescents and young adults (aged 15–49 years) worldwide.⁽¹⁾ In Europe, data from the European Centre for Disease Prevention and Control (ECDC) indicate that, in 2022, 35,391 confirmed cases of syphilis were reported across the 29 EU/EEA Member States, corresponding to a crude notification rate of 8.5 cases per 100,000 inhabitants. This represents a 34% increase compared with 2021.⁽²⁾ Portugal is one of the 21 countries where an upward trend has been observed, mirroring the broader European landscape.⁽²⁾

Described as the “great imitator,” syphilis can present with a wide range of symptoms, including renal complications.⁽³⁾ Nephrotic syndrome is a rare but well-documented complication of secondary syphilis, with case studies highlighting this association.⁽⁴⁾ Membranous nephropathy (MN), characterised by subepithelial immune complex deposition along the glomerular basement membrane, is the most common histopathological correlate of nephrotic syndrome in secondary syphilis.⁽⁵⁾

Clinically, nephrotic syndrome in these cases presents suddenly, typically without hypertension and with preserved renal function. It may be transient, with spontaneous remission, or persist over time.⁽⁶⁾

We report the case of an adolescent with nephrotic syndrome secondary to syphilis infection, emphasising the need for thorough evaluation in cases of nephrotic syndrome. Screening to exclude possible STIs is necessary, given the rising prevalence of STIs among youth (15–49 years).

CASE DESCRIPTION

A previously healthy 15-year-old female presented to the Emergency Department with a one-week history of cough, rhinorrhoea, and nasal congestion, accompanied by periorbital and lower limb oedema, both of which had progressed over the previous three days and recent weight gain (although this could not be quantified due to the absence of prior weight measurements). The patient also reported abdominal pain and occasional nausea. On the day prior to admission, she experienced facial oedema, oropharyngeal discomfort, and dyspnoea. There was no history of recent infection, vaccination, or medication use prior to symptom onset.

On physical examination, bilateral periorbital and facial oedema were prominent, along with lower limb oedema with pitting extending up to the knees. Palpation of the abdomen revealed mild periumbilical discomfort, without hepatosplenomegaly. Pulmonary auscultation was unremarkable. Blood pressure was within the normal range

for age. No skin changes, mucosal lesions, alopecia, or lymphadenopathy were observed.

Initial laboratory evaluation revealed hypoalbuminemia (20 g/L; reference range, 35–50 g/L). Urinalysis showed 3+ proteinuria, with an unremarkable urinary sediment. Quantification confirmed nephrotic-range proteinuria, with a urine protein-to-creatinine ratio of 20 mg/mg. Renal function was preserved, with serum urea and creatinine levels within normal limits. Complement studies and autoimmune screening were unremarkable. Laboratory findings are summarised in **Table 1**.

An abdominal ultrasound was performed, showing no evidence of organomegaly or ascites. Renal ultrasound revealed normal-sized kidneys with preserved corticomedullary differentiation and no structural abnormalities.

Based on the clinical and laboratory findings, the patient was diagnosed with new-onset nephrotic syndrome and was admitted for inpatient care. Corticosteroid therapy was initiated with oral prednisolone at a dose of 80 mg/day. After two days of hospitalisation, the patient's condition worsened, with increased pain and cutaneous inflammatory signs in the abdominal region. She developed fever and an increase in inflammatory markers (maximum C-reactive protein 72.2 mg/L and peak procalcitonin level 21 ng/mL). Assuming abdominal wall cellulitis as a complication of nephrotic syndrome, a seven-day course of cefotaxime and clindamycin was started, with complete apyrexia, resolution of the inflammatory signs and normalisation of the laboratory inflammatory markers in 72 hours. She remained hemodynamically stable.

During hospitalisation, and as part of the aetiological workup for secondary causes of nephrotic syndrome, serological screening for infectious diseases, including syphilis, was performed.

