CASE REPORT
SILENT MYOCARDIAL INFARCTION IN WEGENER'S GRANULOMATOSIS

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SUMMARY
Histological cardiac abnormalities in Wegener's granulomatosis can frequently be demonstrated at post-mortem examination, but clinically significant cardiac involvement is rare. We describe a massive silent myocardial infarction, occurring at a time when other features of the disease were responding to aggressive immunosuppression.

KEY WORDS: Wegener's granulomatosis, Myocardial infarction, Vasculitis.

WEGENER’S granulomatosis is an uncommon multisystem disorder characterized by necrotizing granuloma and vasculitis. Prior to the introduction of immunosuppressive therapy the majority of patients died within 1 yr, renal and respiratory disease being the main causes of death [1]. Currently, with treatment the majority of patients survive and even though fulminating cases still occur treatment-related mortality has now become a significant problem [2].

Significant cardiac complications occurring during the course of Wegener's granulomatosis are rare. Even though coronary vasculitis can be demonstrated at post mortem, symptoms associated with myocardial ischaemia or heart failure are very uncommon. In this report we describe the late onset of cardiogenic shock, due to a silent myocardial infarction, in a young male whose disease was responding to immunosuppressive therapy.

CASE REPORT
A 23-yr-old male initially presented to his general practitioner with a 10-day history of left-sided earache and a bloody discharge, symptoms initially thought to be indicative of middle ear infection. When the patient failed to respond to a short course of antibiotic therapy he was referred to an ear, nose and throat (ENT) specialist who noted the presence of a left seventh lower motor neurone facial weakness. Results of investigations performed were as follows: normal blood count, liver and renal function tests, chest radiograph and an erythrocyte sedimentation rate (ESR) of 65 mm/h. An immunological screen, which included antineutrophil cytoplasmic antibodies (ANCA), was negative and the immunoglobulin levels were normal. A computerized tomogram (CT) of the left petrous temporal bone showed soft tissue shadowing in the left middle ear but no bony destruction. He underwent a biopsy and mastoidectomy, histological examination of the left Eustachian cushion. He was again discharged home on symptomatic therapy.

Six weeks later he was readmitted, having developed fever, fatigue, weight loss and haemoptysis. His ESR was now 122 mm/h, his full blood count remained normal, renal and hepatic screen showed no significant abnormality and the cANCA was negative. A plain radiograph and CT scan of the chest revealed mid-zone consolidation/cavitation (Fig. 1). Mantoux test was negative and the serum angiotensin converting enzyme (ACE) levels were within the normal range. Bronchosopic biopsy was performed; the small amount of tissue obtained showed an acute necrotizing ulcerative process with no evidence of vasculitis or granuloma formation. The attending physician made a diagnosis of atypical sarcoidosis initiated treatment for 2 weeks only with 20 mg of oral prednisolone. No resolution in the chest X-ray findings took place and he was subsequently referred to the thoracic surgeons for an open lung biopsy. Whilst awaiting this procedure he developed severe arthralgia, vasculitic lesions over the elbows, nose and cheeks and gangrene of several toes of the left foot. It was at this point that he was referred to the Rheumatology Department at the University Hospital of Wales, Cardiff.

Physical examination revealed multiple vasculitic lesions over the hands, feet, elbows and face, the left foot was cold and the dorsalis pedis pulse was absent. There was no lymphadenopathy, hepatomegaly or splenomegaly. His pulse rate was 120/min, blood pressure (BP) 140/100 and there were normal heart sounds with no murmurs. Auscultation of the lung fields revealed normal breath sounds only. Investigations at this point revealed a haemoglobin 10 g/dl, white blood count 20 x 10^9/l and a platelet count 872 x 10^9/l. The urea was 14.7 mmol/l and creatinine 82 umol/l. Urine testing revealed blood and protein with a creatinine clearance of 46 ml/min. The ESR had increased to 120 mm/h and the C-reactive protein (CRP) to 180 mg/l. The ANCA was now positive at a titre of 1:320 with a cytoplasmic staining pattern. The electrocardiogram (ECG) was normal and an echocardiogram revealed no abnormality other than a tachycardia.

Immunosuppressive treatment was started and comprised three 1g intravenous pulses of methylprednisolone on alternate days, followed by 60 mg of oral prednisolone and 150 mg of cyclophosphamide daily. He also underwent a course of plasma exchange totalling 301 and was in addition transfused with 3 units of packed cells. His clinical state improved within 72 h. The vasculitic skin lesions on the
elbows, nose and cheeks began to resolve and no new lesions appeared. The ESR fell to 50 mm/h after 2 days and continued to fall. After 1 week of treatment the CRP was 13 mg/l. He remained mildly hypertensive, BP 145/100 and in view of the persisting tachycardia a cardiological opinion was sought. This confirmed the presence of a sinus tachycardia with an otherwise normal ECG and no additional evidence of cardiac disease.

