The Journal of Laryngology and Otology
August 1997, Vol. **111**, pp. 746–748

Clinical Records

Misleading clinical features in Wegener's granulomatosis. A case report

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Abstract
Wegener's granulomatosis is a systemic vasculitis that may present with a variety of findings and be difficult to diagnose. We report a case of a patient who presented with serous otitis media and subsequently developed a suspected primary lung tumour. Thoracotomy and pulmonary mass excision were required to establish the diagnosis. Otological manifestations of Wegener's granulomatosis, differential diagnosis, pathological findings and c-ANCA test role are discussed.

Key words: Wegener's granulomatosis; Otitis media with effusion; Granuloma, respiratory tract

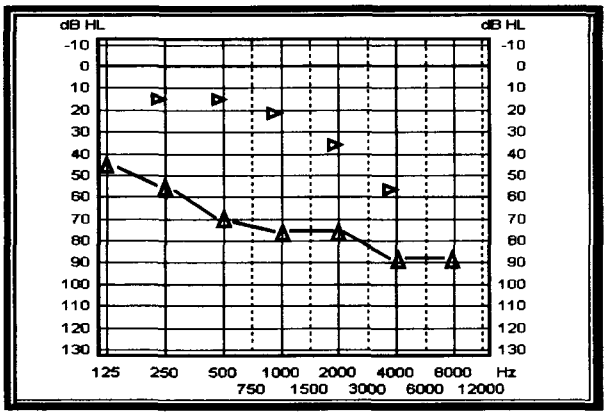
Introduction

Wegener's granulomatosis is a rare systemic disease of unknown aetiology, characterized by necrotizing granulomatous lesions and vasculitis involving both small arteries and veins. It mainly affects the upper respiratory tract where it can remain limited for long periods of time to then spread to other organs, primarily the lung and kidney (Illum and Thorling, 1981; Fauci *et al.*, 1983; Cohen Tervaert *et al.*, 1990; Anderson *et al.*, 1992; Lebovics *et al.*, 1992). Forms of this disease with limited lesions elsewhere and the absence of renal involvement have been described (Lee *et al.*, 1993; Benson-Mitchell *et al.*, 1994).

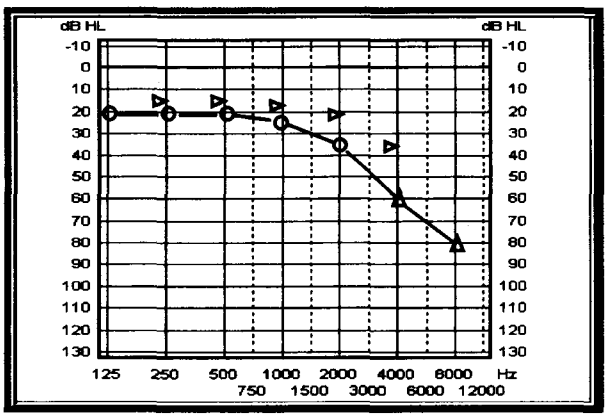
We report a case of Wegener's granulomatosis in a patient who presented with serous otitis media.

Case report

A 53-year-old woman presented with a four-month history of hearing loss, otalgia, fullness of the right ear and nasal obstruction. Otoscopy revealed a hyperaemic right tympanic membrane with middle-ear effusion. Anterior rhinoscopy showed hypertrophy of the turbinates and oedematous nasal mucosa. An audiogram revealed a severe mixed hearing loss in the right ear (Figure 1). Computed tomography (CT) scan showed opacification of the right middle-ear cleft and mastoid air cells and of the left maxillary sinus (Figure 2). A nasopharynx biopsy revealed a picture of the inflammatory type. Laboratory findings revealed only mild eosinophilia and dysproteinaemia. The allergometric tests showed a marked specific skin hyper-reactivity. Allergic rhinopathy with Eustachian tube and sinusal involvement was suspected. The middle-ear effusion, inflammation, and hearing loss were resolved with steroid (40 mg/day methylprednisone i.m.) and antibiotic (1 g/day ciprofloxacin p.o.) therapy. Two months later the patient presented again with the same otological and rhinological symptoms, but she also complained of chest pain and a slight fever (37.8 °C). The audiogram and



(a)



(b)

FIG. 1
(a) Pre-treatment audiogram showing severe mixed hearing loss.
(b) A month post-treatment audiogram after steroidal treatment showing resolution of mixed hearing loss.

