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Clinical Record

Wegener's granulomatosis presenting as acute systemic vasculitis following 20 years of limited tracheobronchial disease

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Abstract

Objective: We report a patient with a 20-year history of apparently idiopathic airways stenoses, who presented with an antineutrophil cytoplasmic antibody (ANCA) associated, acute, systemic vasculitis with necrotising glomerulonephritis, subsequently diagnosed as Wegener's granulomatosis.

Methods: We present a case report and a review of the world literature on airway stenosis in Wegener's granulomatosis.

Results: To our knowledge, this is the first report of Wegener's granulomatosis manifesting as local airway disease for such a prolonged period, before transforming into a systemic vasculitis.

Conclusions: This case highlights the need for physicians to be alert to the possibility of Wegener's granulomatosis as a cause of apparently idiopathic airway stenosis, and to be aware that systemic disease may occur in very long-standing, limited Wegener's granulomatosis.

Key words: Wegener's Granulomatosis; Tracheal Stenosis; Vasculitis; Antineutrophil Cytoplasmic Antibodies; Glomerulonephritis

Introduction

Wegener's granulomatosis is a multisystem vasculitis of small- to medium-sized blood vessels, which may occur in a systemic or limited form. Airway stenosis is a well recognised feature. We report a patient with a 20-year history of tracheal and bronchial stenoses who presented with an antineutrophil cytoplasmic antibody associated, acute, systemic vasculitis with necrotising glomerulonephritis, subsequently diagnosed as Wegener's granulomatosis. We also review the literature on airway stenosis in Wegener's granulomatosis.

To our knowledge, this is the first report of Wegener's granulomatosis manifesting as limited airways disease for such a prolonged period, before transforming into a systemic vasculitis.

Case report

A 55-year-old, retired librarian was referred by her general practitioner with a one-week history of haemoptysis. During the preceding month, she had experienced epistaxis, arthralgia, myalgia, itchy red eyes, mouth ulcers, general malaise, and an episodic rash affecting the arms and legs. She had not experienced chest pain or dyspnoea, and had normal exercise tolerance. She had never smoked and did not drink alcohol or abuse drugs.

Twenty years previously, the patient had been diagnosed elsewhere with idiopathic tracheal and bronchial stenoses, following investigation for a wheezy cough of several years' duration. She had developed left upper lobe collapse, and bronchoscopy had revealed a stricture of the left main bronchus. She had been followed by thoracic surgeons, respiratory physicians and otolaryngologists, and had developed strictures at several sites, requiring repeated bronchoscopies, bouginage and endobronchial stenting.

A year before presenting to us, the patient had received laser treatment to a subcricoid stenosis. No cause had previously been identified for her airways stenoses, and biopsies had revealed only non-specific fibrosis.

The patient's past medical history included well controlled hypertension, bilateral sensorineural hearing loss and mild conductive deafness. Her current medication included amlodipine and omeprazole.

On examination, the patient's pulse was 110/minute and regular, her blood pressure was 143/82 mmHg, her respiratory rate was 20/minute and her oxygen saturation 99 per cent on air. She was hoarse, which was normal for her. Auscultation revealed left mid- to lower zone crackles, with bronchial breathing. A maculopapular, erythematous rash was observed affecting the patient's arms and upper back, with sparing of the face and trunk. The rash on her legs appeared vasculitic, with palpable purpura. There was no clinical evidence of synovitis.

The results of blood tests are displayed in Table I. Urinalysis revealed a 3+ reading for blood and a trace of protein. Urine microscopy confirmed active urinary sediment. Chest X-ray demonstrated left lower lobe opacification. High resolution computed tomography of the chest with contrast revealed a left main endobronchial stent, left lower lobe consolidation, and peripheral nodules in the left upper lobe and right lower lobe which were too small to characterise. Bronchoscopy revealed inflamed, oedematous mucosa in the left main bronchus and an epithelialised stent. Bronchoalveolar washings grew

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TABLE I

PATIENT'S LABORATORY TEST RESULTS AT PRESENTATION AND 12 MONTHS

Test	Normal range	Value	
		At presentation	At 12 mths*
Haemoglobin (g/dl)	11.4–15	9.9	13.0
Mean cell volume (fl)	83–101	79.3	88.6
White cell count ($\times 10^9$/l)	4–11	10.0	6.9
Neutrophil count ($\times 10^9$/l)	2–7.5	8.4	4.5
Platelets ($\times 10^9$/l)	120–400	735	392
ESR (mm/1st hr)	0–20	80	7
Iron status		Deficient	Replete
Biochemistry profile		Normal	Normal
Clotting		Normal	–
CRP (mg/l)	0–10	149	<5
ANCA immunofluorescence		+++ Perinuclear pattern	++ Perinuclear pattern
Anti-MPO Ab titre (u/ml)	0–25	140	20
Anti-PR3 Ab titre (u/ml)	0–25	1	4
Anti-GBM Ab titre (u/ml)	0–25	0	–