Following a positive Venereal Disease Research Laboratory (VDRL) screening test, a *Treponema pallidum* haemagglutination (TPHA) test and anti-*Treponema pallidum* IgM antibody were ordered, confirming *Treponema pallidum* infection. Other STIs were ruled out, including Human Immunodeficiency Virus (HIV), Hepatitis B, Hepatitis C, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae*. Treatment with intramuscular benzathine penicillin G (2.4 million IU) was initiated. There was no evidence of sexual abuse, and the patient reported a sexual partner, who was notified and referred for appropriate evaluation and treatment. Despite the review of the anamnesis during hospitalisation, only during an outpatient appointment did the adolescent reveal a history of risky sexual behaviour and the development of a genital ulcer approximately six weeks prior to hospital admission. In the absence of this information, it was decided to administer Penicillin once weekly for three weeks instead of treating with a single dose. The patient and her mother were informed about the disease and about the importance of contact tracing.

A renal biopsy was performed subsequently to further characterise the underlying aetiology. Histological findings

were consistent with membranous nephropathy (**Figure 1**). No specific staining for *Treponema pallidum* was performed, and no direct bacterial deposits were identified.

The patient was discharged after significant clinical improvement, with complete resolution of oedema, normalisation of serum albumin, and improving proteinuria (protein-to-creatinine ratio 0.1 mg/mg). Complete remission

of nephrotic syndrome was achieved one week after initiation of benzathine penicillin G. Corticosteroid therapy was subsequently tapered to prednisolone 60 mg/day for four weeks, followed by 40 mg on alternate days, and discontinued after a total of eight weeks. At three-month follow-up, the patient remains in complete clinical remission, with an eightfold decline in VDRL titres (1:16).

Table 1 - Laboratory test results.

Laboratory parameters	Results	Reference range
Haemoglobin (g/L)	13.8	12 - 16
Leucocytes (x10 ⁹ /L)	19.5	4.5 - 13
Neutrophils (x10 ⁹ /L)	16.3	4.5 - 13
Platelets (x10 ⁹ /L)	543	150 - 450
PT (seconds)	11.1	10.2 - 12.0
aPTT (seconds)	29.8	26 - 37
Fibrinogen (g/L)	4.6	1.54 – 4.88
Urea (mg/dL)	34	18 - 45
Serum creatinine (mg/dL)	0.9	0.5 - 0.9
Serum albumin (g/L)	20.0	32.0 - 45.0
Sodium (mmol/L)	135	136 - 146
Potassium (mmol/L)	4.8	3.40 - 4.70
Calcium (mg/dL)	8.1	8.40 - 10.20
Total proteins (g/L)	46.7	60 - 80
AST (U/L)	23	<23
ALT (U/L)	11	<18
LDH (U/L)	312	0.00 - 240
Total cholesterol (mg/dL)	248	112 - 207
LDL-cholesterol (mg/dL)	150	<130
C-reactive protein (mg/L)	5.5	<5.0
Immunoglobulin G (g/L)	7.69	6.5 - 18.50
Immunoglobulin M (g/L)	2.30	0.40 - 2.30

Immunoglobulin A (g/L)	2.68	0.70 - 4.00
C3 complement fraction (g/L)	1.47	0.90 - 1.80
C4 complement fraction (g/L)	0.20	0.10 - 0.40
ANA	Positive (1:80)	
Anti-ds-DNA	Negative	
C-ANCA (PR3)	Negative	
Rapid plasma reagin (RPR)	Positive (1:128)	
Respiratory pathogen PCR panel	Rhinovirus (+)	
Serologies for EBV, CMV, HIV, HBsAg, and HCV	Negative	
Chlamydia trachomatis & Neisseria gonorrhoeae PCR	Negative	
Urine protein-to-creatinine ratio (mg/mg)	20	<0.2

