A previously healthy 33-year-old heterosexual male with rectal pain and bleeding and profuse nocturnal sweating was admitted to the gastroenterology department of our hospital. He appeared moderately ill with a normal temperature of 37.0 °C, a blood pressure of 120/70 mmHg and a regular pulse of 70 beats/min. Subtle periorbital oedema and a firm rectal mass, suspicious for carcinoma, were the only remarkable clinical findings. Relevant laboratory tests were as follows: erythrocyte sedimentation rate 75 mm/hour (<15), haemoglobin 7.7 mmol/l (8.7 to 10.9), creatinine 59 μmol/l (70 to 110), total protein 58 g/l (60 to 80), albumin 21 g/l (34 to 48), cholesterol 6.60 mmol/l (3.0 to 6.4) and urine was dipstick positive for protein. A suspected nephrotic syndrome was confirmed by a 24-hour urine collection with 19 grams of protein and a selectivity index of 12, indicating selective proteinuria. A kidney biopsy was performed. Light microscopy revealed sporadic irregularity of the glomerular basement membrane consistent with spikes (figure 1). Furthermore, an abundant accumulation of silver positive granules in the tubular cells were seen. Immunofluorescence showed a diffuse, weak, deposition of IgG in a granular pattern and to a lesser extent of IgM and C3 (figure 2). According to the Churg classification, a mild membranous glomerulopathy stage I was present.

Meanwhile colonoscopy had been performed and an ulcer was seen at 5 cm, of which the biopsies showed granulomatous inflammation (figure 3). Computer tomography of the abdomen showed, in addition to a localised rectal lesion, perirectal, presacral and iliaca lymphadenopathy.

**What is your diagnosis?**

See page 377 for the answer to this photo quiz.
**DIAGNOSIS**

The diagnosis of nephrotic syndrome associated with secondary syphilis was made. Serological tests were positive, while no other sexually transmitted diseases (HIV, lymphogranuloma venereum) were found (table 1). A causal relationship was strongly supported by complete resolution of proteinuria within one week after initiating benzylpenicillin. Before the penicillin-era renal involvement was a well-recognised complication of syphilis, with an incidence varying from 0.3 to 8%<sup>1</sup>. Nephropathy usually occurs in the secondary stage, four to ten weeks after the initial chancre. Since syphilis became a well-treatable disease, advanced stages of syphilis – and thus associated renal involvement – have become rare. However, since 2001 a rising incidence of syphilis has been reported in Western countries, often accompanied with HIV co-infection. Proteinuria is usually found and may vary from transient mild albuminuria to a fulminating nephrotic syndrome.<sup>1</sup> Presentation with acute nephritic syndrome, acute renal failure<sup>1</sup> or salt-losing nephropathy<sup>2</sup> are less commonly reported. Membranous nephropathy as histopathological substrate is frequently reported, but minimal change nephropathy, rapidly progressive glomerulonephritis with formation of crescents<sup>3</sup> or interstitial nephritis<sup>2</sup> may also occur in association with syphilis. Immunofluorescence studies show granular deposition of immunoglobulins, mainly IgG, and C3, along the basement membrane and at electron microscopy subepithelial electron dense deposits are seen.<sup>1</sup> These findings suggest syphilis-related nephropathy is caused by immune-complex deposition. This hypothesis is supported by the identification of elutable anti-treponemal antibodies or a treponemal antigen in the glomeruli of patients with syphilis-related kidney disease.<sup>2</sup> Diagnosis of a syphilis-related nephropathy may be difficult and requires thorough questioning and physical examination. Diagnostic criteria include a recent infection, co-existence of kidney disease with a late primary or secondary stage, positive serological tests, remission after initiating penicillin therapy and exclusion of other potential causes such as other underlying diseases or co-medication.<sup>4</sup>

**CONCLUSION**

Sexually transmitted diseases, including syphilis, remain an important cause of secondary forms of the nephrotic syndrome. Recognition of syphilis-related nephropathy is important, as complete recovery can simply be achieved by initiating antibiotic therapy.

**REFERENCES**