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Clinical Report

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cANCA-associated aortitis

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Abstract
Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is traditionally viewed as a small vessel disease. We report a patient with cANCA antibodies directed against proteinase-3 with asymptomatic aortic involvement, in combination with diffuse alveolar haemorrhage and pauci-immune, necrotizing crescentic glomerulonephritis. A review of the literature is discussed.

Keywords: aortitis; cANCA; vasculitis; Wegener's granulomatosis

Introduction

Vasculitis comprises a group of clinical conditions linked by blood vessel inflammation. The Chapel Hill Consensus Conference Classification System classifies vasculitis according to vessel size and characteristic clinical and histopathological features [1]. Anti-neutrophil cytoplasmic antibodies (ANCA) have been used to further characterize the small-vessel vasculitides.

Large-vessel vasculitis comprises fewer clinical syndromes than medium- or small-vessel vasculitides, most commonly Giant Cell arteritis and Takayasu's arteritis. Large vessel involvement in ANCA-associated vasculitis is uncommon and, when present, often portends a poor prognosis, with outcomes involving aortic dissection, rupture and, possibly, stenosing arteritis. We describe a case of asymptomatic large vessel involvement in a biopsy-proven cANCA-associated small-vessel vasculitis.

Case

A 64-year-old Greek man, previously well, presented with a 4-week history of fever, malaise, dysuria and haematuria. He described intermittent pleuritic chest pain but no abdominal pain. A trial of antibiotics (roxithromycin and cephalexin) from his local doctor had not improved his symptoms. At presentation, he was normotensive. Relevant physical findings included crackles at the left lower lung field and minimal oedema in the lower extremities. Initial laboratory investigations demonstrated a serum creatinine of 92 μmol/L, with elevated inflammatory markers (C-reactive protein 29 mg/L; erythrocyte sedimentation rate 93 mm/h). Initial urine microscopy revealed heavy isomorphic haematuria without cellular casts and an *Escherichia coli* infection on culture. After treatment of the infection, urine microscopy demonstrated $>1000 \times 10^6$/L dysmorphic red cells and 24-h urine collection revealed significant proteinuria (1.05 g/day), with a creatinine clearance of 33 mL/min. A blurred outline of the abdominal aorta was revealed on computerized tomography (CT) scan, and subsequent CT aortogram revealed near circumferential soft tissue oedema of both the thoracic arch and inferior to the origin of the renal arteries. There was no narrowing or obliteration of the vessel lumen (Figure 1a).

His renal function deteriorated quickly, serum creatinine reaching 230 μmol/L. Renal biopsy confirmed the presence of a pauci-immune, necrotizing crescentic glomerulonephritis with fibrocellular crescents present in 40% of the glomeruli. A positive ANCA titre was subsequently detected with granular cytoplasmic staining showing specificity for proteinase-3 (55 U/mL).

Oral cyclophosphamide (1.5 mg/kg/day) and intravenous methylprednisolone (500 mg/day) were commenced; however, within a week, the patient developed diffuse alveolar haemorrhage. He required a total of six plasma exchanges $>$10 days. Despite treatment, the serum creatinine continued to rise (peaking at 650 μmol/L), and haemodialysis support was required for 1 week. The patient was discharged on cyclophosphamide (1.5 mg/kg/day) and prednisolone (60 mg/day). Serum creatinine on discharge was 342 μmol/L.

Two months after discharge, investigations revealed a serum creatinine of 167 μmol/L (cANCA 30 U/mL), Figure 2. A CT aortogram showed reduced aortic inflammation (Figure 1b). Clinical remission was evident after 3 months' treatment with cyclophosphamide, and methotrexate was commenced after the patient proved intolerant to azathioprine. Twenty months later, the patient has remained well with a serum creatinine of 115 μmol/L, with negligible haematuria (5×10^6/L erythrocytes on urine microscopy) and proteinuria (protein:creatinine ratio 0.010 g/mmol). There is no evidence of aortic vasculitis on CT scan, although the mid-thoracic and abdominal aorta remain mildly tortuous and ectatic.