Abbreviations: **ALT**, alanine transaminase; **ANA**, antinuclear antibody; **Anti-ds-DNA**, anti-double-stranded deoxyribonucleic acid antibodies; **aPTT**, activated partial thromboplastin time; **AST**, aspartate transaminase; **C-ANCA**, antineutrophil cytoplasmic autoantibody; **CMV**, cytomegalovirus; **CRP**, C-reactive protein; **EBV**, Epstein-Barr virus; **HBsAg**, Hepatitis B surface antigen; **HCV**, Hepatitis C virus; **HIV**, Human Immunodeficiency Virus; **LDH**, lactate dehydrogenase; **PCR**, polymerase chain reaction; **PT**, prothrombin time; **RPR**, rapid plasma reagin; **VDRL**, venereal disease research laboratory.

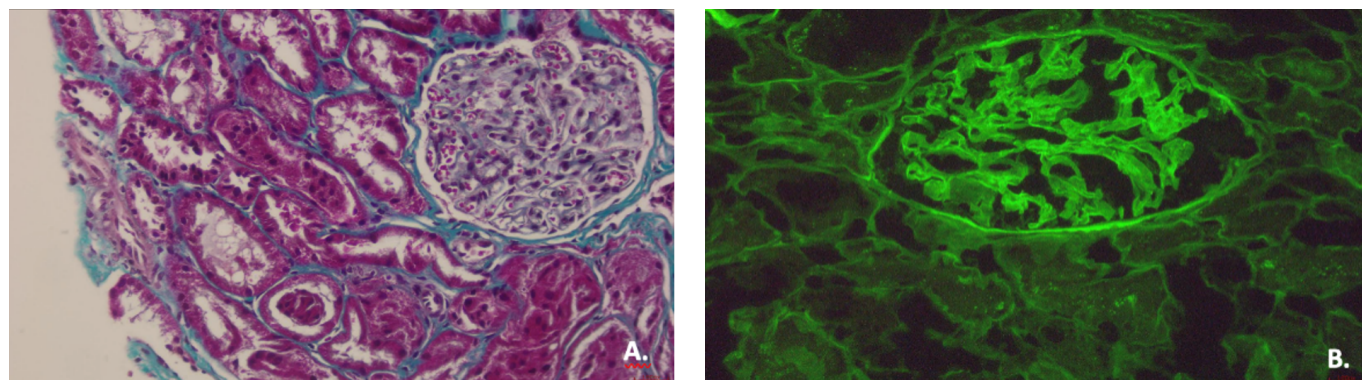


Figure 1- **A** – Masson's trichrome stain in the light microscopic study: The paraffin-embedded sample consisted of two cortical fragments containing 11 glomeruli, without the capsule, medulla, or medium-calibre arteries. All glomeruli exhibited mild thickening of the capillary walls and podocyte hypertrophy. **B** – Immunofluorescence study performed on frozen sections revealed granular parietal deposits of IgG (++), IgM (+), C3 (++), C1q (++), kappa (++), and lambda (++).

DISCUSSION

This case describes a previously healthy adolescent who presented with new-onset nephrotic syndrome associated with *Treponema pallidum* infection. A review of the literature reinforces the need to consider sexually transmitted diseases in the differential diagnosis of nephrotic syndrome, particularly

in sexually active adolescents.⁽⁷⁾

The association between secondary syphilis and renal complications can manifest as acute kidney injury, membranoproliferative glomerulonephritis, interstitial nephritis, or nephrotic syndrome. Secondary syphilis can affect the kidney through several mechanisms, with histological patterns including membranous nephropathy,

membranoproliferative glomerulonephritis, and interstitial nephritis, which may present clinically as nephrotic syndrome, nephritic syndrome, or acute kidney injury.⁽⁵⁾ In most cases of nephrotic syndrome secondary to syphilis, renal pathology reveals a pattern consistent with membranous nephropathy.⁽⁸⁾ It would have been valuable to search for anti-neuron-derived neurotrophic factor (NDNF) antibodies in kidney biopsy tissue, as seen in patients with syphilis and membranous nephropathy.⁽⁹⁾ However, this test is not available at our hospital.

