To the Editor:

Wegener's granulomatosis (WG) is a multisystemic disease with a complex genetic background. The clinical presentation is characterized by necrotizing granulomatous inflammation of the upper and lower respiratory tract, glomerulonephritis, and small-vessel vasculitis. We describe an unusual primary manifestation of WG with salivary gland swelling.

A 68-year-old man who was admitted to the hospital presented with progressive swellings of his right cheek and bilateral submandibular space over a period of several weeks. Extraoral examination revealed a bilateral enlargement of both submandibular glands and the right parotid gland, which were solid, plain, and painless to pressure (Figure 1.1). The oral cavity showed no pathologies of the mucosa, and no putrid secretion from the Stenon's duct was determined. His history was notable for eye complications with dryness and reddening, ear complaints with bilateral hearing impairment, severe headache, night sweats, muscular weakness, and weight loss of about 8 kg during the 6 weeks before presentation. Blood tests revealed increased values for erythrocyte sedimentation rate (110/115 mm), C-reactive protein (203.7 mg/l), and leukocytes (13.18/nl). On magnetic resonance imaging (MRI), the right parotid gland and the submandibular glands were enlarged, demonstrating low signal intensity in T1-weighted and T2-weighted imaging (Figure 1.2 a and b, and Figure 1.3).

Figure 1. 1.1: Note the massive bilateral enlargement of submandibular space and the right cheek. 1.2: Axial noncontrast enhanced T1-weighted (a) and T2-weighted, fat-suppressed sequences (b) show a markedly enlarged right parotid gland with hypointense signal. There is homogeneous enhancement in T1-weighted fat-suppressed imaging after intravenous contrast media application (c). 1.3: In contrast to T1-weighted imaging (a), T2-weighted fat-suppressed (b) and contrast enhanced T1-weighted fat-suppressed (c) sequences reveal inhomogeneous signals of the enlarged submandibular glands, leading to suspicion of presence of small necrotic parts.
a and b). After intravenous application of contrast media, marked enhancement was found in the affected sites, with inhomogeneous signals in the submandibular glands (Figure 1.2c and Figure 1.3c). There was no evidence of abscess formation or malignancy in which small areas of necrosis could be found. The patient left the clinic without a firmly established diagnosis and refused further diagnostic measures. He underwent medical examinations at regular intervals by his general practitioner. A presumptive diagnosis of Heerfordt syndrome was made (an acute syndrome presentation of sarcoidosis, presenting with fever, uveitis, and swelling of the parotid and/or other salivary/lacrimal glands) and longterm treatment with a reducing regime of prednisolone was started (beginning with 60 mg daily). The swelling of the salivary glands disappeared after 3 months, but general symptoms persisted. Meanwhile, a further laboratory analysis revealed elevated cytoplasmic antineutrophil cytoplasmic antibodies (cANCA; 1/276) and proteinase-3-ANCA (196.0 U/ml), results that raised the suspicion of WG. However, the patient again refused further medical examinations to confirm the diagnosis. A definite diagnosis of WG was confirmed at autopsy by histological evaluation of renal specimens following unexpected cardiac death about 1 year later. The autopsy showed pauci-immune extracapillary proliferative glomerulonephritis (Figure 2).

Salivary gland swelling is a frequent symptom reflecting different pathologies. If the enlargement is not confined to 1 salivary gland, a systemic cause must be assumed. In spite of that, even other diseases usually causing unilateral salivary gland swelling may occasionally induce bilateral swelling. So it is appropriate to keep all these diseases in mind when establishing an accurate diagnosis (Table 1). We observed an unusual primary manifestation of WG with bilateral enlargement of both submandibular glands and the right parotid gland. Accurate diagnosis of WG is based on clinical, histopathological, and blood chemical investigations. Additionally, classification according to the criteria of the American College of Rheumatology (ACR)\(^2\) seems apt. However, there are cases in which the ACR criteria are not fulfilled. In particular, so-called localized WG, possibly initially present in our patient, is not considered in the ACR criteria. According to the European Vasculitis Study Group, “localized disease” is defined as WG without vasculitis outside the ear, nose, and throat tract and the lung, without threatened vital organ function, and without constitutional symptoms\(^3\).

In these cases, an early cANCA test may aid diagnosis and provide essential information for early therapy and thus prevent disease progression. A disadvantage is that the sensitivity depends largely on the extent of the disease. For systemic WG, the sensitivity approaches 96%, while in localized forms, sensitivities of about 67% or less are described\(^4\). In the case of localized WG, ANCA could also be negative\(^5\). Hence it is appropriate to consider other symptoms that can help to establish the diagnosis of WG, such as salivary gland enlargement. Review of the literature revealed that salivary gland swelling, as described above, is a rare feature in WG, which is mostly confined to the parotid and submandibular glands\(^6\), but even sublingual salivary glands can be affected\(^7\). Descriptions of salivary gland enlargement as an initial symptom of systemic manifestation of WG are rare but some cases have been published\(^8\).

MRI findings in our patient were unspecific, consistent with an inflammatory process. Nevertheless, low signal intensity of the involved salivary glands in T2-weighted imaging has been described in other granulomatous lesions and may be assessed at least as an indicator for WG\(^9\).

The disastrous course of disease in this patient shows that today, survival rates in untreated patients are as low as initially described. Fauci, et al revealed that in the mid-1980s, nearly 90% of untreated patients with WG died within 2 years\(^10\). With up-to-date treatment, the standardized mortality rate for a patient with WG is not increased\(^11\).

Salivary gland involvement in WG is very rare, but it should be considered in the differential diagnosis of this symptom. Early diagnosis is important, as immediate treatment can dramatically improve the prognosis and prevent complications.

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Table 1. Diseases accompanied by salivary gland enlargement.

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Infection</td>
<td>Bacterial (Acute purulent), Chronic recurrent, Viral (Epidemic parotitis), Specific bacterial (Tuberculosis)</td>
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<tr>
<td>Neoplastic disease</td>
<td>(Kaposi sarcoma herpesvirus, Epstein-Barr virus, etc.)</td>
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<td>Obstructive electrolyte sialadenitis</td>
<td>(+/- sialolithiasis)</td>
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<td>Sialadenosis</td>
<td>Endocrine disturbance (e.g., diabetes mellitus), Psychogenic disturbance (e.g., bulimia), Dystrophic disturbance (e.g., cachexia)</td>
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Figure 2. Kidney autopsy section showing cellular crescent formation in the right part of the glomerulus (arrow). In this periodic acid-Schiff stain, bar represents 50 µm.
REFERENCES
Correction