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Original Article

Evaluation of tuberculous parotitis cases with the pooled analysis method

Sevil Alkan Çeviker[1], Emine Kübra Dindar Demiray[2], Mustafa Yılmaz[3], Dursun Mehmet Mehel[4]

[1]*Department of Infectious Diseases and Clinical Microbiology, Çanakkale Onsekiz Mart University Faculty of Medicine, Çanakkale, Turkey*
[2]*Department of Infectious Diseases and Clinical Microbiology, Bitlis State Hospital, Bitlis, Turkey*
[3]*Department of Infectious Diseases and Clinical Microbiology, Kütahya Health Sciences University, Evliya Çelebi Training and Research Hospital, Kütahya, Turkey*
[4]*Department of Otorhinolaryngology, Samsun Training and Research Hospital, Samsun, Turkey*

ABSTRACT

Objectives: Tuberculous parotitis (TP) is a disease that should be considered in the differential diagnosis along with parotid malignancy and other parotid inflammatory diseases due to its clinical features. Advanced diagnostic methods have made the diagnosis of tuberculous parotitis much easier. The purpose of this study was to evaluate the reported TP cases in Turkey.

Materials and methods: The pooled analysis method was used in the study. Using the keywords, a total of 23 articles were found in five databases. The study included 18 articles, with five articles published before the year 2000 being eliminated.

Results: The articles were all case reports and case series. A total of 18 articles were used to evaluate data from 26 cases. The mean age of the cases was 37.7 (9-72) years, with 8 males and 18 females. In 13 of the cases, the localization was on the right side, 11 on the left, bilaterally in one, and unspecified in one. The most common complaints in terms of symptoms were facial swelling (96%), neck swelling (11.5%), high fever (7.7%), eye swelling (3.8%), painful jaw movements (3.8%), and shoulder swelling (3.8%). The average duration of symptoms was 32.3 months (10 days-30 years). Concurrent HIV infection was never reported. There was no history of tuberculosis in any of the cases. Four cases had a tuberculosis family history, while 15 did not. In addition to localized physical examination findings, fever was reported in two cases, as were ocular findings in two cases, weight loss in one case, shoulder pain in one case, and cough and sputum in one case. One patient had cervical vertebra tuberculosis with retropharyngeal abscess and parotid gland involvement.

Conclusion: Tuberculous parotitis should be considered in the differential diagnosis of parotid gland involvement, particularly in endemic regions such as our country.

Keywords: Mycobacterium tuberculosis, tuberculous parotitis, Turkey.

Tuberculosis (TB) is a chronic disease that affects people all over the world, particularly in developing countries, and is characterized by granulomatous inflammation, mainly in the pulmonary involvement. Extrapulmonary tuberculosis accounts for around 20% of all active tuberculosis cases and can affect any organ in the body. However, salivary gland involvement is extremely rare.[1,2] The first case was reported by De Pauli in 1893.[2]

Tuberculous parotitis (TP) is a disease that, due to its clinical similarities, can be confused with parotid malignancy and other inflammatory parotid gland diseases. Advanced diagnostic technologies have made tuberculous parotitis easier to diagnose, and clinicians should consider it in their differential diagnosis.[3] According to data from our country, the incidence of TB was 29.4/100,000 in 2005 but has now decreased to 14.1/100,000 in 2018.[4]

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Correspondence: Sevil Alkan Çeviker, MD. Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları Anabilim Dalı, 17020 Çanakkale, Türkiye.
Tel: +90 506 - 687 37 68 e-mail: dr.alpersener@gmail.com

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The purpose of this study was to evaluate articles about tuberculous parotitis that had been published in domestic and international journals in the previous 19 years, to examine the characteristics of this infection using the pool analysis method, and to compare the results with data from other countries.

