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Granulomatosis with polyangiitis and constrictive pericarditis – a case report

[1]AE Horne, [2]PA Henriksen, [3]EN Amft
[1]Rheumatology Registrar,[3]Rheumatology Consultant,Rheumatic Diseases Unit, Western General Hospital, Edinburgh, UK; [2]Cardiology Consultant, Cardiology Department, Western General Hospital, Edinburgh, UK

ABSTRACT
Polyangiitis with granulomatosis, previously known as Wegener's granulomatosis, is a systemic necrotising granulomatous vasculitis. It predominantly affects the upper and lower respiratory tracts and the kidneys, but can potentially affect any organ system. It is diagnosed by clinical features, immunology (anti-neutrophil cytoplasmic antibodies) and histology. Cardiac involvement occurs in 6 to 44% of cases. We present a case of polyangiitis with granulomatosis and constrictive pericarditis, which occurred despite vigorous immunosuppression and which required surgical pericardectomy.

KEYWORDS breathless, GPA, pericardial constriction, pericardial stripping, Wegener's granulomatosis

DECLARATION OF INTERESTS No conflict of interest declared.

Correspondence to ***A Horne***
Rheumatic Diseases Unit
Western General Hospital
Crewe Road
Edinburgh EH4 2XU
UK

e-mail ***annamariehorne@nhs.net***

CASE REPORT

A 42-year-old woman, diagnosed with polyangiitis with granulomatosis (GPA) in 2010, presented with polyarthritis, bloody nasal discharge, maxillary sinus pain, multiple mononeuropathies (mononeuritis multiplex), sicca symptoms and Raynaud's disease. Investigations showed proteinase 3 anti-neutrophil cytoplasmic antibody >100 U/ml. Baseline computed tomography of the sinuses showed changes consistent with polyposis, with no bony erosions; however, subsequent magnetic resonance imaging (MRI) of the sinuses in 2011 did show paranasal erosion. Two nasal biopsies showed inflammation with no granulomatous tissue. Of note, the baseline echocardiogram was normal.

The patient was treated with steroids (oral and intravenous) and intravenous cyclophosphamide (6 pulses). Iloprost was given a month after diagnosis for severe Raynaud's disease. Maintenance treatments with methotrexate and then azathioprine were discontinued due to gastrointestinal problems and abnormal liver function tests, respectively. In March/April 2011 a course of rituximab was given for ongoing sinus and joint symptoms, followed by mycophenolate mofetil (MMF). As IgG was low (4.74 g/L), a subsequent disease flare in February 2012 was treated with a further course of cyclophosphamide. Thereafter the patient had combination treatment of ciclosporin and MMF. The patient was administered prednisolone continuously throughout this period, the dose varying from 20mg to 60mg. Sinus and joint symptoms worsened in July/August 2013, and the patient was re-treated with rituximab. A chest X-ray at that time was normal.

From July 2013 the patient developed persistent and progressive dyspnoea and, subsequently, peripheral oedema and orthopnoea. She presented to the medical team on three occasions. The chest X-rays over that time progressed from a small costophrenic effusion and possible pneumonia, which was treated with antibiotics, to pulmonary oedema in August. Three echocardiograms were carried out between July and August; the first scan showed a small pericardial effusion measuring 1.5cm at maximum diameter, indirect pulmonary artery pressure 34mmHg above right atrial pressure, with a suggestion of a pericardial fat pad and normal left ventricular function. Subsequent scans were unchanged. Ciclosporin and MMF were discontinued in July/August 2013 due to inefficacy. The patient had received rituximab in July, and continued on 50mg prednisolone.

An outpatient rheumatology review prompted readmission in September 2013. The patient was clinically and radiologically in congestive cardiac failure. Oxygen saturations were 98% on room air at rest. An ECG on admission was normal and a chest X-ray showed moderate cardiomegaly with perihilar congestion. An echocardiogram demonstrated good biventricular systolic function, a diastolic septal bounce, dilated atria, exaggerated respiratory variation of Doppler forward flows and normal early diastolic myocardial relaxation velocity (Figure 1).