*In clinic. Mths = months; hr = hour; – = not tested; ANCA = anti-neutrophil cytoplasmic antibody; MPO = myeloperoxidase; Ab = antibody; PR3 = proteinase 3; GBM = glomerular basement membrane

normal respiratory tract flora only. Pulmonary function tests showed a forced expiratory volume in 1 second (FEV_1) of 1.7 litres (74 per cent of the predicted value), a vital capacity (VC) of 2.85 litres (96 per cent of the predicted value), and an FEV_1/VC of 60 per cent. Previous pulmonary function testing had shown no reversibility to salbutamol. Gas transfer was normal and not significantly changed from measurements made four years previously. Flow volume loop was in keeping with tracheal/bronchial stenoses. Renal ultrasound revealed normal-sized kidneys. Percutaneous renal biopsy demonstrated pauci-immune, focal necrotising glomerulonephritis with crescents, consistent with ANCA associated systemic vasculitis. The patient's Birmingham vasculitis activity score on presentation was 21 (the normal value being zero).

The patient was diagnosed with Wegener's granulomatosis on the basis of her clinical features and immunopathology. Prednisolone was commenced, with rapid resolution of her rash and improvement in arthralgia and systemic malaise. She subsequently received a course of pulsed intravenous cyclophosphamide. Her symptoms completely resolved, and her C-reactive protein levels and Birmingham vasculitis activity score normalised. Following completion of the cyclophosphamide course, she was converted to maintenance azathioprine and low dose steroids. She remained strongly positive for ANCA, with a perinuclear pattern, but levels of anti-myeloperoxidase antibodies decreased to normal.

Discussion

Wegener's granulomatosis is a multisystem, autoimmune vasculitis of small- to medium-sized blood vessels, with an incidence of 3–14 per million.[1] Typical features include epistaxis, sinusitis, nasal crusting, haemoptysis, deafness due to serous otitis media and mucosal ulceration. Patients are usually positive for antineutrophil cytoplasmic cytoplasmic antibodies directed against proteinase-3, with a cytoplasmic pattern of staining on immunofluorescence. The classic, generalised form described by Wegener consists of the triad of necrotising granulomas of the respiratory tract, small vessel angiitis and focal necrotising glomerulonephritis. This generalised form can be life-threatening and requires systemic immunosuppression. A limited form of Wegener's granulomatosis, with lesions localised to the lung, was later identified.[2] Tracheal and bronchial stenoses are a less common but well described feature[3,4] which can cause airway compromise. Airway strictures in the absence of systemic disease may be managed by local therapy, including intralesional steroids, balloon dilatation and laser surgery.[5] Tracheal stenosis as the presenting symptom of Wegener's granulomatosis was described in a series of 10 patients.[6] It may develop later in the disease course, even when the systemic inflammation has been successfully controlled by immunosuppression.[7,8]

- **Wegener's granulomatosis is a rare, multisystem vasculitis of small- to medium-sized blood vessels which causes necrotising granulomatous inflammation**
- **It may occur in a limited or systemic form**
- **Systemic disease can be life-threatening and requires immunosuppressive therapy**
- **Upper respiratory tract symptoms are common**
- **Tracheal and bronchial stenoses are well described manifestations of Wegener's granulomatosis, and may be treated with intralesional steroids, balloon dilatation, stenting or laser therapy**
- **Wegener's granulomatosis should be considered as a cause for apparently idiopathic airway stenosis**
- **Limited Wegener's granulomatosis may transform into systemic vasculitis, even after a very long time period – in our patient, more than 20 years**

Our patient had suffered limited airways disease for over 20 years before developing acute, systemic involvement, with joint, eye, skin, mucosal and renal disease with crescentic glomerulonephritis. To our knowledge, this is the first report of Wegener's granulomatosis manifesting as local airway disease for such a prolonged period, before transforming into a systemic vasculitis. The patient's initial presentation had preceded the discovery of ANCA, and she had never previously been tested for this autoantibody. Unfortunately, no stored serum samples were available for retrospective testing, so we do not know at what point she became ANCA-positive. Fienburg has described 12 cases of Wegener's granulomatosis in which localised

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mucosal lesions preceded the onset of systemic features, although none had tracheal stenosis or such a prolonged period of limited disease.[9] Our patient's case highlights the fact that Wegener's granulomatosis should be considered in the differential diagnosis of airway strictures. Furthermore, in a series of 73 patients with apparently idiopathic laryngotracheal stenosis, six were ultimately shown to have Wegener's granulomatosis.[10] The possibility of the development of systemic disease must be borne in mind in this condition, even in cases of very longstanding, limited Wegener's granulomatosis.

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