Why is a shrunken bladder and a nephrotic kidney an expression of the same disease?

Case

A 29-year-old Chinese woman presented with a 4 week history of progressive urinary frequency, dysuria and leg edema. She was forced to urinate every 10 min, resulting in great irritability and sleeplessness. Furthermore, she felt mild abdominal fullness and dyspnea. She was therefore referred to our department for evaluation. Her abdomen was bulging without tenderness or bowel sounds arrest. There was no erythema, joint swelling or Raynaud’s phenomenon. On admission, her urinalysis showed heavy proteinuria. She was found to have nephritic syndrome (proteinuria 4.5 g/24 h, serum albumin level 2.8 g/dl) and active urinary sediment (6–8 red cells/high power field, but no leukocytes or casts). Repeated urinary cultures showed no bacteria. Renal function was altered: serum creatinine was 3.9 mg/dl and creatinine clearance rate was 20 ml/min. There was no anaemia, but blood lymphocyte count had decreased to 900/ml. No fluid levels were seen on plain abdominal X-rays. Ultrasonogram and abdominal scan CT showed severe bilateral hydroureteronephrosis and hydroureter (Figure 1a). Cystoscopy revealed a bladder capacity of 25 ml with a contracted thickened bladder wall, diffuse hyperaemia, edema and friability of mucosa without visualization of both ureteral orifices. Voiding cystourethrogram showed a small and contracted bladder with thickened and irregular walls without diverticula, and no vesicoureteral reflux was demonstrated (Figure 2). Biopsy of the bladder wall revealed changes of interstitial cystitis disclosing diffuse edema of the submucosal tissue, and no active vasculitis. At that time an antegrade pyelography confirmed bilateral hydroureteronephrosis. We immediately inserted a bilateral ureteral JJ tube. However, because renal function was stable 3 weeks later, we removed the JJ tubes and no further surgical procedure was performed.

Although her antinuclear antibodies were positive, there was no other finding suggestive of active systemic lupus erythematosus (SLE). Renal biopsy specimens obtained 1 week after admission showed mild mesangial proliferative glomerulonephritis (Figure 3).

Urodynamic studies that were performed 3 weeks after hospitalization were normal. The patient was treated with 1 mg/Kg/day of prednisone, and her lower urinary tract symptoms markedly improved. Serum creatinine decreased to 0.7 mg/dl within 2 months with a marked improvement in the bilateral hydroureteronephrosis (Figure 1b), and gastrointestinal symptoms completely abated. Prednisone was tapered and the patient was maintained on prednisone at 12.5 mg/day. Her urinary protein excretion decreased markedly as she recovered from her contracted bladder condition.

Question

What is your diagnosis?
Answers to the quiz on the preceding page

Pathological diagnosis: SLE with lupus cystitis associated ureterohydronephrosis and class 2, WHO classification lupus nephritis

The association of urinary frequency with ureterohydronephrosis + mild abdominal fullness and mesangial proliferative glomerulonephritis in an Asian young woman led to two major diagnoses a lupus cystitis and/or chronic intestinal pseudo-obstruction (CIPO).

Interstitial cystitis, which itself is an uncommon lesion of the urinary bladder, was first described by Nitze [1] in 1907. The first case of interstitial cystitis with SLE, in which the urinary bladder contained deposits of IgG, IgM, IgA, and complement was called lupus cystitis by Orth et al. [2], and this nomenclature has been widely accepted. In SLE patients, interstitial cystitis was found in 11 out of 35 autopsies, and is estimated to occur in 0.5–1% of all SLE cases. Lupus cystitis may occur as an initial and/or isolated manifestation of SLE as in our patient.

Chronic interstitial cystitis (CIC) occurs mainly in middle-aged women who present with frequency and urgency. Of 34 patients with CIC, 25 were ANA positive among whom seven had SLE [3]. The manifestations of lupus cystitis in adults and children are similar and include vomiting, weight loss, frequency and urgency. Urinalysis reveals either no abnormality or only microscopic haematuria and is characterized by a negative cytology. The precise mechanisms involved in lupus cystitis remain obscure. Bladder biopsies of lupus cystitis show granular deposits of immune complex (IgG, IgA, IgM and C3, C1q) with monoclonal and polymorphonuclear leukocytes along blood vessel walls [4]. These findings suggest that immune complex-mediated vasculitis is one of the attributable causes of lupus cystitis. Segawa et al. [5] noted the elevation of interleukin-8 and monocyte chemotactic and activating factors, such as urinary chemokines, and their resolution after treatment. These findings provide insight into the mechanism of lupus cystitis. In contrast to idiopathic cystitis, lupus cystitis is frequently associated with hydroureteronephrosis, which is usually due to fibrosis of the ureterovesical junction, and to detrusor muscle spasm secondary to inflammation [2]. Mild gastrointestinal manifestations are common in SLE. Nausea, vomiting, diarrhoea and abdominal pain are found in more than 50% of these patients. These symptoms associated with ureterohydronephrosis in our patient mimicked an intestinal pseudo-obstruction syndrome.

Chronic intestinal pseudo-obstruction is a syndrome defined by the presence of chronic intestinal dilation and dysmotility in the absence of mechanical obstruction or gross inflammatory disease. The megacystis-microcolon intestinal hypoperistalsis syndrome was first described in 1976 as a cause of intestinal obstruction in the newborn. Neonatal presentation of this syndrome includes intestinal occlusion, abdominal distension and bilious vomiting. Late manifestations include abdominal bloating constipation and bilious vomiting with an initially normal intestinal transit [6]. The incidence of urological involvement varies from 33 to 92% and includes megacystis, hydronephrosis, urinary retention and infection [7]. There is an apparent association between lupus-related CIPO and ureterohydronephrosis: 66.7% (12/18) of patients had a concomitant dilated urinary pelvicalyceal system and a contracted urinary bladder, 33.3% (6/18) of these
patients had documented histological features of CIPO and 38.8% had glomerulonephritis (7/18) [8].

We believe that our patient presented with SLE with lupus cystitis and without CIPO evidence for this is the absence of megacystis and because plain abdominal X-ray films showed no gaseous distension of the small bowel and, in the upright films, no presence of fluid in the bowel loops. Treatment of SLE is with corticosteroids and immunosuppressive drugs. These are used and improve the prognosis of lupus cystitis [9] as in our patient.

Conflict of interest statement. None declared.

References

Sophie Georgin-Lavialle
Hassane Izzedine
Vincent Launay-Vacher
Benoît Barrou
Thierry Petitclerc
Gilbert Deray
1Department of Nephrology,
2Department of Urology,
Pitié Salpêtrière Hospital,
Paris, France,
Email: hassan.izzedine@psl.ap-hop-paris.fr