

A case of ANCA associated vasculitis in a patient presenting with chest pain

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Abstract

Antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is a group of multisystem autoimmune small vessel diseases. We report here a case of a 68-year-old woman who initially presented with 29-day history of chest pain, malaise and anorexia. Cardiac problems were ruled out and she was considered to have pneumonia. Her symptoms persisted and blood tests showed renal impairment and evidence of an inflammatory response. A kidney biopsy, chest computed tomography (CT) scan and ANCA testing confirmed a diagnosis of AAV renal injury. She was treated with glucocorticoids and cyclophosphamide (CTX) for six months at which time her kidney function had improved and she avoided the need for dialysis. This case study illustrates that the clinical manifestations of AAV are complex, varied, and prone to misdiagnosis.

Keywords

ANCA, AAV, rapidly progressive glomerulonephritis

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Introduction

Antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is an inflammatory disease of small blood vessels.¹

The clinical manifestations of AAV are varied, complex and may involve several

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body systems.^{1,2} The acute phase of the disease with accompanying severe symptoms is often preceded by a prodromal phase with aspecific symptoms.³ The relative rarity and heterogeneous nature of AAV poses diagnostic challenges and clinical misdiagnosis and mortality rates are high.^{4,5} Kidneys are one of the major target organs to be affected by AAV and renal involvement may be as high as 80%.⁶ Early diagnosis and initiation of effective treatment will lead to be a better outcome.³

We report here on patient who initially presented with chest pain, malaise and anorexia, and was suspected to have pneumonia. She deteriorated but her condition was identified and she was successfully treated with immunosuppressive therapy.

Case report

A 68-year-old woman was referred to our hospital with a 29-day history of chest pain accompanied by malaise and anorexia. She had previously been admitted to the Respiratory Medicine Department at Heyuan People's Hospital with sudden onset of chest pain, general fatigue and anorexia. At the previous hospital, she had undergone a medical examination that included a computed tomography (CT) scan of the chest, electrocardiograph (ECG) and blood tests for levels of cardiac troponin (cTn), creatinine kinase-MB isoenzyme (CK-MB) and inflammatory markers. No evidence of a myocardial infarction (MI) was found and the patient was suspected to have pneumonia. She received antibiotics (not specified) and a mucolytic agent and was discharged from hospital after 11 days later. At discharge her creatinine levels were elevated 152 $\mu\text{mol/l}$ (normal values, 44-75 $\mu\text{mol/l}$).⁷

Over the next few weeks, the patient showed no obvious improvement in her fatigue or anorexia. A blood sample taken by her local practitioner, 13 days after

discharge showed that her creatinine (429 $\mu\text{mol/l}$), potassium (2.9 mmol/l) and blood urea nitrogen (BUN; 18.7 mmol/l) were elevated and so she was referred to our hospital for further investigations.

Review of her medical history showed that she had experienced a transient ischemic attack two years previously and had been prescribed once daily simvastatin 40 mg and aspirin 0.1g. Her body weight was 47 kg, height 160 cm, body mass index (BMI) 18.3 kg/m^2 , systolic/diastolic blood pressure 123/77 mmHg and pulse rate 86 beats/min. Physical examination showed she was mildly anaemic, had no evidence of goitre, clinically palpable lymph nodes, gynecomastia or pruritus. Her visual fields were normal with no evidence of papilledema. Overall, the results of her physical examination were unremarkable. However, laboratory tests showed low serum levels of haemoglobin and potassium and elevated levels of white blood cells, phosphate, parathyroid hormone and creatinine (Table 1). Her estimated glomerular filtration rate (eGFR) was elevated and urinalysis showed high levels of protein, albumen and beta²-microglobulin. Nevertheless, her 24-hour urine output was within the normal range (1000–2000 ml) as was her urine osmolarity (296 $\text{mOsm/kg}\cdot\text{H}_2\text{O}$ [range 280 ~ 310 $\text{mOsm/kg}\cdot\text{H}_2\text{O}$]). Her serum was positive for perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) and myeloperoxidase (MPO)-ANCA and negative for hepatitis B and C viruses and human immunodeficiency virus (HIV).

Based on clinical and laboratory findings, the patient received a presumptive diagnosis of ANCA associated acute glomerulonephritis. To confirm this diagnosis, a kidney biopsy was performed. Comprehensive imaging of the tissues using light microscopy, immunofluorescence and electron microscopy plus results of the clinical examination confirmed the diagnosis of AAV renal injury. Lung

imaging was also performed and a few fibrous foci were found in both lungs.

Oral prednisone was prescribed at an initial dosage of 1 mg/kg/day with subsequent slow tapering to 0.5-0.25 mg/kg/day. The patient also received cyclophosphamide (CTX) by intravenous infusion 800 mg/m² every four weeks. Treatment continued for six months during which time she showed significant improvement from her initial assessment (Table 1). Her chest pain abated and she had no MPO-ANCA at 3 months but pANCA persisted for 5 months. Although some of her blood parameters were still elevated above normal levels at six months, her kidney function was

returning to its original level and she had avoided the need for dialysis.

The patient provided written informed consent before publication of this article and ethical approval was not necessary because the case was part of standard health care practice.