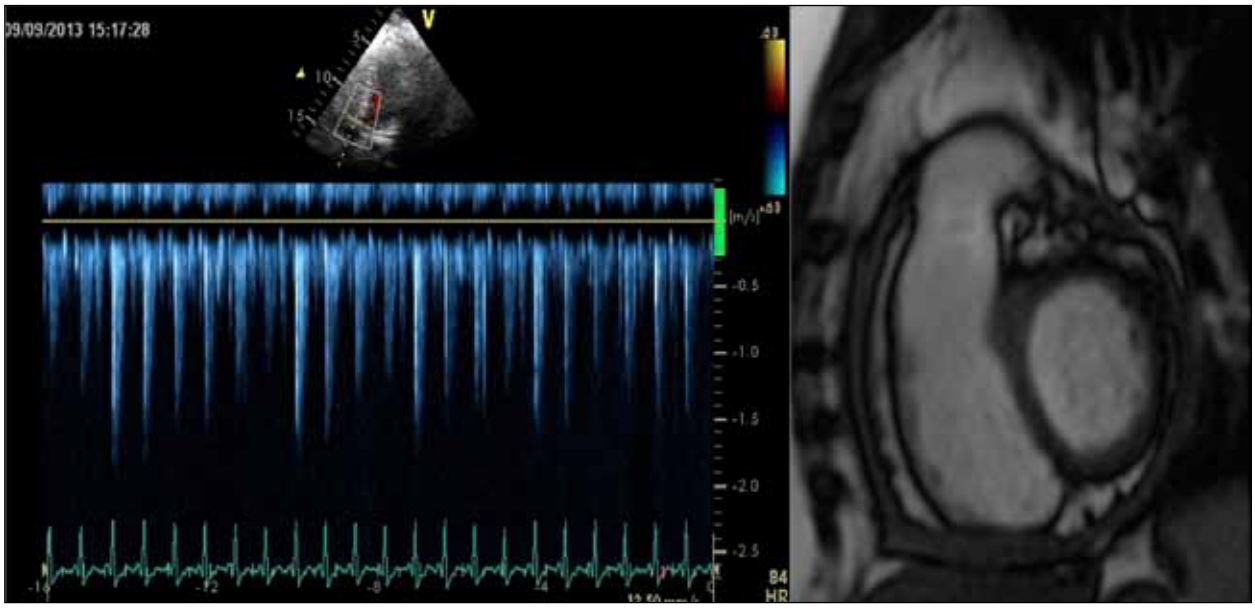

FIGURE 1 (Left) Exaggerated respiratory variation of left ventricular outflow Doppler velocities on transthoracic echocardiogram. This results from the thickened and fibrotic pericardium limiting expansion and filling of the ventricles during diastole. During inspiration, negative intrathoracic pressure increases blood flow into the right ventricle. Constriction of the right ventricular free wall leads to bulging of the interventricular septum with consequent reduction of left ventricular chamber size and filling. This ventricular interdependence results in reduced flow (and velocity) across the aortic valve during inspiration with a consequent fall in systolic pressure during inspiration. (Right) Circumferential pericardial thickening on cardiac MRI

From the echocardiogram, a diagnosis of constrictive pericarditis was felt likely. Cardiac MRI revealed pericardial thickening (7mm), and inspiratory septal flattening with no evidence of infiltrative/inflammatory myocardial disease, corroborating the diagnosis (Figure 1). Cardiac catheterisation confirmed constrictive haemodynamics.

As there was no other evidence of active GPA, and as the patient had had recent intense immunosuppression, a tissue biopsy was carried out to clarify whether the underlying cause was inflammatory or fibrotic. The biopsy revealed collagenous fibrous tissue with no evidence of inflammation or vasculitis; therefore immunosuppression for the pericarditis was not warranted and the steroid dose was reduced.

The patient continued to complain of limiting dyspnoea and had ongoing evidence of congestive cardiac failure despite a period of diuretic therapy. She was therefore referred for surgical pericardectomy. This was performed, without complication, in February 2014. She has recovered well from surgery; her symptoms have improved and she no longer has evidence of congestion. Pathology from the pericardectomy showed non-specific fibrosis with some areas of prominent neovascularisation possibly relating to previous inflammation with maturing granulation tissue. There was no evidence of active vasculitis or inflammation. Cardiac involvement occurs in 6–44% of polyangiitis with granulomatosis (GPA) cases;[1,2,3] 50% are pericarditic; coronary vasculitis, myocarditis, conduction defects and endocarditis make up the rest.[1,3] It is worth mentioning that connective tissue disorders, including GPA, account for only 2–7% of constrictive pericarditis cases.[4] This patient had active GPA prior to the development of progressive dyspnoea, despite intense immunosuppression. It is possible that she had subclinical pericarditis as part of GPA which only manifested symptomatically when fibrosis ensued. MMF is noted for its anti-fibrotic action in other conditions such as systemic sclerosis. MMF was stopped after the first presentation of dyspnoea and it is questionable whether discontinuation contributed by facilitating progressive fibrosis. Rituximab has been associated with increased risk of pulmonary fibrosis[5] but there is no reported association with pericardial fibrosis. Tuberculosis was considered as a potential cause of pericardial constriction given the history of immunosuppression but the pericardium was not calcified and the tuberculosis interferon gamma release assay was negative. The latter excludes latent tuberculosis and, unfortunately, the sample sent from pericardial biopsy was insufficient for mycobacteria film/culture.

Finally, colchicine is effective for treatment of acute symptomatic pericarditis and is recommended in guidelines for recurrent or relapsing symptoms.[6] It is not known whether colchicine therapy further reduces the low incidence of subsequent pericardial constriction in patients with acute pericarditis. There was no pericarditic chest pain symptom or evidence of acute pericardial inflammation in this case, and therefore colchicine was not considered a therapeutic option.

This case underlines the importance of vigilance to changing symptoms in GPA, and to remember that all organ systems can be affected. In addition it highlights the importance of evidence, clinically and/or histologically, of active vasculitis before treating constrictive pericarditis with immunosuppression. As cardiac complications can occur in up to 44% of GPA patients,[1,2,3] screening echocardiograms on a regular basis may be appropriate, particularly in those patients with persistently active GPA. Equally however, given that connective tissue diseases account for such a small proportion of constrictive pericarditis,[4] one must be vigilant in excluding other causes, in particular infection.

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