CASE REPORT

Secondary syphilis: a rare cause of nephrotic syndrome

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SUMMARY

A 59-year-old man with a history of type 2 diabetes and a left nephrectomy following trauma reported of malaise and weakness. He reported a penile ulcer 2 months earlier, but there had been no lymphadenopathy or fever. His speech was slurred, he was breathless on minimal exertion and there was ankle swelling. Twenty-four hours later he developed a generalised maculopapular rash. Laboratory investigation confirmed syphilis and nephrotic syndrome. He was treated with a single injection of benzylpenicillin following which there was a rapid and complete recovery. The temporal association and improvement with treatment suggest that syphilis caused his illness. The incidence of syphilis is increasing and doctors should remain alert to syphilis as a possible cause of the nephrotic syndrome.

BACKGROUND

A severe presentation of nephrotic syndrome is not frequent, and its association with syphilis, although reported in the past, is rarely seen in modern times. The increasing incidence of syphilis suggests that we will see more patients with associated complications.

CASE PRESENTATION

A 59-year-old fisherman, married and living in a rural area, with a medical history of type 2 diabetes mellitus diagnosed 5 years earlier, medicated with oral antidiabetics, with poor compliance. He had a left nephrectomy 30 years earlier from firearm-related trauma.

He presented at the emergency department reporting of progressive general malaise and muscle weakness, without loss of consciousness or sphincter incontinence, with peripheral oedema. He also mentioned a penile ulcer 2 months prior to this episode, with local pruritus, already healed. He denied fever or adenopathies, tick bites, risky sexual behaviour and non-steroidal anti-inflammatory drugs intake.

At admission, examination showed a drowsy patient with slurred speech, but awake and without focal deficits. He was eupneic at rest but breathless on slight exertion, showing an enlarged abdomen, distended but depressible and not painful and lower limbs with exuberant oedema without dermatological features. He had blood pressure of 138/88 mm Hg, regular pulse rate of 77 bpm and tympanic temperature of 36°C. He had a body weight of 92 kg, about 10 kg above his usual weight.

His initial laboratory workup was positive for white cell count (WBC) in the urine and proteinuria. He was started on antibiotics for urinary tract infection and admitted to the ward for investigation of probable nephrotic syndrome.

On day 2, we observed a cutaneous disseminated maculopapular non-pruritic rash (figure 1), with involvement of torso, limbs and palmoplantar regions. At this point, rickettsiosis was suspected (although no tick bite like injury was found), but the next day we discovered lesions in the genital area, with inflammatory balanitis, purulent exudate and paraphimosis, leading to the clinical diagnosis of secondary syphilis.

INVESTIGATIONS

On initial workup, blood and serum test showed white cell count (WBC) 14 900/µL, C reactive protein <0.3 mg/dL, Cr 2.6 mg/dL and blood urea nitrogen 174 mg/dL (previously normal), albumin 0.6 mg/dL, normal glutamic-oxalacetic transminase, glutamic pyruvic transminase and lactate dehydrogenase, total cholesterol 394 mg/dL. C3, C4 and IgA levels were normal. Urinary analysis showed protein (4+), WBC (2+), proteinuria 27 g/24 h, without haematuria. Chest X-ray showed only diaphragm elevation.

We screened the patient for sexually transmitted diseases: Venereal Disease Research Laboratory test (VDRL) (+) treponema pallidum particle agglutination assay (TPPA) (+), syphilis IgM antibody (+), HBs-Ag (+), HBe-Ag (–), HBe-Ab (+), HBc-Ab (+), HBs-Ab (+). HIV and hepatitis C testing were negative.

Renal biopsy had relative contraindication because of a solitary kidney, and we decided not to perform it.

Renal ultrasound showed right kidney with compensatory hypertrophy and ascites.

Autoimmune study was negative for antinuclear antibodies, anti-dsDNA antibody, rheumatoid factor and antineutrophil cytoplasmic antibody. C3, C4 and IgA levels were normal.

Head CT and lumbar punction were performed, and the result was unremarkable.

DIFFERENTIAL DIAGNOSIS

This patient had several comorbidities that could result in a nephrotic syndrome:

Hyperfiltration due to a solitary kidney can cause secondary focal and segmental glomerulosclerosis. This usually presents with insidious proteinuria and clinical course, more commonly associated with non-nephrotic proteinuria. In the rare cases that it courses with nephrotic levels, it is usually without peripheral oedema or hypoalbuminaemia.

Diabetic nephropathy also presents with insidious proteinuria and is associated with other disease-related complications, usually in patients with long-standing diabetes.