Discussion

AAV is a group of multisystem autoimmune small vessel diseases.⁶ The conditions are characterised by formation of granulomas and inflammation of small arteries, arterioles, venules, and capillaries. Untreated, the disease can be fatal and it is often

Table 1. Laboratory results for the patient at initial presentation and during the six-month follow-up period.

Variable	Initial visit	Follow-up					
		1 mo	2 mo	3 mo	4 mo	5 mo	6 mo
Blood							
Haemoglobin, g/l (120–160)	89	96	102	109	111	108	112
WBC, × 10 ⁹ /l (4–10)	14.1	12.1	11.1	10.8	9.8	7.5	8.4
Platelets, × 10 ⁹ /l (125–350)	231	150	191	212	234	179	190
Creatinine, μmol/l (44–75 μmol/l)	429	172	118	110	101	108	100
eGFR, ml/min/1.73m ² (CKD-EPI) (80–120 ml/min/1.73 m ²)	9.4	25.7	40.7	44.8	49.7	45.4	50.1
Potassium, mmol/l (3.5–5.3)	2.9	3.6	4.2	3.7	4.1	4.4	4.0
Sodium, mmol/l (137–147)	138	142	142	146	143	138	138
Chloride, mmol/l (96–108)	98	103	105	110	110	101	105
Phosphate, mmol/l (0.85–1.51)	2.15	1.29	1.28	1.37	1.29	1.35	1.36
Calcium, mmol/l (2.11–2.52)	2.29	2.37	2.34	2.21	2.31	2.17	2.15
Magnesium, mmol/L (0.75–1.02)	0.96	0.77	0.87	0.84	0.98	1.02	0.97
PTH, pg/ml (15–65)	190	–	–	144	–	–	102
pANCA	+ve	+ve	+ve	+ve	+ve	–ve	–ve
MPO-ANCA	+ve	+ve	+ve	–ve	–ve	–ve	–ve
Urine							
Calcium, mmol/24h (0.0–6.2)	0.6	0.6	0.6	0.7	0.5	0.7	0.6
Protein, mg/24h (<150)	1345	1408	788	644	424	355	248
Albumen, mg/24h (<30)	359	557	413	359	214	198	102
Beta-2 microglobulin, mg/l (<0.4)	17	–	–	10	–	–	112

*Normal range for each laboratory variable is given in parenthesis

WBC, white blood cells; eGFR, estimated glomerular filtration rate; CKD-EPI, Chronic kidney disease-epidemiology collaboration equation; PTH, parathyroid hormone; pANCA, perinuclear anti-neutrophil cytoplasmic antibodies; MPO-ANCA, myeloperoxidase anti-neutrophil cytoplasmic antibodies; +ve, positive; –ve, negative

misdiagnosed because of its relative rarity and non-specific presentation.⁵ The most commonly affected body systems include the upper airways, lungs, kidneys, eyes, and peripheral nerves, although almost any part of the body can be affected.⁶ Indeed, multisystem involvement is often the clue for diagnosis.⁵

Investigations should include laboratory assessments of inflammatory markers, kidney function and serological testing for ANCA.⁵ ANCAs have a key role in the pathogenesis of AAV because they can directly or indirectly activate inflammatory cells such as neutrophils and promote the release of various inflammatory factors, which results in injury to small vessels.^{8,9} In addition, a chest X-ray should be taken and CT or magnetic resonance imaging (MRI) may be required to assess the chest, brain and head and neck structures in detail. It is recommended that a kidney biopsy should be considered to confirm the diagnosis.⁵

The characteristics of the case presented here were in accordance with previous studies.^{3,5} Initially, the patient presented with chest pain, malaise and anorexia, all symptoms that could be attributed to more common diseases. Although her creatinine levels were elevated, she was suspected to have pneumonia and was discharged from hospital with a course of antibiotics. The persistence of her symptoms prompted her local physician to refer her to our hospital for further tests. Her urinalysis was positive for protein, albumen and β^2 -microglobulin, and blood tests showed renal impairment (serum creatine 429 $\mu\text{mol/l}$, eGFR 9.4 ml/min/1.73m²) and evidence of an inflammatory response (haemoglobin 89 g/l, WBC $14 \times 10^9/\text{L}$). A kidney biopsy, chest CT scan and ANCA testing confirmed diagnosis of AAV renal injury.

The patient improved following treatment with high-dose glucocorticoids and CTX which is a standard therapy for

ANCA-associated vasculitis.^{5,8} Indeed, immunosuppressive therapy has improved disease outcome for patients with AAV, but the chronic condition requires long-term treatment.¹⁰ Guidelines recommend a gradual withdrawing of the initial immunosuppressive therapy and replacing with a maintenance regimen of either azathioprine or methotrexate.⁵ However, the precise duration of the maintenance regimen is unclear. Patients with AAV are at risk of complications from both the disease and its treatment.

In summary, early diagnosis and treatment are vital for improving the prognosis of patients with AAV. As illustrated by this case study, the disease is prone to misdiagnosis because it often involves several body systems with aspecific clinical features. Importantly, patients with pulmonary involvement at presentation have a high disease burden and poor prognosis.^{10,11} Early diagnosis and initiation of effective treatment will lead to be a better outcome for affected patients.³



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Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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