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Accepted for publication: 20 May 1997.

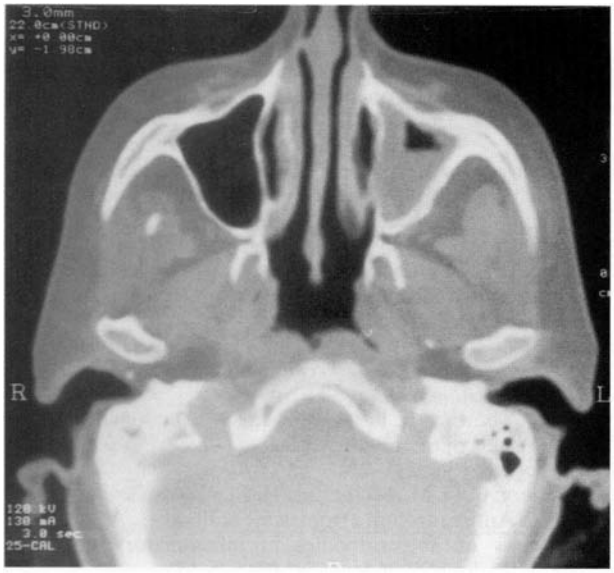

FIG. 2
Axial CT scan showing opacification of the right mastoid air cells and of the left maxillary sinus.

tympanogram had worsened, and a temporal bone CT scan confirmed an inflammatory picture without evidence of bony erosion on the right side. Chest CT revealed a roundish opacity with irregular borders, about 3 cm in diameter and without signs of calcification, in the apical segment of the right upper lobe (Figure 3). No adenopathy or other sign were seen. Microbiological examination of the sputum excluded infection with *Mycobacterium tuberculosis*. Bronchoscopy revealed an inflammatory cytological picture. Lung scintigraphy showed a reduced perfusion of the pulmonary region corresponding to the lesion detected by radiography, and a 99 m TC-MDP skeletal scintiscan revealed a radiophosphate uptake in the right mastoidal area of the skull, suggesting a secondary localization.

A primary lung tumour was then suspected by a thoracic surgeon and the patient underwent thoracotomy and a $3 \times 3 \times 2$ cm nodular mass was removed. Pathological examination showed necrotizing granulomas with scattered giant cells. Nasal obstruction and swelling of the sinonasal mucosa, associated with a granulomatous neoformation in the lung suggested the diagnosis of Wegener's granulomatosis. A serum specimen was submitted for antineutrophilic cytoplasmic antibody (c-ANCA) assay and proved to be positive. After about three months there

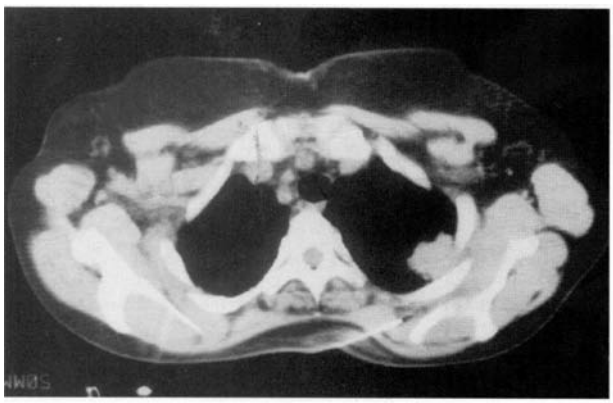

FIG. 3
Axial chest scan showing a roundish opacity with irregular borders in the apical segment of the right upper lobe.

