Do Not Ignore Tuberculosis of the Parotid Gland When Meeting Obvious Infiltration of Neutrophils in a Suspicious Swelling by FNAC

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Abstract
Parotid gland tuberculosis constantly results in unnecessary medical examinations and surgery because of its similarities in the presentation to neoplasms of the parotid gland. Although parotid gland involvement is extremely rare even in tuberculosis-endemic countries, accurate diagnosis of this clinical entity is of great significance because tuberculous parotitis can be successfully treated medically without surgical therapy. Fine needle aspiration cytology (FNAC) and molecular identification of the parotid swellings are efficient in making a rapid diagnosis. Herein, we report an early misdiagnosis of malignancy from a renal transplantation patient on long-term immunologic inhibitor therapy, who ultimately proved to have tuberculosis of the parotid gland by FNAC and molecular identification. The aim of this study is to describe and analyze the etiologic characteristics, epidemiology, clinical presentations, diagnostic methods, histopathologic findings, and pathogenic mechanisms of these rare infections.

Keywords
Mycobacterium tuberculosis, parotid gland, fine needle aspiration, molecular identification, ultrasonography

Introduction
Tuberculosis is a prevalent necrotizing granulomatous disease caused by Mycobacterium tuberculosis from the skin and oropharynx, which can invade any organ.¹ However, parotid gland involvement is extremely unusual, even in countries where it is widespread.² Furthermore, the similarities in the presentations of parotid tuberculosis and tumors frequently lead to misdiagnosis. Thus, feasible and effective methods to make the diagnosis of parotid gland tuberculosis are particularly important both to physicians and patients. Fine needle aspiration cytology (FNAC) in combination with molecular identification has gained widespread acceptance and popularity in the assessment of neck masses, as they can accurately confirm the suspicion of parotid gland tuberculosis even in the absence of a history of pulmonary tuberculosis and relevant clinical symptoms.³

Case Presentation
Clinical Features
A 52-year-old male with no medical history of personal or family tuberculosis presented to us with painful swelling in the left parotido-mastetectic region of 2 months’ duration. The diagnosis was neoplasm of the parotid gland in primary hospital, so he was recommended to come to Zhejiang Provincial People’s Hospital for review and further pathological examination. The patient had no other symptoms or complaints, such as night sweats or weight loss, and his facial nerve function was normal. However, he had taken prograf (FK506), which has long been used for immunosuppression in kidney transplant patients to prevent rejection of the new kidney. His blood pressure, pulse rate, routine blood, erythrocyte sedimentation rate, and urine investigations were within normal limits. Sputum was collected after inhalation of saline aerosol, and sputum culture was negative for M tuberculosis. His serum was non-reactive for HIV, and chest X-ray was also normal.
Local Physical Examination

The patient presented to a doctor with a 2-month history of painful swelling in the left parotidomasseteric region that was approximately the size of an egg. Ultrasonography revealed many firm and tender hypoechoic nodules over the left parotid and parotidomasseteric region, and the largest mass was measured at 2.0 × 1.3 cm. The results indicated that the superficial lymphadenopathy might be caused by the irregular and heterogeneous mass of the left parotid gland (Figure 1).

Fine Needle Aspiration Cytology Findings and Differential Diagnosis

A breakthrough diagnostic result was made by means of FNAC of the peripheral lesions. The detailed procedures of FNAC have been described in the literature. White viscous pus obtained by aspiration of the swelling was examined microscopically after Wright-Giemsa staining and acid-fast staining. The Wright-Giemsa staining results are shown in Figure S1 in Supplementary Material, and detailed procedures for Wright-Giemsa staining have been described in the literature. Obvious infiltration of neutrophils in the Wright-Giemsa staining result suggested that bacterial inflammation should be excluded, so a direct smear of the pus was conducted with Ziehl-Neelsen acid-fast staining to detect tubercle bacillus (Figure 2). The detailed procedures of Ziehl-Neelsen acid-fast staining have been described in the literature. The presence of *M. tuberculosis* in the pus was further confirmed by microbiological investigation according to methods reported in the literature.

Molecular Identification

Molecular identification using a PCR-Fluorescence Diagnostic Kit for *M. tuberculosis* DNA (DANA, Cat. # DA-B052) was used to specifically detect the amount of *M. tuberculosis* DNA (Figure S2 in Supplementary Material). Assays were performed using the LightCycler 480 II Real-Time Polymerase Chain Reaction System using commercially synthesized primers and fluorescently labeled probes that the kit included.