Clinical improvement was sustained until 5 days after commencing treatment when he suddenly developed abdominal pain with rebound tenderness and guarding. Bowel perforation was suspected clinically and at laparotomy perforation of an infarcted area of the caecum was identified. A right hemicolecotomy was subsequently performed. Histological examination of this tissue revealed infarction with granulomatous vasculitis. Post-operatively the lung cavities became colonized by *Staphylococcus aureus* and he required antibiotic treatment with cefuroxime 1.5 g t.d.s., metronidazole 500 mg t.d.s. and flucloxacillin 1 g q.d.s. He made a slow clinical response. Two weeks after initiation of immunosuppressive therapy his condition deteriorated suddenly, his pulse rate increased to 150/min and was associated with hypotension and a gallop rhythm. A repeat ECG showed the changes of a recent extensive anteroseptal myocardial infarct with established Q waves (Fig. 2). A review of the ECG carried out on admission confirmed that this trace was normal. A creatine kinase level carried out some 4 days earlier as part of a routine biochemical screen was 908 IU. At the time this was attributed to skeletal muscle damage, but subsequent analysis of the cardiac isoenzyme CK-MB showed a small increase in the proportion at 15% (normal <5%). Serial enzymes were not investigated. Transthoracic echocardiography confirmed anteroseptal akinesia. At no time had the patient complained of chest pain. Despite maximal inotropic support the patient's clinical course was that of worsening cardiogenic shock, which led to his death 4 days later. Permission for post-mortem examination was refused.

**DISCUSSION**

The diagnosis of Wegener's granulomatosis was made 4 months after the initial presentation at a time when pulmonary inflammation, systemic vasculitis and a positive cANCA were all present. Initial diagnostic confusion may have been due to the absence of typical pathological features on biopsy material obtained from the mastoid region and the lung. However, a delay in diagnosis is not an uncommon finding in patients with this disorder; less than 45% of patients are diagnosed within 3 months of the onset of symptoms [2]. Although highly specific for Wegener's granulomatosis, a negative cANCA in patients with limited active disease should not be regarded as excluding this condition since a positive result occurs in only 70-80% of cases [3]. Our patient improved with aggressive immunosuppressive therapy but succumbed to the late vasculitic complications involving the heart.

Clinically significant cardiac involvement in Wegener's granulomatosis is rare. A comprehensive recent review of 158 patients reported that 10 (6%) had developed pericarditis, eight of whom had typical clinical symptoms and signs [2]. There are smaller studies which report similar clinical and ECG findings [4]. One patient became hypotensive with a tachycardia but echocardiography demonstrated that these signs were secondary to a large pericardial effusion, and resolved following urgent pericardectomy [5]. There is one report of constrictive pericarditis [6]. Arrhythmias associated with Wegener's granulomatosis are unusual but when they do occur supraventricular arrhythmias are the commonest. Although some arrhythmias may be secondary to pericarditis, others have been attributed to vasculitis of the vessels supplying the cardiac conduction system and in some cases this has been confirmed at post-mortem examination [7, 8]. One report demonstrated abnormalities of the sinoatrial and the atrioventricular node with the most extensive pathological changes of vasculitis and fibrosis being located in the sinoatrial artery. Microinfarcts were also demonstrated in the atrioventricular node [7]. Similar findings have been reported in systemic lupus erythematosus [9], rheumatoid arthritis [10, 11] and polyarteritis nodosa [12]. Complete heart block secondary to atrioventricular nodal involvement in Wegener's granulomatosis has been described in one case, the abnormality being corrected following treatment with cyclophosphamide [13]. Aortic valvulitis has also been demonstrated by echocardiography and this process also improved following the introduction of treatment [14].

Cardiac muscle and vessel involvement is much rarer clinically, occurring in less than 2% of the 158 cases followed over a mean period of 8 yr [2]. Pathological examination of tissue, however, demonstrates that cardiac abnormalities are much more common. An early review of necropsy findings in Wegener's granulomatosis reported abnormalities in 30% of cases, although the majority of patients had no cardiac symptoms whilst alive and died from non-cardiac causes [13]. The commonest histological abnormalities were those of coronary arteritis and pericarditis, both occurring in approximately 50% of cases with cardiac involvement [13]. The true frequency of these abnormalities, however, is difficult to establish since the proportion of cases undergoing detailed post-mortem histological examination is variable.

Our case is unusual in that the cardiac complications occurred several days after the commencement of treatment, at a time when the patient's clinical state was improving. We have attributed these to the disease since there were no other identifiable risk factors. The initial presentation was that of a persistent tachycardia in the absence of fever and associated with a reduction in blood pressure. Clinically significant myocardial infarction is extremely rare in Wegener's granulomatosis and there is only one reported case. This was a 28-yr-old male who experienced typical cardiac pain, a finding which contrasts with our patients [15]. The reason why such an extensive anteroseptal infarct was not associated with symptoms is not known.

Although the acute event in this patient was not diagnosed until the development of cardiogenic shock, it is unlikely that the clinical outcome would have been different had the infarct been diagnosed earlier. However, the majority of patients with myocardial infarction associated with Wegener's granulomatosis could
benefit from early detection and appropriate therapy with ACE inhibitors. Whilst it is not feasible to admit all patients with this condition to a coronary care unit for continuous monitoring it is important to be aware that the potential for serious cardiac involvement exists, and that it should be considered in asymptomatic patients if there are any changes in pulse or blood pressure recordings. More frequent ECG recordings and a low threshold for requesting echocardiography would appear appropriate.

REFERENCES