MATERIALS AND METHODS

In this study, three national databases (Ulakbim Turkish Medical Literature database, http://www.turkishmedline.com, http://medline.pleksus.com.tr) and two international databases [Pubmed and ScienceCitation Index Expended (SCI)] were searched for TP cases conducted in Turkey and published in domestic and international journals in the last 19 years. In national databases, the keywords "tuberculous parotitis" and "Mycobacterium tuberculosis" were used.. Three researchers searched international databases using the keywords “Turkey” and “tuberculous parotitis” as well as “Mycobacterium tuberculosis”. Duplicate publications were excluded from the study. The evaluation did not include any studies that were published before 2000. All included articles were case reports and case series. The female-to-male ratio, mean age, history and family history of tuberculosis, parotitis localization, accompanying physical examination findings (local or systemic), laboratory findings, diagnostic methods (direct examination, culture, and biopsy), applied treatment methods (medical/surgical), and screening for and positivity rates of purified protein derivative (PPD) of the TP cases were all evaluated. Since the study was conducted online, no ethics committee permission was required.

RESULTS

A total of 23 articles were found in the search using the specified keywords. A total of 18 papers were included in the study, with five articles published before the year 2000 being eliminated. All articles were case reports or case series. In total, the data from 26 cases of the 18 articles were evaluated (Table 1-3). According to the clinics of the responsible authors who published the studies, eleven were ear nose and throat clinics, two were pediatrics clinics, two were chest diseases clinics, one was a radiology clinic, one was a plastic surgery clinic, and one was an infectious disease clinic. Three articles were published in 2006 and 2008, two in 2007, 2013, and 2016, and one in 2000, 2002, 2003, 2005, 2011, and 2020 according to the study distribution by year. The mean age of the cases was 37.7 (9-72) years, and the cases consisted of 8 males and 18 females. Localization was right side in 13 cases, left side in 11 cases, one case had bilateral localization, and unspecified in one case. According to symptoms, the most common complaints were swelling of the face (96%), swelling of the neck (11.5%), fever (7.7%), swelling of the eye (3.8%), painful jaw movement (3.8%), and swelling of the shoulder (3.8%). The average duration of symptoms was 32.3 months (10 days-30 years). Concurrent HIV infection was not reported in any of the cases. There was no previous tuberculosis history in 26 of the cases. Four patients had a family history of tuberculosis, while 15 others did not. In addition to localized physical examination findings, fever was reported in two cases, as were ocular findings in two, weight loss in one, shoulder pain in one, and cough and sputum in one case. Cervical vertebral tuberculosis with retropharyngeal abscess and parotid gland involvement was seen in one case.

Superficial parotidectomy was performed in 16 of 21 patients who underwent surgery. According to pathology reports, granulomatous

Table 1. Characteristics of tuberculous parotitis

	n	%
Palpation findings		
Tender	3	11.5
Moderately firm	1	3.8
Firm	1	3.8
Unspecified	21	80.7
Mobilization		
Mobile	13	50
Semi-mobile	3	11.5
Immobile	3	11.5
Unspecified	7	27
Pain		
Painless	12	46.1
Painful	7	27
Unspecified	7	27
Increased redness and heat		
Yes	5	19.2
No	4	15.4
Unspecified	17	65.4
Concomitant fistula	2	7.7
Neck lymphadenopathy	3	11.5
Antibiotic use	7	27

Table 2. Evaluation of diagnostic methods, exposure, and pulmonary tuberculosis in the cases

	Number of cases examined	Number of detected cases	%
Culture positive	7	3	11.5
ARB positive	14	6	23.1
Biopsy diagnosis			
PPD test positive	20	16	61.5
QuantiFERON positive	1	0	0
Tuberculosis PCR positive	4	3	11.5
Positive findings in chest radiography/thorax CT	22	4	15.4

ARB: Acid-resistant bacilli; PPD: Purified protein derivative; PCR: Polymerase chain reaction; CT: Computed tomography.

Table 3. Applied invasive diagnostic method

	n	%
Fine needle aspiration biopsy	16	61.5
Surgery	21	80.7

inflammation was detected in 15 (57.7%) cases.

Considering the rate of use of radiological methods for diagnosis, it was determined that a single imaging method was used in 24 patients, two imaging methods were used in eight patients, and three imaging methods (ultrasound, computed tomography [CT], and magnetic resonance imaging [MRI]) were used in three patients.

