Teaching Point
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A 63-year-old man with acute abdominal pain and laboratory signs of rapid progressive renal disease

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Case

A 63-year-old previously healthy man complained of increasing dyspnoea for 2 weeks. A cardiologist saw him, and an echocardiograph showed a mild pericardial effusion. Serum creatinine concentration was 4.6 mg/dl, and the patient was admitted to our clinic for further diagnostic work-up. He had no history of renal disease, a routine serum creatinine was normal 6 months previously, and he was taking no regular medication. In addition to the dyspnoea, the patient complained of abdominal pain in the right lower quadrant that began 24 h before admission. Physical examination revealed normal pulmonary and cardiac findings (BP 150/90 mmHg), but a local tenderness in the lower right abdomen. Ultrasound showed fluid-filled bowels with reduced peristalsis; the kidneys appeared swollen and increased in size. Serum creatinine was 6.3 mg/dl, BUN 99 mg/dl, haemoglobin 12.1 g/dl, leukocytes 22.9 × 10⁹/l and C-reactive protein 210 mg/l. Urinalysis showed red blood cell casts, acanthocytes, and a proteinuria > 300 mg/dl (dipstick; a subsequent 24 h urine collection contained 1000 mg of albumin). Chest radiography was normal. A working diagnosis of an acute nephritic syndrome was made. The patient was scheduled for percutaneous renal biopsy the next day. However, during the night, he developed an abdominal emergency with signs of generalized peritonitis. Laparotomy revealed several ischaemic- and necrotic-appearing segments of the distal jejunum (Figure 1A) that were removed, and end-to-end anastomosis was performed. Histopathology showed necrotizing vasculitis of submucosal small vessels (arterioles and venules), infiltration of the vessel walls with neutrophils (Figure 1B) and hyaline thrombi. Medium size and larger vessels were normal. The patient was treated with intravenous methylprednisolone pulse therapy, followed by oral prednisolon. At this time, the results of further serological tests were obtained showing negative ANA, ENA and anti-GBM antibodies, normal C3 and C4, but a p-ANCA (antineutrophil cytoplasmic antibodies) against myeloperoxidase (MPO) of 32 (positive > 9), whereas c-ANCA (against proteinase 3) was negative. There was no serological evidence for hepatitis B or C, and no cryoglobulins could be detected.

Renal biopsy was performed 5 days later and showed a focal necrotizing glomerulonephritis with diffuse endothelial and mesangial proliferation with crescents (Figure 1C). However, some glomeruli were already sclerosed, suggesting ongoing disease for some time. Immunohistology showed deposition of fibrin (Figure 1D) but no granular or linear immunoglobulin deposits. Oral cyclophosphamide (75 mg) was added to his regimen. This reduced dose was selected because of severe reduction in renal function (serum creatinine was 7.8 mg/dl at this time). Unfortunately, renal function deteriorated further. The patient is now on maintenance haemodialysis. He is currently being treated with azathioprine, and so far has had no recurrence of abdominal pain. The p-ANCA recently was < 10.

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Discussion

This is an atypical case of microscopic polyarteritis with intestinal and renal, but not pulmonary, manifestations. More than 50 years ago, this disease was distinguished from classical polyarteritis nodosa that does not directly involve glomeruli and is a disease of medium-sized vessels [1]. In addition, microscopic polyarteritis differs from Wegener’s granulomatosis in the lack of granuloma formation and the less common occurrence of nasopharyngeal involvement. It has been argued that an increasing number of patients present with ‘overlap syndrome’ in which there is medium as well as small vessel involvement [2,3]. However, the bowel resection specimen in our case revealed only the presence of small vessel vasculitis without evidence of medium size vasculitis. Thus, we do not think that the present case represents an ‘overlap syndrome’ with jejunal polyarteritis nodosa manifestation.

Microscopic polyarteritis, the Churg–Strauss syndrome and Wegener’s granulomatosis are all associated with ANCA [2,3]. There is a prevalence of MPO ANCA in patients with microscopic polyarteritis [4]. Accumulating evidence suggests that ANCA are not only markers of small vessel vasculitis, but may play a pivotal role in pathophysiology [2]. ANCA induce
primed neutrophils and monocytes to undergo a respiratory burst, resulting in the release of toxic granule constituents into the local microenvironment [2]. Moreover, interaction of ANCA with leukocytes also triggers the transcription of a distinct subset of genes potentially involved in the injury of small vessels [5]. A recent animal model has been established that clearly demonstrates that MPO ANCA alone was able to cause pauci-immune glomerular necrosis and small vessel vasculitis [6]. This fascinating observation may eventually lead to the development of more specific therapies targeting primarily ANCA.

Vasculitis syndromes still present a major diagnostic challenge because diverse organ systems could be involved and the patient presents with an array of puzzling symptoms. The heterogeneity as well as overlap among the different subtypes of vasculitis contribute to the difficulties. Small vessel vasculitis could exhibit life-threatening extra-renal manifestations. Alveolar capillaritis with pulmonary haemorrhage has been considered as one of those complications, but other organ complications such as in this case also contribute to a high morbidity and mortality. Therefore, an early diagnosis is of considerable clinical importance because some types of vasculitis such as microscopic polyarteritis exhibit a high morbidity and require aggressive immunosuppressive therapy. The present case also shows that renal involvement may progress for some time unnoticed, and renal function deteriorates despite consequent immunosuppressive therapy. Immune complex-mediated or cryoglobulinemic vasculitis, various infections and inflammatory bowel diseases with treatment-associated renal problems are the major differential diagnosis of syndromes involving both the abdomen and the kidneys.

Teaching points

(i) Organ involvement in microscopic polyarteritis may vary from that commonly described in textbooks.
(ii) Abdominal involvement which can lead to life-threatening complications has to be considered.
(iii) The diagnosis of a microscopic polyarteritis has at least to be excluded in patients with an acute renal insufficiency and acute abdominal pain.

Conflict of interest statement. None declared.

References