Recurrent sinusitis: think granulomatosis with polyangiitis

Introduction

This article presents the case of a 52-year-old man who was treated in primary care on four different occasions with repeated courses of antibiotics for presumed sinusitis. This occurred for 3 months without specialist ear, nose and throat advice being sought. He developed rapidly progressive systemic symptoms and on rheumatology assessment his anti-neutrophil cytoplasmic antibody-proteinase 3 (ANCA-PR3) antibody levels were elevated with active renal involvement.

Subsequent renal biopsy confirmed a rapidly progressive crescentic (extracapillary) glomerulonephritis. He was treated with pulsed methylprednisolone for 3 days and then switched to high dose oral prednisolone and oral cyclophosphamide. The patient responded well to treatment with a marked improvement in renal function and resolution of systemic symptoms.

Discussion

A diagnosis of granulomatosis with polyangiitis was made based on clinical symptoms, positive serology and histology. The previous name for this condition, Wegener's granulomatosis, was revised to granulomatosis with polyangiitis in 2012. It is a worldwide disease with a variable incidence of 4–9 per million. Granulomatosis with polyangiitis is a necrotizing vasculitis of the small and medium-sized vessels involving the upper and lower respiratory tract, and the kidneys (Jennette et al, 2013).

Vasculitis is a systemic illness that can affect various organ systems. Over 90% of patients with granulomatosis with polyangiitis have ear, nose and throat symptoms which can precede the systemic systems of generalized disease for a long time and lead to a delay in diagnosis. Otolaryngological presenting symptoms of granulomatosis with polyangiitis are commonly misdiagnosed as infectious or allergic in aetiology.

Some of the earliest upper respiratory tract features include obstruction from mucosal swelling and serosanguinous discharge as well as epistaxis. In the later stages of presentation there may be septal cartilage destruction leading to the classic 'saddle' shaped deformity of the nasal bridge. Patients can also present with sensorineural deafness, as well as conductive hearing deafness (Hakim et al, 2011). Magnetic resonance imaging or computed tomography should be arranged to assess the extent of sinus involvement. Further assessment of patients with active ear, nose and throat symptoms should include formal endoscopy by an otolaryngologist and biopsies obtained from areas of inflammation, although histology in active disease is often non-specific and difficult to distin-

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Case Report

A 52-year-old Caucasian male, previously well, consulted his GP over a 3-month period with recurrent bilateral headaches, intermittent episodes of epistaxis and bilateral hearing loss. He was treated with antibiotics for recurrent sinusitis on four different occasions with no symptomatic improvement. Despite the persistent symptoms he was never referred to an ear, nose and throat specialist for further investigation.

Three months after the onset of his symptoms he was admitted to the acute medical unit. He complained of progressive fatigue, malaise, night sweats and fevers and of having dropped two belt sizes. He was dyspnoeic on exertion, but no chest pain or haemoptysis was reported. His urine production was low which he attributed to his recent poor appetite. There was nil else on systemic enquiry. He had a history of skin psoriasis, no significant family history and was not taking any medication. He worked as an agricultural fitter, did not consume alcohol or smoke cigarettes and had no recent history of travel.

On examination, he appeared plethoric; his pulse was 110 beats per minute and his blood pressure was 128/74 mmHg. There was no lymphadenopathy, sinus tenderness or peripheral synovitis. He had well-demarcated psoriatic plaques on his elbows but no vasculitic rashes or purpura. Full neurological, cardiac, respiratory and abdominal examinations were normal.

Full blood count was normal; his serum creatinine was 125 umol/litre (normal range 36–107 umol/litre) with an estimated glomerular filtration rate of 52 ml/min. C-reactive protein was 189 mg/litre (normal range 0–5 mg/litre). His anti-neutrophil cytoplasmic antibody-proteinase 3 (ANCA-PR3) antibody level was elevated at 5.9 U/ml (normal range 0–2 U/ml). Urine dip showed protein and blood with dysmorphic red cells on microscopy.

Chest radiograph did not show obvious cavitations or infiltrates with normal cardiomediastinal contours. Computed tomography of the sinuses (*Figure 1*) showed diffuse mucosal thickening within the right maxillary sinus and polypoidal mucosal thickening in the base of the left maxillary sinus (see white arrows).

