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Wegener's granulomatosis presenting as major salivary gland enlargement

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Abstract
Salivary gland involvement is rare in Wegener's granulomatosis. We report the first case of widespread major salivary gland enlargement as part of the presentation of this disease. A review of the few reported cases in the literature suggests that salivary gland involvement may be associated with a limited form of the disease and an improved prognosis. The anti-neutrophil cytoplasmic antibody (c-ANCA) assay remains the gold standard of diagnosis but care should be exercised in the interpretation of results. This patient responded well to current immunosuppressive therapy.

Key words: Wegener's granulomatosis; Parotid gland; Submandibular gland

Introduction

Wegener's granulomatosis (WG) is a systemic disease characterized by the triad of necrotising granulomatous vasculitis of the upper and lower respiratory tracts and the kidneys. The progress of the disease can be unpredictable if left untreated. Most patients respond well to steroids and/or cyclophosphamide with the possibility of long-term remission (Hunder and Lie, 1990). Some success has been reported with trimethoprim-sulphamethoxazole especially in cases with limited disease (Specks *et al.*, 1991). The term 'limited' refers to preservation of renal function and has a good prognosis when treated.

The discovery of the c-ANCA auto-antibody, which has a high degree of specificity for WG, has played a significant role in aiding diagnosis and monitoring treatment (van der Woude *et al.*, 1985).

Salivary gland involvement is a rare mode of presentation for WG. In the past 10 years there have been only two papers describing major salivary gland involvement (Specks *et al.*, 1991; Benson-Mitchell *et al.*, 1994). All reports, however, were of either parotid or submandibular gland involvement. We report a case which is, to our knowledge, the first with bilateral parotid and submandibular gland enlargement as a presenting symptom in WG.

Case report

A 48-year-old lady was admitted as an emergency to the ENT department with a 48-hour history of painful bilateral parotid and submandibular gland enlargement. This was associated with general malaise and lethargy. Two weeks earlier she had attended the ENT out-patient department with a history and symptoms of acute rhinosinusitis. This initially responded well to topical decongestants and oral antibiotics.

On admission her nasal symptoms had recurred. In addition she was complaining of a recent cough productive of clear sputum.

On examination she was mildly pyrexial at 37.5° C. She looked unwell with bilateral nasal obstruction and a markedly congested nasal mucosa. She had prominent bilateral tender enlargement of both parotid and both submandibular glands. She had enlarged jugulo-digastric lymph nodes bilaterally. Her blood pressure and pulse were stable and normal.

Pertinent laboratory results included: ESR 76 mm/h; haemoglobin 12 g/dl; white cell count 18.6×10^9/l; platelets 570×10^9/l. Her urea and electrolytes were normal as were the liver function tests. Urinalysis revealed microscopic haematuria and moderate proteinuria. A chest X-ray on admission was normal while sinus X-rays revealed opacification of the maxillary sinuses. Serology for mumps, cytomegalovirus (CMV) and Epstein-Barr virus

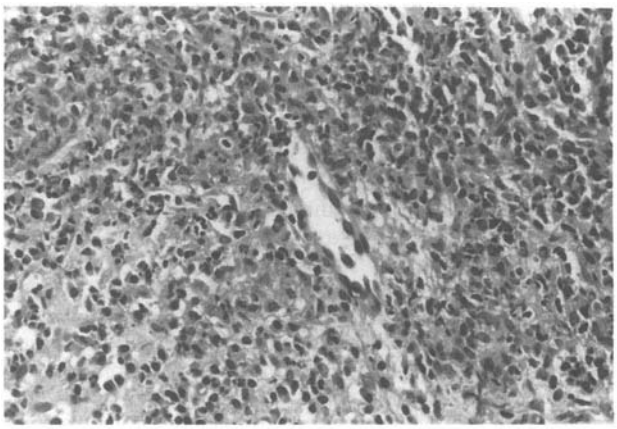

FIG. 1
Biopsy from nasal septum shows a diffuse inflammatory infiltrate with a vasculocentric pattern. (H & E; × 25).

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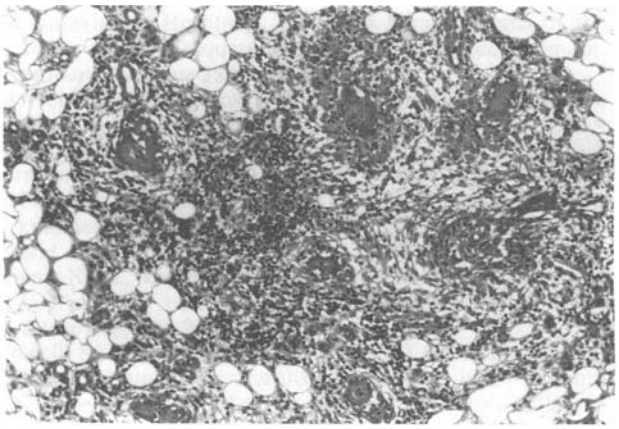

FIG. 2

The biopsy from the parotid gland shows considerable acinar destruction. There is a combined microscopic vasculitis and intense inflammatory infiltrate of salivary ducts and acini. (H & E; × 10).