Discussion

Tuberculosis mostly affects the lungs, but extrapulmonary forms of the disease may present in concurrence with a focus in the lungs or may present primarily without pulmonary involvement. Tuberculosis of the parotid gland is one type of extrapulmonary tuberculosis that is difficult to diagnose due to the absence of systemic signs and symptoms of the infection.
Therefore, it is generally overlooked by physicians, and most patients undergo unnecessary surgery due to indistinctness from a malignancy. Ascertaining the clinical likelihood of tuberculosis of the parotid gland based on elementary parameters is of great significance because it can be successfully treated medically, without surgical therapy. Although the precise pathogenic mechanism of parotid tuberculosis remains unclear, and the complete source of parotid tuberculosis remains controversial, it has been confirmed that the formation of necrotic foci is caused by *M. tuberculosis*, which is mainly liberated from the oral cavity or primary foci and ascends into the salivary gland via lymphatic drainage. Confirming the pathogenesis of parotid tuberculosis has important significance for clinical therapy and merits further exploration.

In this case, the patient was experiencing the side effects of immunosuppressive therapy, which are the major drawbacks to renal transplantation. It eventually led to a decrease in his immunity and contributed to the infection and the difficulty of treatment. Thus, when *M. tuberculosis* invaded the parotid gland through the blood or lymphatic system, it induced inflammatory infiltration around most irregular white necrotic foci.

The etiology, clinical manifestations, pathogen treatment, and prognosis of parotid tuberculosis are variable among patients. It usually appears as a localized, uniform, unilateral, firm-to-hard nodular parotid mass resulting from mycobacterial infection of intracapsular or pericapsular lymph nodes and gradually increases in size over several months or may exist for decades without any systemic symptoms. Diffuse glandular enlargement with the involvement of glandular parenchyma as acute parotitis has commonly been described. Besides, it also presents as a periauricular fistula or an abscess in the parotid gland.

Unilateral tuberculous parotitis is clinically indistinguishable from a primary neoplasm, especially in the absence of pulmonary tuberculosis. Furthermore, it is difficult to make a differential diagnosis using only ultrasonographic observation or histopathological examination. Fine needle aspiration cytology, which has always been neglected, is accurate in distinguishing parotid tuberculosis from neoplasms and is helpful in differentiating chronic swelling from acute suppurative parotitis by Wright-Giemsa staining and acid-fast staining. Fine needle aspiration cytology is a technically simple procedure with fewer complications and side effects than traditional parotidectomy. High sensitivity and specificity in the diagnosis of parotid tuberculosis makes surgeons increasingly interested in FNAC findings. However, the limitations of FNAC are that it is occasionally nondiagnostic with false negatives due to uncertainty factors; it is therefore necessary to utilize other techniques for definitive diagnosis.

![Acid-fast staining result under an oil immersion lens](image-url)

**Figure 2.** Acid-fast staining result under an oil immersion lens. Positive acid-fast stain results showed that among the pus, there were numerous rod-shaped *Mycobacterium tuberculosis* bacteria specifically stained red, while others were stained blue. Approximately 20 *Mycobacterium tuberculosis* bacteria could be seen in one view.
diagnostic aids such as computed tomography, ultrasonographic examination, and magnetic resonance imaging.19

In our patient, we could not find any evidence of active disease elsewhere, and FNAC was essential to initiate prompt treatment, as it discovered numerous M tuberculosis bacteria in the abscess. Finally, the patient started effective antitubercular chemotherapy with rifampicin, isoniazid, ethambutol, and pyrazinamide.

Conclusion
Parotid gland tuberculosis should be emphasized because it can be successfully treated medically without surgical therapy. Medical practitioners or paramedical personnel should be aware that normal chest X-ray and negative sputum culture results do not rule out extrapulmonary tuberculosis, including parotid gland tuberculosis. Clinicians and experts should consider tuberculosis in the differential diagnosis of any patients with suspicious swelling of the parotid gland. Fine needle aspiration cytology is not only a technically simple procedure with few complications and side effects but also a reliable method in the evaluation of tuberculosis of the parotid gland, with fairly high specificity and sensitivity rates. This study suggests its utility in attempting to assess the probability of parotid tuberculosis and thus in adopting the most efficient therapeutic strategies.

Authors’ Note
The study was approved by the Committee of Ethics and Academic and Scientific Deontology of Zhejiang Province People’s Hospital, and the patient in this case has approved the publication of this study. Written and informed consent was obtained from the patient for publication of this Case Report and any accompanying images.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This paper was financially supported by the Medical Scientific Research Foundation of Zhejiang Province (No. 2017KY004).

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Supplemental Material
Supplemental material for this article is available online.

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