According to the treatments administered to the patients, 22 (84.6%) received a 4-drug antituberculosis treatment regimen (rifampin + isoniazid + pyrazinamide + ethambutol) and 1 (1.8%) received a 3-drug regimen (rifampin + isoniazid + pyrazinamide). Data on the treatment method was unavailable for three of the cases. In terms of the duration of treatment, it was determined that treatment lasted between 3 and 12 months (mean 7.07 months).

DISCUSSION

Tuberculosis is a necrotizing granulomatous disease with a wide range of clinical symptoms and a wide geographic distribution, with the lungs being the most common site of infection. Extrapulmonary tuberculosis accounts for about 20% of all active tuberculosis cases. Extrapulmonary involvement is mostly observed in the kidneys, bone, meninx, and lymph nodes.[5,6] The most prevalent form of extrapulmonary involvement is tuberculosis of the head and neck region, which accounts for roughly 15% of all mycobacterial infections. It has been determined that approximately 70% of the parotid gland is involved when the salivary glands are primarily involved. Even in countries where tuberculosis remains endemic, tuberculosis of the parotid gland is a very rare clinical condition.[7] It is usually unilateral, with only a few cases of bilateral involvement.

Although the pathogenesis of the spread of tuberculosis to the parotid gland is still unclear, two hypotheses have been proposed. According to the first hypothesis, mycobacteria spreads from an infection of the teeth or tonsils to the parotid parenchyma and/or lymph nodes via autoinoculation, duct, or afferent lymphatics. Simply put, the constant flow of saliva can cause mycobacteria to reach the gland parenchyma. The second hypothesis proposes that tuberculosis infection spreads from the lungs via a hematogenous or lymphatic route.[7] Tuberculin skin test using PPD is helpful in the diagnosis of tuberculosis. The PPD skin test, acid-fast bacilli (ARB) staining of sputum, and appropriate cultures can all be used to differentiate between these two hypotheses. However, even in patients with a positive PPD test and histological confirmation, ARB staining and cultures can sometimes be detected as negative.[5,7]

There are two types of TP manifestations in terms of pathogenic involvement: localized and diffuse. While the intraglandular and periglandular lymph nodes are usually involved in the localized form, the parenchyma of the parotid gland is commonly involved in the diffuse form as a result of lymph node infection.[8] The diffuse form is uncommon, suggesting that the majority of the infection originates from the hematogenous

route.[8] However, because there may be no active disease elsewhere in the diffuse type, parenchymal involvement may be caused by the secondary spread of primary nodal disease to the nearby gland.

When the disease starts as diffuse parotid inflammation, the PPD test is weakly positive, and it is generally thought to be caused by atypical mycobacteria; however, when the parotid lymph nodes are more affected, the PPD test is strongly positive, and M. tuberculosis infection from another site is considered in such a situation.[5,7,8]

The clinical symptom is a slow-growing swelling that is often confused for a parotid neoplasm. While swelling usually emerges within a period of 3-6 months, a case of painless parotid gland swelling that grew slowly over a 10-year period has also been reported. Although parotid tuberculosis can be made diagnosed with a high degree of clinical suspicion, doctors commonly overlook it. In addition to tuberculosis, tularemia, syphilis, leprosy, cat scratch disease, fungal infections, lymphogranuloma venereum, sarcoidosis, brucellosis, and toxoplasmosis induce granulomatous inflammation in the salivary gland.[8] Malign lymphoma, chronic lymphadenopathy, sialosis, Sjögren's syndrome, and acute or chronic suppurative parotitis should all be considered, in the differential diagnosis.

