*The Journal of Laryngology & Otology (2012)*, **126**, 207–209.

doi:10.1017/S0022215111002209

CLINICAL RECORD

# Wegener's granulomatosis presenting as meningitis

G THIEL, M SHAKEEL, K AH-SEE

*Department of Otorhinolaryngology, Aberdeen Royal Infirmary, Scotland, UK*

## Abstract

*Background*: Wegener's granulomatosis is a rare but well recognised autoimmune necrotising vasculitis. Presentation of disease in the head and neck is common and mostly consists of nasal crusting, blockage and bloody discharge. Neurological presentation is very uncommon.

*Methods*: We report a patient who presented to the medical emergency services with signs and symptoms of meningitis, but who was eventually diagnosed with Wegener's granulomatosis. A literature search on this topic was carried out using Medline and Embase (1996 to 2011), searching for 'Wegener's granulomatosis' and 'meningitis'.

*Results*: After thorough neurological and medical investigation, a combination of brain computed tomography, lumbar puncture, nasal biopsy and laboratory results refuted the diagnosis of meningitis and confirmed the diagnosis of Wegener's granulomatosis.

*Conclusion*: To the best of our knowledge, this is the first English-language case report of a patient with Wegener's granulomatosis presenting with symptoms of meningitis unconfirmed on computed tomography and lumbar puncture.

**Key words:** Wegener's Granulomatosis; Meningitis; Nasal Cavity; Diagnosis

## Introduction

Wegener's granulomatosis is a rare but well recognised autoimmune necrotising vasculitis affecting the respiratory and renal tract to varying degrees.[1,2]

Presentation of disease in the head and neck is common and mostly consists of nasal crusting, blockage and bloody discharge.[1,2] However, varied presentations have been reported, including neurological symptoms and meningitis, although the latter is very rare and few reports exist in the literature.[3,4]

We report a woman who presented with clinical signs of meningitis, but with normal computed tomography (CT), magnetic resonance imaging (MRI) and lumbar puncture findings. She had previously undergone excision of a melanoma from her nostril, further complicating the diagnosis. Biopsies and circulating antineutrophil cytoplasm antibody levels confirmed the correct diagnosis, and the patient recovered on immunosuppressant treatment.

## Case report

A 60-year-old woman had initially presented complaining of increasing headache over the previous two weeks, together with flu-like symptoms and a blocked nose. She had been treated with doxycycline and subsequently clarithromycin, in conjunction with chlorphenamine, pseudoephedrine and xylometazoline, without clinical benefit.

The patient's past medical history consisted of hypothyroidism, osteoporosis, and a lentigenous malignant melanoma removed from the left nostril four years previously (Clarke level two, Breslow thickness 0.1 mm). The melanoma had been completely excised with a 4 mm margin, and the patient had been discharged from follow up the year before the current presentation.

Her only medication was thyroxine 200 µg once daily. She was a non-smoker and moderate drinker.

On the day of admission, the patient complained of severe headache, blurred vision, photophobia and neck stiffness. Her vital signs were unremarkable, except for a pulse rate of 120 beats per minute. Her temperature at the time of referral was 38.3°C, but had been 37°C on admission.

Examination revealed neck stiffness and photophobia. Kernig's sign was negative, the cranial nerves were grossly intact, and the pupils were equal and reactive to light, with equivocal fundoscopy.

The patient was admitted to the infectious diseases unit with a provisional diagnosis of meningitis possibly secondary to sinusitis.

Accepted for publication 21 March 2011 First published online 14 September 2011

Serological analysis revealed elevated liver function test results and C-reactive protein (CRP) levels but no other abnormality, in particular no renal derangement.

Blood cultures and a lumbar puncture were both negative.

A computed tomography brain scan was carried out urgently on the day after admission. This did not show any intracranial abnormalities, but did show opacification of the left maxillary sinus and left nostril.

The patient was commenced on intravenous ceftriaxone, but continued to suffer swinging pyrexia of approximately 38°C.

An ENT opinion was sought. Nasal endoscopy was found to be impeded by a friable mass filling both nostrils. The rest of the ENT examination was unremarkable.

An MRI scan revealed signs of inflammatory changes in the left maxillary sinus and both nostrils.

An ultrasound scan and abdominal CT were undertaken to exclude possible metastatic disease from the patient's previous melanoma; both were normal.

An urgent examination of the nose under anaesthesia was conducted, and biopsies taken. Both nostrils were blocked by a friable, bleeding, irregular mass with extension into the left maxillary sinus.

Histopathological examination of the biopsies demonstrated a haemorrhagic appearance, granulomata and a heavy inflammatory infiltrate. There were also areas of necrosis and acute inflammation, some centred around small vessels. There was no immunohistochemical evidence of carcinoma, lymphoma or melanoma. The findings were in keeping with Wegener's granulomatosis.

Analysis for circulating antineutrophil cytoplasm antibodies proved highly positive.

The patient was commenced on prednisolone and cyclophosphamide and showed signs of improvement within five days. After this initial treatment, she was commenced on methotrexate.

She was finally discharged two months after her initial hospital admission.

