Case Report

Salt loss and hyponatraemia in a patient with syphilitic nephritis

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Keywords: hyponatraemia; interstitial nephritis; salt-losing nephropathy; syphilis

Introduction

The relationship between syphilis and nephropathy has been recognized for >100 years [1]. Nephropathy may appear in either congenital syphilis or the secondary stage of an acquired infection [2,3]. Nephropathy is an infrequent complication of acquired syphilis but may develop clinically in the secondary stage of the infection [3]. Most patients display a nephrotic syndrome [4]. Membranous glomerulonephritis or diffuse endocapillary glomerulonephritis with or without crescent formation were the main pathological findings in adults with acquired syphilis [5]. Interstitial nephritis, being the dominant feature, was rarely documented in the literature.

We report an unusual occurrence of secondary syphilis with interstitial nephritis due to recurrent hyponatraemia from salt-losing nephropathy. Penicillin treatment completely resolved the salt-losing nephropathy and intractable hyponatraemia.

Case

A 67-year-old male had hypertension with β-blocker control for many years. Around 6 months before admission, he had left side numbness, dizziness and mildly slurred speech. Magnetic resonance imaging (MRI) of the brain revealed a small ventral medullary infarct. On examination, he was dehydrated in appearance. Blood pressure was 130/90 mmHg with a pulse rate of 90/min. Meanwhile, hyponatraemia (Na 129 meq/l), renal insufficiency [blood urea nitrogen (BUN) 16 mg/dl, creatinine (Cr) 1.6 mg/dl] and positive rapid plasma reagin (RPR)/treponema pallidum haemagglutination (TPHA) (1:1/1:80) were found. Urinalysis revealed a specific gravity of 1.005, pH 7.0, no protein, no red blood cells and no white blood cells. The urinary sodium was 73 meq/l. Serum sodium and serum creatinine were normal (Na 138 meq/l, Cr 1.4 mg/dl) following normal saline infusion for 2 days, while all other symptoms improved concurrently.

Two months later, the patient presented with comparable symptoms (numbness of the extremities of the limbs, dizziness on postural change) to the emergency department. He appeared dehydrated with orthostatic hypotension. Hyponatraemia (Na 118 meq/l), renal insufficiency (BUN 16 mg/dl, Cr 1.8 mg/dl) and positive RPR/TPHA (1:1/1:80) were recorded. The survey of haemogram, biochemical data and urinalysis appeared normal. Urinary sodium was 70 meq/l. Numbness, dizziness, renal insufficiency (Cr 1.5 mg/dl) and sodium concentration (134 meq/l) improved following normal saline infusion for 7 days afterwards.

During the following month, hyponatraemia, renal insufficiency and disturbance of consciousness appeared several times and improved uneventfully following saline infusion. The serum creatinine was as low as 0.9 mg/dl following saline infusion. The positive RPR/TPHA (1:1/1:80) persisted. The hormone survey revealed normal serum thyroxine, thyroid-stimulating hormone and cortisol levels, but high normal serum renin (58.3 µU/ml) and aldosterone (84.8 pg/ml) levels. The clinical profile also indicated the relatively hypovolaemic status of the patient at each presentation.

On the day of admission, he was found unconscious again on the street. On admission, he was totally disoriented and in delirium status. His temperature was 36.5°C. pulse 74 beats/min and the respiration 18/min. Blood pressure was 160/80 mmHg. Physical examination showed a flat jugular vein in the supine position. Skin and mucosa were dry. Examination disclosed a painless erosion over the penis, scrotum and sacral area. The haemogram indicated red blood cells 3.85 × 10⁶/ml, haemoglobin 11.5 g/dl, haematocrit 31%, platelets 234 000/ml and white blood cell count 5.5 × 10⁹/l (with the segment 66.4%, and lymphocyte 23.4%). Biochemical data showed serum creatinine 1.3 mg/dl, BUN 15 mg/dl, sodium 117 meq/l and potassium 4.0 meq/l. Serum albumin was 3.9 g/dl, taken ~2 weeks preceding this admission. Serum RPR/TPHA was raised to 1:2/1:160. Urinalysis revealed a
specific gravity of 1.007, pH 7.0, with no protein, no red blood cells and no white cells. Urine sodium concentration was 70 meq/l on admission. Serum sodium concentration returned to 131 meq/l following 2 days of saline infusion. Meanwhile, the urinary sodium concentration was raised to the level of 169 meq/l during saline infusion. A study of the cerebrospinal fluid (CSF) was normal without evidence of neurosyphilis. Antidiuretic hormone (ADH) was low (0.8 IU/l) on recovery of volume status. The low ADH level implied that his hyponatraemia was not caused by inappropriate secretion of ADH. Postural dizziness and delirium diminished following saline infusion and improvement of hyponatraemia.