Due to the development of resistant strains and HIV coinfection, the incidence of TP has increased in developed countries in recent years. However, parotid gland tuberculosis in children is quite rare. However, among children living in tuberculosis-endemic areas, TP should not be neglected in the differential diagnosis of slow-growing, fistulized parotid masses, especially after contact with an adult tuberculosis patient.[5,8]

Isolating mycobacteria from the parotid tissue provides a definitive diagnosis of parotid tuberculosis. Generally, surgeons prefer excisional biopsy, and in cases of complete parotid gland involvement, the diagnosis can be made by performing a total parotidectomy operation. Intraoperatively, facial nerve damage and local fistula may develop.[7,9]

In order to diagnose tuberculosis, radiological imaging, fine-needle aspiration biopsy (FNAB), and tuberculosis polymerase chain reaction test (TB-PCR) are essential. The FNAB method for detecting lymphadenopathy caused by cervical tuberculosis is effective, inexpensive, and less invasive. Another advantage of FNAB is that it may be used to examine the drug sensitivity of cultures obtained from biopsy samples. In parotid lesions, FNAB has a sensitivity of 81-100% and the specificity of 94-100%.[6,9] Other imaging modalities, such as ultrasound, CT, and MRI, are sensitive in detecting tuberculous lesions in the parotid gland, they are not specific. The majority of the imaging findings were found to be neoplasms. In cases of pulmonary tuberculosis, chest radiography may be useful. Although superficial ultrasound can accurately identify the lesion, the appearance of the lesion (hyperechoic/hypoechoic) has been described as variable in the literature. The lesions' Color Doppler findings are also non-specific, ranging from avascular to highly vascular lesions. For determining the size of the lesion and detecting associated deeper lesions, computed tomography and magnetic resonance imaging (MRI) are useful. However, while CT and MRI findings are highly sensitive, they are not specific and cannot distinguish lesions from neoplasms. When CT reveals linearly arrayed nodules in the superficial lobes of the glands in patients with unilateral parotid nodules, which is a pathognomonic finding, tuberculosis should be considered.[5,6,9] On MRI, lesions are usually observed as non-specific, homogeneous hypointense on T1-weighted images and hyperintense on T2-weighted images.[5,9,10] Since imaging findings are indistinguishable from neoplasms, surgical intervention, such as superficial parotidectomy, can usually be performed and the diagnosis made postoperatively.[6,10] Large necrotic masses or abscess formations can be treated with anti-tuberculosis medications, despite conventional clinical practice, with the exception of cases that are unresponsive to treatment.[11]

Epithelial cells, giant cells and epithelioid granuloma structures with caseous necrosis are typical tuberculosis histological features. Acute inflammatory changes can occasionally be observed, particularly in the early stages of the disease, which can make it difficult to distinguish between various inflammatory causes.[5,11] Furthermore, ARB may not be detected in biopsy specimens, presumably due

to low bacillus concentrations in extrapulmonary tuberculosis lesions. When clinical suspicion of tuberculosis is high despite negative diagnostic testing, anti-tuberculosis medication is usually started to assess the patient's response to the anti-tuberculosis regimen. Isoniazid, rifampin, ethambutol, and pyrazinamide are still used as first-line medication and have proven to be effective. Extrapulmonary tuberculosis is usually treated with a total of nine months of treatment (4-drug regimen in the first two months followed by 2 applications of isoniazid and rifampin).[12,13] In some cases, certain drug combinations (such as clarithromycin, amikacin, and ciprofloxacin) have been shown to be effective against resistant strains.[14] Pre-treatment FNAB is still important, especially in the identification of tuberculosis from malignant lesions, in order to reduce potential complications of surgical procedures using the least invasive method possible.[15]

Researches on TP began in 1977, and by 1985, almost 100 new cases had been reported to the literature till 2003, mostly based on parotidectomy materials.[6,16-18]

In a retrospective study conducted by Vayısoğlu et al.[19] in our country, 48 patients with tuberculosis in the head and neck region were examined and their clinical findings, treatment methods, and treatment outcomes were evaluated between January 2000 and June 2009. Parotid gland tuberculosis was diagnosed in two (4%) cases. Excisional biopsy was used to diagnose all of the patients in the study, antitubercular treatment resulted in regression of all lesions. We believe that evaluating our country's data has added to our national literature as a consequence of reviewing publications related to tuberculous parotitis published in domestic and international journals during the last 19 years; however, more research is needed.

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