Discussion

ANCA-associated large-vessel vasculitis (ALV) has rarely been reported in European and North American populations [2]. Large vessel involvement may precede small

vessel changes and may also occur in isolation [2]. The pathogenesis of ALV is unknown. It is possible that common pathological processes are involved in both large- and small-vessel vasculitis. Intimal injury may be the initial insult, progressing to inflammation of the medial layer and then adventitia, with resulting transmural aortitis [2]. Alternatively, the large vessel wall changes seen on imaging may be a result of vasculitis of the vasa vasorum of the aortic wall [3–5].

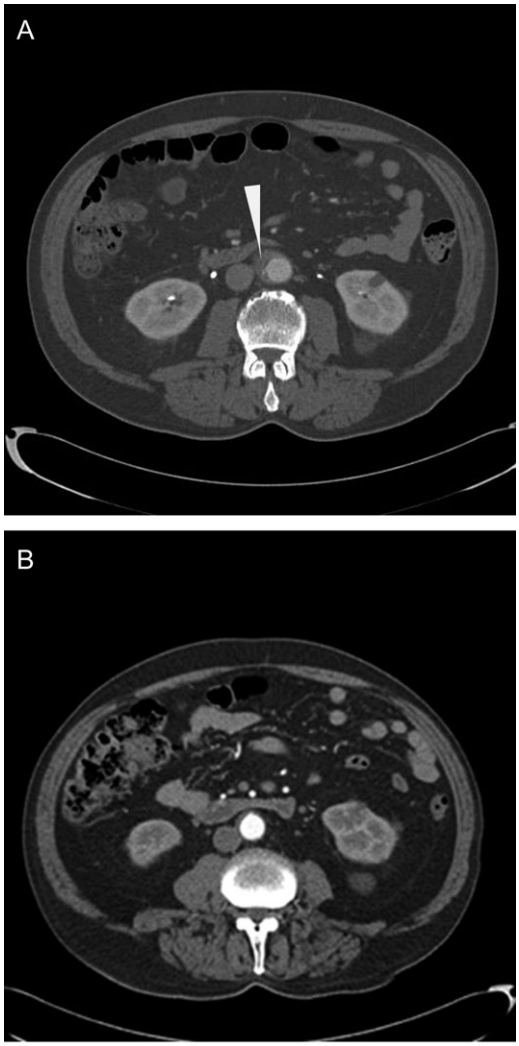

Fig. 1. (**A**) CT scan showing periaortic oedema of the abdominal aorta at diagnosis. (**B**) CT scan of abdominal aorta at 2 months (inflammation indicated by arrowheads).

The presentation of ANCA-associated large-vessel vasculitis is diverse but appears intrinsically different from the stenosing lesions of Takayasu's vasculitis [6–9]. Previous reports include prominent perivasculitis, arterial dilatation and aortic dissection and/or rupture. Case reports of Wegener's granulomatosis with large vessel involvement also include periaortitis, with resultant aortic aneurysm and dissection [2, 10].

Given the infrequent number of reports, there is no consensus on the management of patients with ALV. However, apart from surgical intervention for dissection or rupture, the finding of large vessel involvement does not appear to require additional treatment. Most patients have been managed with an extended period of immunosuppression using corticosteroids and cyclophosphamide, following similar regimens for small vessel disease. It also remains unclear how the aortitis should be followed. Our patient underwent a follow-up CT aortogram 2 and 20 months after diagnosis. For patients with significant renal impairment, contrast CT scans may risk contrast-induced nephropathy, and alternative options include magnetic resonance imaging or positron emission tomography scanning [8].

While ANCA-associated disease is often considered to be limited to small vessels, this case highlights that large vessels can also be affected. Its true frequency is unknown as involvement appears to be asymptomatic; however, though not seen in our patient, it can be associated with a poor outcome due to vessel rupture or dissection. This case illustrates the need for awareness of potential large vessel involvement in ANCA-associated small vessel disease.

Conflict of interest statement. None declared.

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Day	Creatinine (μmol/L)	Urinary RBC (x 10^6/HPF)	Total PCR (g/mmol)	ESR (mm/hr)	CRP (mg/L)	ANCA (U/mL)
1	95	>1000	0.06	67	39	
5	119	>1000	0.06	107	81	
10	213	>1000	-	107	119	55
15	326	>1000	0.07	-	195	
20	605	>1000	-	-	67	
31	342	500	0.05	29	4	31
60	144	100	0.04	27	<2	10

Fig. 2. Biochemical markers and response to treatment. RBC, red blood cells; HPF, high power field; PCR, protein:creatinine ratio; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

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