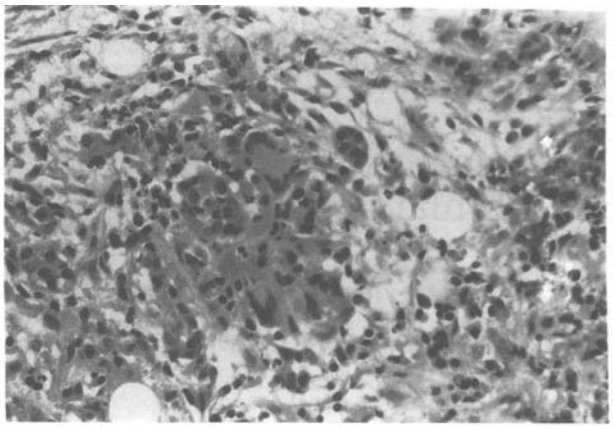

FIG. 3

The acinocentric inflammatory destruction produces a granulomatous appearance with multinucleate giant cells in the parotid. (H & E; × 40).

(EBV) was negative.

Open biopsies of the right parotid gland and nasal septal mucosa revealed florid inflammatory changes. In the nasal septum there was an obliterative vasculitis with transmural infiltration of lymphocytes and scattered eosinophils and neutrophils (Figure 1). Giant cells were not observed. Despite this, however, the site and presence of a mixed lymphocytic eosinophilic vasculitis was suggestive of WG. The parotid gland showed a destructive inflammatory infiltrate in which giant cells were seen. The inflammatory component was only partly vasculocentric and the major involvement seemed to relate to salivary ducts and acini (Figure 2). At the sites of acinar destruction the giant cell aggregation produced a granulomatous appearance (Figure 3). Taking the two biopsies together a diagnosis of granulomatous vasculitis seemed the only tenable explanation.

Serology for c-ANCA was obtained using the two available assays. Interestingly, the immunofluorescent assay was negative for elevated titres of the antibody while the ELISA assay was strongly positive (67 U., normal <4U.).

The patient was treated immediately with oral high dose prednisolone and subsequently with cyclophosphamide and responded well.

Discussion

To our knowledge this is the first case of widespread major salivary gland enlargement as a presenting feature of Wegener's granulomatosis.

Fahey *et al.* (1954) were the first to report parotid gland involvement while submandibular gland involvement was reported in 1976 (Smith and Konrad, 1976). Only two papers have appeared in the past 10 years reporting salivary gland involvement in WG (Specks *et al.,* 1991; Benson-Mitchell *et al.,* 1994). None of these, however, involved widespread salivary gland disease. All five cases reported by Specks *et al.* (1991) had preservation of renal function and as such were defined as limited WG.

A recent report described tumefactions in various parenchymal sites including retroperitoneum, mediastinum, retro-orbit, gingiva and breast (Goulart *et al.,* 1995). The salivary gland was not among the organs involved in that report.

The gold standard for the diagnosis of WG remains the c-ANCA assay. In our case however the immunofluorescent assay proved negative while the ELISA assay was strongly positive. These tests may be negative in 15–33 per cent of cases, particularly those without renal disease (Nolle *et al.,* 1989). c-ANCA alone therefore is not sufficient to make the diagnosis of WG and a tissue biopsy is recommended (Rao *et al.,* 1995).

The differential diagnosis included sarcoidosis but this was excluded on both clinical (normal chest X-ray) and histological grounds. While salivary gland granulomata would be expected in sarcoid the degree of parenchymal destruction related to the mixed acute and chronic infiltrate which was ductulo- and acinocentric would not be found. Moreover, the histological features seen in the nasal septal biopsy were quite unlike those of sarcoidosis.

The renal function in this case has remained normal while urine culture revealed a coliform infection which was successfully treated with antibiotics and the haematuria resolved. The introduction of immunosuppressant therapy has vastly improved the prognosis for these patients and this lady, in particular, remains well following prednisolone and cyclophosphamide therapy.

In summary while salivary gland involvement in WG is rare we recommend a degree of clinical suspicion so that an early diagnosis is obtained and early treatment commenced. Salivary gland involvement may indicate an association with preserved renal function and as such a better prognosis on treatment.

Finally c-ANCA remains the definitive diagnostic test but we recommend that both the immunofluorescent and the ELISA forms of analysis are requested and that if possible histological confirmation should also be obtained.

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