## Discussion

To the best of our knowledge, this is the first case report in the English-language literature of a patient with Wegener's granulomatosis presenting with symptoms of meningitis unconfirmed by CT scan and lumbar puncture.

A literature search was carried out using the Medline and Embase databases, searching 1996 to week nine of 2011, using the search terms 'Wegener's granulomatosis' and 'meningitis'.

### *Aetiology*

Wegener's granulomatosis is an autoimmune necrotising vasculitis of as yet unknown aetiology, first described by Wegener in 1936.[5]

The classical clinical triad of the disease consists of necrotising granulomatous inflammation of the respiratory tract, necrotising glomerulonephritis, and necrotising systemic vasculitis affecting predominantly small vessels.

Histologically, Wegener's granulomatosis has a characteristic triad of granulomatous inflammation, irregularly patterned necrosis and vasculitis.

Untreated, the outcome is potentially rapidly fatal due to systemic involvement.[1]

The European Vasculitis Study Group has defined the disease stages as: localised (i.e. restricted to the upper and/or lower respiratory tract); early systemic (i.e. any organ involvement except renal, and except imminent organ failure); and generalised (i.e. renal involvement and/or imminent organ failure).[6] Localised disease is found in under 5 per cent of patients.[2]

Wegener's granulomatosis is observed in children as well as adults, but the peak incidence is in the fourth and fifth decades of life.[2] The disease is rare, with an incidence of one per 100 000 and a prevalence of up to five per 100 000.[7,8]

### *Diagnosis*

The diagnosis of Wegener's granulomatosis is based on a combination of clinical features, laboratory tests and histology.[2]

Head and neck presentations of the disease vary, but commonly comprise nasal crusting, bloody discharge and obstruction. Middle-ear, laryngeal and neurological manifestations have been reported but are rather uncommon.[1]

In view of the great clinical variety of the disease, a high index of clinical suspicion is paramount in order to make the diagnosis.

Serological results are often non-specific, with raised CRP levels and erythrocyte sedimentation rate, and, in cases of renal involvement, elevated creatinin levels, hypercalaemia and metabolic acidosis.[2]

Detection of circulating antineutrophil cytoplasm antibodies plays an important role in the diagnosis. Analysis is positive in approximately 50 per cent of patients with localised disease, but in approximately 95 per cent of patients with generalised disease.[2] The antibody titre often correlates with the disease activity.

Histologically, Wegener's granulomatosis is characterised by three findings: necrosis, granulomatous inflammation and vasculitis. The combination of all three criteria is found in only 15 to 25 per cent of biopsies from the ENT area.[9] In most cases, only one criterion is found.[1]

### *Treatment*

Treatment of Wegener's granulomatosis consists of immunosuppressant therapy, which should be initiated as soon as possible as the disease can be rapidly fatal. Surgical therapy plays only a very limited role.

At present, the Fauci protocol represents the standard treatment. This consists of a combination of

https://doi.org/10.1017/S0022215111002209 Published online by Cambridge University Press

prednisolone and cyclophosphamide, and leads to remission rates of over 90 per cent.[10]

However, these drugs (especially cyclophosphamide) lead to considerable morbidity and mortality (due to serious infections, lymphoma, bladder carcinoma and myelodysplastic syndrome).[11] The extent of such pathology is directly correlated to the cumulative dose of cyclophosphamide. Thus, the total exposure should be as low as possible.

- **Wegener's granulomatosis is a rare but well recognised autoimmune necrotising vasculitis**
- **As an acute presentation it is an emergency, due to potentially fatal renal impairment**
- **Presentation can vary; the presented case mimicked the signs and symptoms of meningitis, without actual meningeal involvement**

Alternatives to cyclophosphamide comprise methotrexate and trimethoprim plus sulfamethoxazole, and can be used in patients in remission or with localised disease processes.

*Outcome*

Despite the fact that Wegener's granulomatosis is a potentially fatal disease, the use of immunosuppressant therapy has enabled reported remission rates as high as 90 per cent.[10]

## Conclusion

Wegener's granulomatosis is a rare and potentially fatal immune vasculitis, but immunosuppressant therapy can give good results.

Presentation is very varied, and a high index of clinical suspicion is paramount in order to initiate treatment as soon as possible.

We present a case of Wegener's granulomatosis which posed a diagnostic dilemma as the presentation clinically mimicked meningitis, although there were no radiological or bacteriological indicators of central nervous system disease. A second misleading factor was the previous excision of a malignant melanoma from the patient's external nose.

In this patient, a combination of clinical presentation, histological findings and laboratory tests (specifically circulating antineutrophil cytoplasm antibody levels) led to the diagnosis of Wegener's granulomatosis. Treatment was commenced and good results achieved within a short period of time.

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Address for correspondence:
Dr Gundula Thiel,
University Department of Otorhinolaryngology,
Lauriston Building,
Lauriston Place,
Edinburgh EH3 9HA, Scotland, UK

E-mail: gundulathiel@doctors.org.uk



Dr G Thiel takes responsibility for the integrity of the content of the paper
Competing interests: None declared