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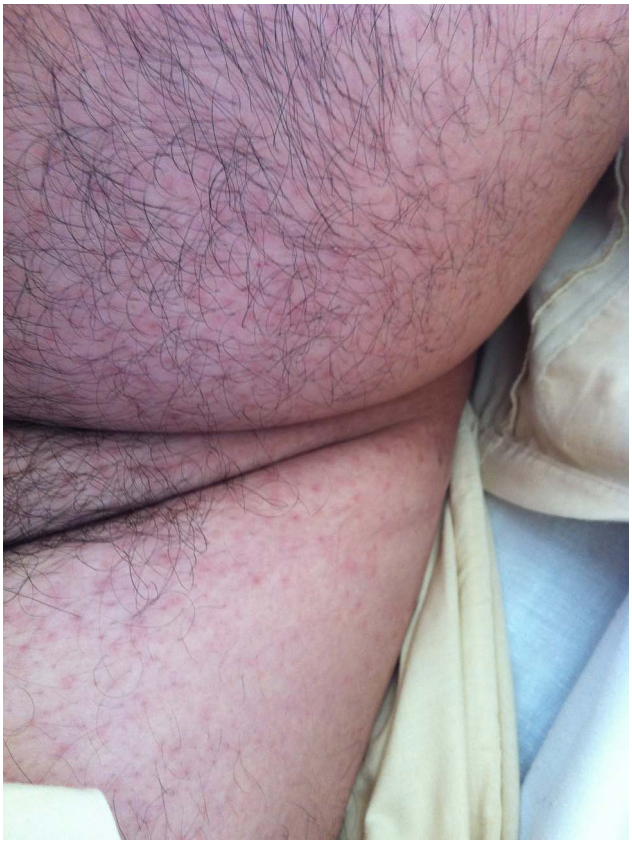

Figure 1 Cutaneous disseminated maculopapular non-pruritic rash.

Secondary membranous nephropathy is usually associated with autoimmune diseases, but it can also be caused by infections, certain medications and tumours. Among the infectious causes hepatitis B is relatively common, but nephrotic-range proteinuria occurs in the acute phase of this disease when elevated liver enzymes and positive Hbe antigen can also be found.

Another rare but known infectious cause of nephritic syndrome is secondary syphilis, usually with a severe clinical presentation and heavy proteinuria, as found in this patient. It is characterised by clinical and laboratorial resolution within months after aetiological treatment.[1]

TREATMENT

The patient was initially started on amoxiclavulanate for urinary tract infection, and then added doxycycline for suspected rickettsiosis.

After clinical diagnosis of secondary syphilis, he was given a single intramuscular dose of 2,400.000 UI benzathine penicillin. The initial antibiotics were suspended at this point.

For the nephrotic syndrome, the patient was started on enalapril, furosemide, simvastatine and enoxaparine (full anticoagulation dose), and he did not receive any steroids or any immunosuppressive agent.

OUTCOME AND FOLLOW-UP

The patient showed clinical improvement, with diuresis over 120 mL/h, decreasing abdominal volume, and weight loss of 9.5 kg in the first week. The neurological findings disappeared shortly after admission.

He was re-evaluated weekly after discharge, and 6 weeks later he had: TPPA (–), creatinine 0.7 mg/dL, albumin 2.4 g/dL, proteinuria 2.5 g/24 h, with no oedema. He maintained clinical and laboratorial improvement resulting in complete recovery 4 months after the diagnosis (creatinine 0.8 mg/dL, albumin 3.9 g/dL, total cholesterol 212 mg/dL and without significant proteinuria).

DISCUSSION

Our patient presented with a nephrotic syndrome at the same time as he was diagnosed with secondary syphilis. This association has been recognised for a long time. In 1935, in a series of over 1000 patients with syphilis, Herman and Marr described 7.1% patients with proteinuria and 0.28% patients with nephrotic syndrome.[2] We found about 10 cases with this association in the last 25 years,[3–12] proving this to be a rare complication of syphilis. In most of these cases, the clinical presentation was exuberant and patients showed recovery within months after treatment. When renal biopsy was performed, the diagnosis was membranous glomerulonephritis.[4 5 8 9 11 12]

Although proof is not possible, remission following treatment with penicillin is consistent with a causal relationship. Doctors should remain alert to the possibility of syphilis as a cause of the nephrotic syndrome.

Learning points

- Syphilis remains a rare cause of the nephrotic syndrome.
- Patients may deny risky sexual behaviour.
- The nephrotic syndrome of syphilis may recover completely following treatment of the underlying condition.

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