Secondary syphilis presents with highly heterogeneous symptoms, typically including fever, lymphadenopathy, hepatosplenomegaly, and a skin rash.⁽⁴⁾ Nephrotic syndrome is usually characterised by a sudden onset of oedema, proteinuria, and hypoalbuminemia, without hypertension, and with preserved renal function.⁽⁶⁾ In our case, the clinical and laboratory presentation is consistent with reports in the literature, presenting with normal blood pressure, preserved renal function, hypoalbuminaemia, and nephrotic-range proteinuria. Since our patient did not exhibit other symptoms of secondary syphilis, we assumed the nephrotic syndrome was the first manifestation. Direct identification of *Treponema pallidum* in renal tissue is not routinely performed and was not available in our case, with diagnosis relying on serological findings and clinicopathological correlation.

Treatment with benzathine penicillin G is effective, leading to resolution of both the infection and its associated renal manifestations.^(4,5,8) Similar favourable renal outcomes were observed in the recent series reported by Fang *et al.*, in which treatment of the underlying infection was associated with significant improvement in kidney manifestations across different histopathological patterns.⁽⁹⁾ Most cases of NDNF-associated membranous nephropathy respond to penicillin treatment and do not require immunosuppression.⁽¹⁰⁾ Clinical reports prior to the discovery of this antibody also revealed a good response to penicillin without the need for immunosuppression. In our case, corticosteroid therapy was initiated before the diagnosis of syphilis was established, in line with standard management of idiopathic nephrotic syndrome. However, following confirmation of syphilis and the rapid remission observed after initiation of benzathine penicillin G, continuation of corticosteroid therapy for a total of 8 weeks may be questioned. Given that most cases of syphilis-associated membranous nephropathy respond to antibiotic therapy alone, prolonged corticosteroid use may have been unnecessary and could expose patients to avoidable adverse effects.

These findings are consistent with previous reports documenting a favourable prognosis when early diagnosis is achieved and appropriate therapy is initiated.⁽¹¹⁾

The clinical history revealed significant risk factors for STIs, such as unprotected sexual intercourse with multiple partners and a previous genital lesion. This underscores the importance of a thorough clinical history and physical examination, as well as routine STI screening in patients with risk factors – particularly adolescents, who may be reluctant to disclose

risky behaviours, thereby hindering the recognition of STIs. Delayed diagnosis of infections such as syphilis can lead to inappropriate treatment and complications.

CONCLUSION

The incidence of STIs, including syphilis, is increasing worldwide. This case reinforces the importance of considering infectious causes, including STIs, in the differential diagnosis of nephrotic syndrome, particularly in adolescent patients. Integrating testing for syphilis and other STIs into the aetiological workup of glomerulopathies may facilitate early diagnosis and prevent therapeutic delays. Among adolescents, raising awareness of safe sexual practices and promoting screening programmes are essential to prevent complications such as those observed in this case.

AUTHORSHIP

Swasilanne Bandeira - Conceptualization; Writing – original draft; Final approval

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Maria Sotto-Maior Costa - Clinical data interpretation; Writing – review & editing; Final approval

Madalena Almeida Borges - Clinical data interpretation; Writing – review & editing; Final approval

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Gisela Neto - Clinical data interpretation; Writing – review & editing; Supervision; Final approval

PATIENT CONSENT FOR PUBLICATION

Assent from the patient and written informed consent from the patient's legal guardian were obtained for publication of this case report and any accompanying images.

PUBLICATION ETHICS

This clinical case has not been previously presented or published and is not under consideration by any other journal. An abstract of this case report has been submitted for presentation at the upcoming 58th Annual Meeting of the

European Society for Paediatric Nephrology (ESPN), to be held from 15–18 October 2025 in Athens.

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