Within 24 hours of admission his estimated glomerular filtration rate rapidly fell to 19 ml/min and his creatinine level increased to 229 umol/litre. He was referred urgently for nephrology assessment and renal biopsy. Histology (*Figure 2*) showed a rapidly progressive crescentic (extracapillary) glomerulonephritis (pauci-immune type) consistent with vasculitis.

Pulsed intravenous methylprednisolone 500 mg was administered on three consecutive days, followed by oral prednisolone (60 mg). Oral cyclophosphamide 150 mg once daily was commenced as induction immunosuppressive therapy.

He was in remission after 5 months with complete normalization of his renal function, and is presently on azathioprine 150 mg once daily as maintenance therapy.

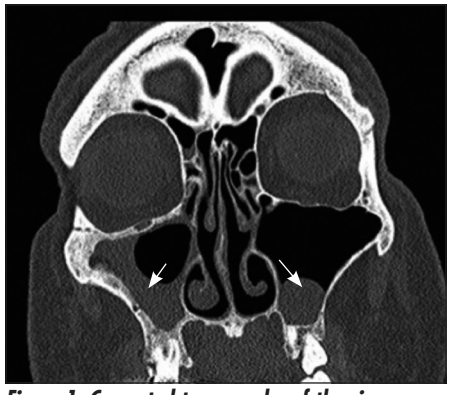

Figure 1. Computed tomography of the sinuses shows right maxillary thickening with basal predominance and polypoidal mucosal thickening in the base of the left maxillary sinus (white arrows).

guish from chronic infection (Watts and Dharmapalaiah, 2012).

In this case, the patient was treated with antibiotics by his GP for refractory recurrent sinusitis. Unfortunately an ear, nose and throat opinion regarding these frequent episodes was never instigated until he developed systemic manifestations and presented to the emergency department of his own accord. Although only a small proportion of sinusitis patients will actually have granulomatosis with polyangiitis this diagnostic delay can be avoided by earlier referral to a rhinologist if patients are presenting with recurrent sinusitis. Moreover 90% of granulomatosis with polyangiitis patients are ANCA positive, therefore measurement of ANCA may be useful to help the clinician, although ANCA is sometimes negative in more localized cases (Watts and Scott, 2012).

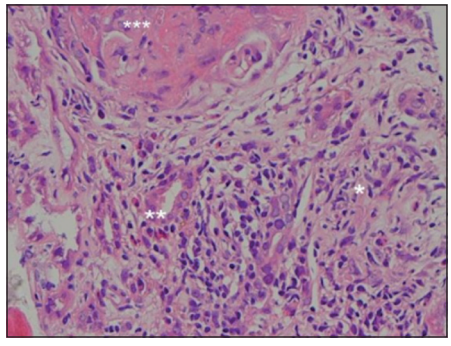

*Figure 2. Renal biopsy. * Interstitial inflammation (slight granulomatosis); ** eosinophils adjacent to tubule; *** fibrinoid necrosis associated with a cellular crescent.*

Conclusions

Early detection and treatment of granulomatosis with polyangiitis is essential. The mortality rate for patients with renal failure at presentation is approximately 25% in the first year and highest in the first 3 months when the vasculitis is at its most active and when immunosuppressive therapy is maximal (Jennette et al, 2013). Patients presenting with unusual sinonasal symptoms that include nasal crusting, deformities or a suspicion of septal perforation should be referred urgently. Ideally, the ear, nose and throat surgeon and the rheumatologist will work closely together to optimize the diagnosis and management of the patient. **BJHM**

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LEARNING POINTS

- Clinicians should have a low threshold for referring patients with recurrent sinusitis to an ear, nose and throat specialist for further investigation if they are not responding to antibiotics.
- Diagnosis of vasculitis can be challenging – a detailed history and a careful physical examination supported by laboratory results are essential in making a diagnosis.
- Urinalysis is the single most important investigation – proteinuria and/or haematuria in a patient with systemic illness requires further investigation and is a medical emergency in the context of vasculitis.
- Tissue biopsy is important to confirm the diagnosis before treatment with potentially toxic immunosuppressive drugs.
- Chest X-ray should be performed in all patients with suspected vasculitis to look for any evidence of infiltrates, haemorrhage or cavitation and to exclude infection.
- The treatment of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis consists of induction and then maintenance of remission. Treatment depends on the extent of the disease.