Primary tonsillar tuberculosis – case report

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Abstract

We report the case of a 44-year-old male patient with tonsillar tuberculosis (TB) diagnosed in the Department of Ear, Nose & Throat (ENT), “Victor Babeş” University of Medicine and Pharmacy, Timișoara, Romania. The patient addressed to our Clinic with intense odynophagia, referred otalgia, sore throat, fever periods and weight loss. During the ENT clinical exam, we identified an enlarged left tonsil, partially covered with yellowish-white plaque, with ulceration and bleeding spots localized on tonsillar inferior pole. A high suspicion of tonsillar malignancy was raised, and a biopsy was performed revealing extrapulmonary TB. Taking into consideration the normal chest X-ray, a primary tonsillar TB diagnosis was established. The patient was addressed to Department of Pneumophthisiology for anti-tuberculous therapy for six months. At the end of the treatment, the patient was symptoms-free.

Keywords: tonsillar tuberculosis, odynophagia, epithelioid macrophages, multinucleated cells.

Introduction

World Health Organization (WHO) considers tuberculosis (TB) to be a very important cause of death worldwide [1]. In 2017, 10 million people were affected by TB and 1.6 million died from TB. WHO estimated one million children TB infected in the same year, with a total number of 230 000 deaths [together with human immunodeficiency virus (HIV)-associated TB]. The same organization estimates approximately half a million Rifampicin resistance new cases, of which 82% had multidrug-resistant (MDR) TB. Globally, TB incidence is falling at about 2% per year, with a purpose of ending the TB epidemic by 2030 as health targets of the Sustainable Development Goals.

Estimated rate of TB per 100 000 people, compiled from WHO data for each country, published by Public Health of England, revealed an incidence in Europe of 144 (estimated rate per 100 000 population) in Kyrgyzstan, 116 in Greenland, 95 in Republic of Moldova, 86 in Georgia, 85 in Tajikistan, 84 in Ukraine, 73 in Uzbekistan and on the 8th place Romania with an incidence of 72/100 000 people [2].

From all TB cases extrapulmonary ones (EP-TB) are seen in only 10–15%. From EP-TB lymph nodes has the highest incidence [3]. Oral cavity TB is even rarer and palatine tonsil TB being extremely rare. In cases of tonsil TB, the most common form is the secondary one [4]. Approximately 0.05–5% of the total TB patients have oral signs and symptoms [5]. In the oral cavity and oropharynx, TB may be primary or, more often, secondary. Most frequent localization of oral and oropharyngeal TB is the tongue, still the Mycobacterium tuberculosis infection may also affect other oropharyngeal structures [5].

Other EP-TB sites include gastrointestinal organs, bones and joints, central nervous system (CNS), and genitourinary organs. In the same time, due to numerous factors, the real incidence of EP-TB is considered to be much higher than reported [6].

We present a case of primary tonsillar TB that raised great problems of positive and differential diagnosis, being an extremely rare form.

Case presentation

We report a 44-year-old male patient diagnosed with a rare case of tonsillar TB diagnosed in the Department of Ear, Nose & Throat (ENT), “Victor Babeş” University of Medicine and Pharmacy, Timișoara, Romania, on March 26, 2018. In 2018, in our Department of ENT were admitted 2317 patients. In 2018, there were diagnosed 12 patients with TB and ENT determinations: nine laryngeal TB (eight secondary and one primary), one nasal TB (primary), one middle ear (secondary) and our patient (primary tonsillar TB).

The patient was referred to our Clinic with a two
months history of intense odynophagia, referred otalgia, sore throat, foetor, subfebrile periods, weight loss (approximately 6 kg in two months) and intermediate uveitis at the right eye. A seven days treatment with Clarithromycin 1 g/day (0.5 g at 12 h) was implemented prior to our Department admission without any improvement. The patient was admitted in the Hospital and clinical and paraclinical exams were performed. The anamnesis revealed a conjunctival-palpebral Kaposi’s sarcoma, anterior ischemic optic neuropathy, and glaucoma as concomitant pathologies.

On ENT clinical exam on buccopharyngoscopy, we identified an enlarged left tonsil, covered partially with yellowish-white plaque, with an ulceration and bleeding spots localized on tonsillar inferior pole, the posterior wall of the oropharynx was of normal aspect. Indirect laryngoscopy and 700 endoscopic laryngoscopy completed the exam, without revealing other pathological aspects. The patient temperature was 38°C, heart rate (HR), 95 beats/minute, blood pressure (BP) 130/75 mmHg and respiratory rate (RR), 17 breaths/minute.