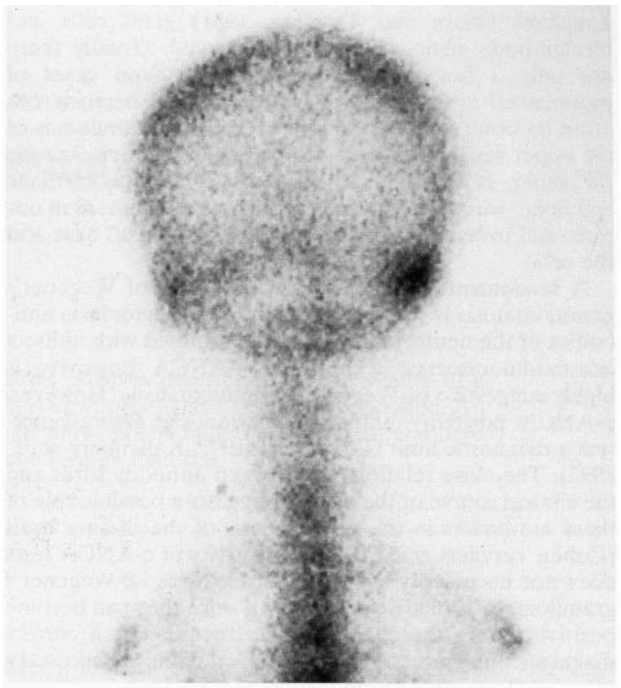

FIG. 4
Skeletal 99mTC-MDP scintiscan showing a radiophosphate uptake in the right mastoidal area.

was an initial deformation of the nasal pyramid which strongly supported a diagnosis of Wegener's granulomatosis. Steroidal treatment was instituted and the outcome was good.

Discussion

Otological symptoms can represent the onset of Wegener's granulomatosis in 20–25 per cent of cases, whereas aural lesions may develop during the course of the disease in 14 to 45 per cent of cases (Illum and Thorling, 1981; Kornblut *et al.*, 1982; Fauci *et al.*, 1983; Choufani *et al.*, 1991; Lebovics *et al.*, 1992). In the former cases a conductive or mixed, uni- or bilateral hearing loss associated with other objective signs of otitis media with effusion can be the presenting features. Granulomatous obstruction of the Eustachian tube often constitutes the pathological basis of the disease, while a sensorineural hearing loss due to vascular damage (Davenport, 1992), deposits of immune complexes in the cochlear site or granulomatous involvement of the cochlear nerve (Macias *et al.*, 1993) is less frequent.

Early diagnosis is difficult because of the variety of signs and symptoms, which are not always pathognomonic. In our case differential diagnosis excluded the following pathologies: neoplastic disease such as primary or metastatic lung cancer, tuberculosis, nasopharyngeal lymphoma, non-keratinizing squamous cell carcinoma, Hodgkin's lymphoma and Churg-Strauss's disease (Kornblut *et al.*, 1982; Gordon *et al.*, 1993).

Wegener's granulomatosis was initially believed to be an atypical form of polyarteritis nodosa on the basis of its clinical and anatomical features, but Wegener subsequently stressed the importance of necrosis with the formation of granulomas. A granuloma forms primarily in the connective tissue, without vascular involvement, and can remain quiescent for a long time. Subsequently, scattered granulomas can be seen as miliary nodules composed mainly of histiocytes and epithelioid cells, and

https://doi.org/10.1017/S0022215100138502 Published online by Cambridge University Press

Langhans (Illum and Thorling, 1981) giant cells and foreign-body giant cells can be observed. Usually there are only a few eosinophilic leukocytes and cases of pronounced eosinophilia are rare. Central necrosis can often be observed. The rapidly necrotizing granulomas of the upper respiratory tract can cause colliquative necrosis (Wegener, 1990) of the adjacent tissues, such as cartilage and bone, with consequent deformity of the nose, as in our case, and invasion of the paranasal cells of skull base and the orbit.

A fundamental element in the diagnosis of Wegener's granulomatosis is serum-positivity for anti-cytoplasm antibodies of the neutrophils (c-ANCA), studied with indirect immunofluorescence techniques. c-ANCA positivity is highly suggestive of Wegener's granulomatosis. However, p-ANCA positivity, shown by perinuclear fluorescence, sets a diagnostic limit (Davenport, 1992; Kallenberg *et al.*, 1992). The close relationship between antibody titres and the clinical course of the disease suggests a possible role of these antibodies in the pathogenesis of the disease itself (Cohen Tervaert *et al.*, 1990). Negativity of c-ANCA tests does not necessarily exclude the diagnosis of Wegener's granulomatosis (Carrie *et al.*, 1994), since they can become positive during the course of the disease. For a correct diagnostic interpretation of serological data it is necessary to carefully assess the clinical-pathological relationship in the case being examined. Therefore, in the presence of meaningful clinical and pathological parameters, even when the c-ANCA titre is negative, treatment is necessary (Davenport, 1992; Carrie *et al.*, 1994).

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