Parotid Gland Involvement as Initial Presentation of Wegener’s Granulomatosis: A Diagnostic Pitfall

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Wegener’s granulomatosis, or by its new nomenclature granulomatosis with polyangiitis, is included in the group of antineutrophil cytoplasmic antibody-associated vasculitides. Characterized by necrosis, granulomatous inflammation and vasculitis, it typically consists of the classic triad of upper and lower respiratory tract involvement and crescentic glomerulonephritis [1]. Being a systemic vasculitis, other diverse clinical manifestations frequently occur and include fever, joint involvement, ocular abnormalities, skin lesions, central and peripheral nervous system involvement and myo/pericarditis. Involvement of parotid glands is, however, rare.

We present a patient who presented with painful unilateral parotid gland enlargement. Thought of as either an infective or tumorous process, prolonged antibiotic treatment was administered to no avail. Eventually parotid gland biopsy was performed. Follow-up ascertained that the parotid gland involvement was actually the initial manifestation of GPA. October 2011, following a 10 day history of fever, swelling and intractable pain in the right lower mandibular region. Prior to admission he had been treated with oral amoxycillin/clavulanic acid to no avail. A presumptive diagnosis of acute parotitis or an infected Warthin’s tumor was made and the patient was given intravenous antibiotics. Subjectively, a very mild improvement was noted and the patient was discharged on continued oral medication. A fortnight later he was examined in the emergency department complaining of ongoing severe mandibular pain. Examination revealed a solid painful mass of the right parotid gland, and ultrasonography of the gland was recommended upon discharge.

A week later the patient was readmitted with a purulent discharging sinus in the right mandibular area and a lower motor neuron right facial nerve palsy. Serum creatinine, which had not been checked, ranged from 1.0 to 1.3 mg/dl (basal value 0.8 mg/dl a year previously). Culture of the sinus discharge grew methicillin-sensitive Staphyocccal aureus. Acid-fast stain was negative. Fundoscopic examination, chest X-ray and brain computed tomography were normal. Cervical computed tomography demonstrated an enlarged inhomogeneous right parotid gland with numerous calcifications which compressed intraparotid blood vessels with regional lymphadenopathy. Fine needle aspiration of the parotid mass showed a mixed population of small and medium-sized lymphocytes, histiocytes and a few multinucleated giant cells. It was interpreted as being compatible with a reactive process, although the possibility of granulomatous inflammation was considered. The patient was treated with intravenous cefazolin for another 2 weeks without any noticeable improvement. Consequently, biopsy of the parotid gland was performed and the patient was discharged pending histological diagnosis.

Three weeks later, he was readmitted due to the appearance of a new solid mass in the central cervical region and oliguria. Laboratory data revealed serum hemoglobin 8 g/dl, serum creatinine 13 mg/dl, urea 285 mg/dl, serum pH 7.379 with a bicarbonate (HCO3) of 15 mM/L. Dipstick urinalysis showed red blood cells 200/µl, and protein 300 mg/dl. C-ANCA tested positive at a titer of 1/80, anti-proteinase-3 antibodies 92.88 U/ml (normal range 0–5 U/ml). A chest X-ray demonstrated bilateral pulmonary infiltrates.

Emergency hemodialysis was performed. Kidney biopsy demonstrated a pauci-immune crescentic glomerulonephritis [Figure A]. In parallel, the parotid gland biopsy was finally available and showed massive necrosis of the gland and soft tissue with focal acute and chronic granulomatous inflammation [Figure B]. There was no evidence of malignancy.

The diagnosis of GPA was established. The patient was treated with intravenous pulse steroids followed by oral prednisone and cyclophosphamide. Plasmapheresis was not performed. Despite this treatment, the patient remains dialysis dependent. The parotid gland mass and central cervical mass resolved rapidly following the commencement of immunosuppressive treatment.
COMMENT

Although ear, nose and throat symptoms are part and parcel of the upper respiratory tract manifestations in GPA, salivary gland involvement and in particular that of the parotid gland has rarely been documented. In an analysis of 158 patients with GPA, Hoffman et al. [2] reported more than 1% of biopsy-proven parotid gland involvement. When it does occur, it presents with either unilateral or bilateral swelling of the gland usually accompanied by severe pain and fever. As such, it mimics infective conditions of the gland (mumps, tuberculosis, actinomycosis) or non-infective inflammatory conditions, the most common being Sjögren syndrome and sarcoidosis.

In the presence of an ill-defined parotid mass, suspicion of a neoplastic process is also raised. Our patient is a case in point, precisely illustrating this line of thinking. Continued consideration of either an infective or tumorous condition of the gland resulted in a much delayed diagnosis of GPA with severe consequences. Notably, although interpretation of the fine needle aspiration of the gland raised the possibility of a granulomatous process, it did not serve to alert the attending physicians to an alternative diagnosis.

Even a simple urinalysis that might have been indicative of renal involvement was not performed during the early part of the patient’s course. When he eventually presented with renal failure necessitating dialysis, a belated positive C-ANCA and a renal biopsy showing a necrotizing, crescentic, pauci-immune glomerulonephritis established the correct diagnosis of GPA. The parotid gland biopsy demonstrating granulomatous necrosis with vasculitis confirmed the gland’s involvement. Treated with cyclophosphamide and intravenous pulse steroids followed by oral steroids, the patient has remained on dialysis. It may be argued that plasma exchange should have been part of the therapeutic regimen as, according to the Mepex study, it was seen to enhance the recovery of renal function in dialysis-dependent ANCA-associated vasculitis [3].

In summary, we report a patient whose initial manifestation of GPA was involvement of the parotid gland. Due to the rarity of such a presentation of WG, diagnosis was delayed. GPA should be considered in the differential diagnosis of isolated inflammatory parotid enlargement. As exemplified by our patient, salivary gland involvement appears to be an early feature in GPA and the disease can run a very rapid and severe course. A high index of suspicion is therefore warranted. Testing for C-ANCA should be done promptly since antibodies were found to be positive in 67% of cases of limited WG and in up to 95% of systemic GPA [4]. We recommend that a routine urinalysis be performed in patients with parotid gland masses that fail to resolve in the expected time frame after treatment of common causes. The information that hints at renal involvement would lead to a speedier correct diagnosis. Specific treatment could then be rapidly initiated in the hope of preventing irreversible renal failure.

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