Taking into consideration the intense odynophagia and the high rate on TB incidence, a chest X-ray was performed, revealing a normal aspect. Paraclinical exam comprised on: erythrocyte sedimentation rate (ESR) 107 mm/h, hemoglobin (Hb) 7.6 mg%, hematocrit (Ht) 26.6%, serum creatinine 0.9 mg%, blood urea 17 mg%, alanine aminotransferase (ALAT) 139 U/L, aspartate aminotransferase (ASAT) 62 U/L, Na⁺ 134 mEq/L, K⁺ 4 mEq/L, white blood cells (WBC) 4.4×10³/μL, red blood cells (RBC) 3.05×10⁶/μL, platelets (PLT) 260×10³/μL.

The patient underwent a complete ophthalmologic examination and was diagnosed with non-specific uveitis at the right eye. Due to clinical appearance and lack of response to antibiotic and anti-inflammatory treatment, a high suspicion of tonsillar malignancy was raised or a specific inflammatory lesion. For diagnosis, it was decided to perform a tonsil biopsy. The surgical specimens excised were fixed in 4% (v/v) buffered formalin, sent to the Service of Pathology and embedded in paraffin. Four μm sections were cut using Leica RM2235 semi-automated rotary microtome, displayed on SuperFrost™ microscope slides and stained with Hematoxylin and Eosin (HE). For the immunohistochemical (IHC) exam, we used the antibodies: anti-Ki67 (monoclonal mouse anti-human Ki67, clone MIB-1, 1/50 dilution, Dako), anti-p53 (monoclonal mouse anti-human p53 protein, clone DO-7, 1/100 dilution, Dako), anti-cluster of differentiation (CD) 3 (monoclonal mouse anti-human CD3, clone F7.2.38, 1/25 dilution, Dako), anti-CD20 (monoclonal mouse anti-human CD20cy, clone L26, 1/50 dilution, Dako), anti-CD79α (monoclonal mouse anti-human CD79α, clone JCB117, 1/50 dilution, Dako), anti-CD68 (monoclonal mouse anti-human CD68, clone KP1, 1/100 dilution, Dako), anti-CD34 (monoclonal mouse anti-human CD34 Class II, clone QBEnd 10, 1/50 dilution, Dako).

The histopathology exams showed tonsillar parenchyma composed of lymphoid tissue disposed diffusely with rare lymphoid follicles, covered by non-keratinizing squamous stratified epithelium. Quite frequently, in the tonsillar stroma, instead of the lymphoid follicles, we identified granulomatous structures, made of epithelial cells and multinucleate giant Langhans cells, structures that were similar to the Koster tuberculous nodules. There were not highlighted any necrosis and caseification areas (Figures 1 and 2). In some areas of the tonsils, there was highlighted erosion of the surface epithelium and a non-specific inflammatory infiltrate in the sub-adjacent chorion, made of granulocytes, lymphocytes and macrophages (Figure 3).

The IHC exams showed a negative reaction both for the anti-Ki67 antibody and for the anti-p53 antibody, which excluded a malignant lesion. In contrast, multinucleate giant cells and epithelial cells presented a positive reaction to anti-CD68 antibody, thus proving that they are macrophage cells (Figures 4 and 5). Around the giant cells and tuberculous follicles, we highlighted numerous T-lymphocytes and less B-lymphocytes (Figures 6–8).

Figure 1 – Overall image of a palatine tonsil area. Immediately under the covering epithelium, there is observed the presence of a tuberculous nodule formed of various epithelioid cells, arranged around a giant multinucleate cell (the Langhans cell). At the nodule margin, there may be observed a crown of lymphocytes that continues with the tonsillar lymphoid infiltrate. HE staining, ×100.

Figure 2 – Image of tuberculous nodule formed of giant multinucleate cells and epithelioid cells. There are not highlighted any areas of cellular or tissue necrosis. HE staining, ×200.
Evaluating blood microcirculation showed that tuberculous follicles presented a lower microvascular density in comparison to the unaffected areas of the palatine tonsil (Figures 9 and 10). The histopathological aspects were consistent with TB. QuantiFERON-TB test was positive. The sputum smear for acid-fast bacilli was
negative, and pulmonary radiography excluded pulmonary involvement. The final diagnosis was of extrapulmonary primary tonsillar TB.