Salt-losing nephropathy due to syphilis tubulointerstitial disease was considered to be the primary disease causing his recurrent volume depletion. Blood and urine bacterial culture were negative. Percutaneous renal biopsy revealed that most glomeruli were relatively unaffected except for mild hypercellularity. Renal tubules exhibited moderate to severe atrophy, while the interstitium showed severe fibrosis with profound mononuclear cell infiltration. Some unaffected proximal tubules were also observed in the renal cortex. Immunofluorescence sections disclosed >30 glomeruli with all stains negative. Electronic microscopy showed no deposits. Neither non-steroidal anti-inflammatory drugs (NSAIDs) nor other medication capable of causing interstitial nephritis appeared in his medication history. He underwent penicillin therapy intramuscularly with benzathine penicillin G 2.4 × 10⁶ U per week for 1 month under the diagnosis of suspected acute and chronic tubulointerstitial nephritis owing to syphilis. Urinary sodium examination dropped to 37 meq/l 2 weeks later following penicillin treatment, when serum sodium returned to 136 meq/l. Postural dizziness and delirium were absent throughout 12 months of follow-up. The follow-up of serum RPR/TPHA was weakly positive (1:1/1:80) at 6 months and 1:1/1:4 in 12 months.

Discussion

The relationship between syphilis and renal disease was first reported in the 19th century, although it is recognized as unusual. Nephropathy may develop in congenital syphilis [2]. Renal involvement is also an uncommon but well-described complication of secondary syphilis, and may begin to appear in the secondary stage of the infection [3].

The spectrum of renal involvement in the early spirochaetemic stage of syphilis encompasses proteinuria, acute nephrosis and, uncommonly, acute haemorrhagic nephritis [2]. Proteinuria is usually mild and transient. Acute nephrosis is a temporary nephrotic syndrome without marked haematuria, hypertension or azotaemia. The amount of proteinuria may be as large as 53 g/24 h [5]. Most patients manifest a nephrotic syndrome, which becomes clinically apparent contemporaneously with development of typical skin lesions [4]. Microscopic haematuria, hypertension or impaired renal function occurred rarely. Pathologically, most acquired syphilitic nephropathy in adults shows membranous glomerulonephritis on light microscopy, often accompanied by a slight mesangial proliferation. Immunofluorescence discloses subepithelial electron-dense deposits containing IgG and complement [6].

The patient demonstrated a rare presentation of recurrent hyponatraemia resulting from salt-losing nephropathy. No microscopic haematuria or proteinuria occurred. Persistent renal salt wasting must come from the renal tubular defect of sodium reabsorption under normal salt intake. Syphilis-related tubulointerstitial disturbance might be a possible cause of the sodium reabsorption defect without any obvious offending toxins or medications. We then decided to perform a renal biopsy to see if there was an underlying tubulointerstitial disease which could explain the persistent renal salt wasting even with normal urine analysis. Urine analysis usually reveals white cells, red cells and white cell casts in tubulointerstitial disease. However, a relatively normal urinalysis might suggest renal tubulointerstitial disease with mild glomerular involvement. With chronic renal disease, disorders that should be considered include pre-renal disease and tubulointerstitial diseases with minor glomerular disturbance [7]. Bossini et al. [8] also found that 30% of urinalysis was normal in Sjogren’s syndrome patients with tubulointerstitial disease, which was only evidenced by urinary concentrating disorders. It is likely that some of the renal tubulointerstitial diseases present with functional dysfunction without urine abnormality and our patient might have similar clinical presentation. The kidney biopsy of the patient revealed interstitial nephritis without prominent glomerular alteration. The immunofluorescence study found no immunoglobulin or complement deposition. Electron microscopy revealed no subepithelial electron-dense deposit.

It is always difficult to establish a causal relationship between syphilis and renal disease [5]. It has been stated that a diagnosis of syphilitic nephropathy probably can never be established with certainty. Commonly accepted criteria include history of recent infection, co-existence of late primary or secondary syphilis with nephropathy, a positive serological test, spontaneous remission or rapid recovery following antisyphilitic therapy, and absence of other causes of renal disease [2]. The patient fulfilled these criteria without history of exposure to offending drugs, systemic disease or evidence of malignancy. Following the penicillin therapy, there was a dramatic resolution of hyponatraemia without salt supplement. Repeated serology tests revealed positive RPR/TPHA 1:1/1:80 several times before admission and 1:2/1:160 on admission. Penicillin therapy resolved the hyponatraemia which caused salt loss and reduced serology titres from 1:2/1:160 at the time of admission to weakly positive 1:1/1:80 four weeks later, 1:1/1:80 six months later and
1:1/1:4 after 1 year. The observed recovery of hyponatraemia and falling serology titre indirectly imply that syphilis might be related to the salt-losing renal interstitial disease. This patient possibly experienced seldom met tubulointerstitial nephritis in secondary syphilis. Docolomansky et al. also reported a case of secondary syphilis with interstitial nephritis in 1973 [9].

This investigation indicated that the appearance of interstitial nephritis with salt handling impairment might represent a clinical picture of an acquired syphilis with renal involvement. Interstitial nephritis can be treatable and should be taken into consideration when diagnosing a patient with salt-losing nephropathy.

Conflict of interest statement. None declared.

[See related Editorial Comment by van Assen et al. (doi:10.1093/ndt/gfh792)]

References


Received for publication: 8.4.04
Accepted in revised form: 15.2.05