The patient was addressed to the Department of Pneumophthisiology for six months anti-TB therapy. For two months, a daily combination of Rifampicin 600 mg/day (the patient’s weight was 65 kg), Isoniazid 300 mg/day, Pyrazinamide 1500 mg/day, and Ethambutol 900 mg/day was administered followed by four months administration of Rifampicin 600 mg/day and Isoniazid 600 mg/day, three days/week. At the end of the treatment, the patient was symptoms-free.

Figure 9 – Well-represented microvascular network present in an area of normal tonsil. Immunostaining with anti-CD34 antibody, ×100.

Figure 10 – Low microvascular network in the area of tuberculous follicles. Immunostaining with anti-CD34 antibody, ×100.

**Discussions**

Searching the PubMed for the “extrapulmonary tuberculosis” a number of 3709 articles were found, out of which only 29 are related to primary tonsillar TB. Romania occupies the 8th place in Europe regarding TB incidence, after Kyrgyzstan, Greenland, Republic of Moldova, Georgia, Tajikistan, Ukraine and Uzbekistan with an incidence of 72/100 000 people (according to WHO and Public Health of England) [2].

Out of 2317 patients hospitalized in our Department of ENT, 12 (0.51%) patients presented TB and ENT determinations: nine laryngeal TB (eight secondary and one primary), one nasal TB (primary), one middle ear (secondary) and one patient (primary tonsillar TB).

The case presented by us raised problems of clinical diagnosis, as the patient’s medical history did not suggest any infection with a tuberculous bacillus, and the lung X-ray excluded a specific infection at this level. The lack of response to the treatment applied at first suggested the existence either of tumoral pathology or tonsil infection, with a particular pathogen agent. The diagnosis of tonsillar TB was established on the macroscopic and IHC aspects provided by the tonsil tissue harvested through biopsy and by the QuantiFERON-TB test, being confirmed by the disease evolution after the specific treatment for TB.

Our case, the differential diagnosis had to include squamous cell carcinomas, lympho-reticular malignancy, aphthous or traumatic ulcers, actinomycosis, Wegener’s granulomatosis, Plaut–Vincent’s tonsillitis [6–11].

After chemotherapy, TB incidence declined dramatically [5, 12]. Oral and oropharyngeal TB lesions are uncommon. In our series, the incidence of EP-TB was 0.51%, and oropharyngeal incidence of TB was 0.04%. Tonsillar TB is caused either by *M. bovis* infection (unpasteurized milk), or due to contact with infected sputum [6]. Tonsillar TB is classified into tonsil primary TB, without lungs involvement and tonsil secondary TB, where sputum smear-positive pulmonary TB is documented [13]. Some conditions predispose to tonsillar TB: poor dental hygiene, tooth extraction, periodontitis, and oral leukoplakia. Our patient did not undergo any tooth extraction nor had poor dental hygiene, periodontitis or oral leukoplakia.

The differential diagnosis is with oropharyngeal malignancies, which are more common in elderly patients, and on clinical basis, the diagnosis being difficult without the high suspicion of tonsillar TB. An accurate ENT clinical examination is mandatory in order to establish a correct diagnosis [14, 15].

QuantiFERON-TB test, histopathological exam, Ziehl–Neelsen staining and mycobacterial culture should be performed in order to establish the diagnosis [16, 17].

Typical features of tonsillar TB on pathological exam include: epithelioid granulomas with caseous necrosis, Langhans’ and foreign body giant cells with or without acid-fast bacilli. The absence of caseous necrosis imposed the differential diagnosis with sarcoidosis, but positive QuantiFERON-TB test sustained the diagnosis of TB.

A successful treatment for tonsillar TB is consisted in Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol for two months, and Rifampicin and Isoniazid for the next four months, with symptoms-free at the end of the treatment [6].

**Conclusions**

We consider tonsillar TB to be a rare entity, but in cases of unhealing tonsillar lesions associated with intense odynophagia a high suspicion of tonsillar malignancy vs. tonsillar TB should always be raised. A successful treatment for tonsillar TB is consisted in Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol for two months, and Rifampicin and Isoniazid for the next four months, with symptoms-free at the end of the treatment.
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Conflict of interests
The authors declare that they have no conflict of interests.

Authors’ contribution
Nicolae Constantin Balica and Mărioara Poenaru equally contributed to the manuscript.

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