



Primary tonsillar tuberculosis in a pediatric patient

Case report and literature review

Stefana Maria Moisa, MD, PhD, Ingrith Miron, MD, PhD, Anca Adam-Raileanu, MD, Vasile Valeriu Lupu, MD, PhD*, Ancuta Lupu, MD, PhD, Elena Tarca, MD, PhD

Abstract

Rationale: Tuberculosis is an entity that usually affects the lungs, although extrapulmonary sites can also be involved. Tonsils are rarely affected, especially in the absence of pulmonary disease, primary tonsillar tuberculosis being a diagnostic challenge for the clinician.

Patient concerns: We present the case of a 14-year-old female teenager, presented to our Pediatric Service with a 14-day history of dysphagia, odynophagia and left reflex otalgia associated with a 5 kg weight loss. Clinical examination revealed mild pharyngeal erythema, marked enlargement of the left tonsil infiltrating the lateral pharyngeal wall and the uvula and painful, mobile, nonadherent to deep bilateral latero-cervical adenopathy.

Diagnosis: Positive interferon-gamma release assay (QuantiFERON-TB gold). Mantoux test reading was 16 mm.

Interventions: During hospitalization, the patient received Clindamycin and Gentamicin for 3 days i.v., with discrete relief of symptoms and inflammatory markers. On the 4th day of hospitalization, treatment with Imipenem/Cilastin is started for 7 days in micro-perfusion, with tonsil hypertrophy decrease in size and favorable clinical evolution.

Outcome: Tonsil hypertrophy decreased in size and patient had a favorable clinical evolution. At discharge, the patient was given a 6-month course of anti-tuberculous drug.

Lessons: The particularity of this case is represented by the rarity of primary tuberculosis of tonsils in children, with unilateral involvement, displaying at the same time a common issue encountered in the current practice: the limitations and the difficult course of setting the diagnosis due to the involvement of relatives in the medical act.

Abbreviations: AFB = acid-fast bacilli, CBC = complete blood count, CRP = serum C-reactive protein, CT = computer tomography, ESR = erythrocyte sedimentation rate, MDR-TB = multiple drug-resistant tuberculosis, MRI = magnetic resonance imaging, TB = tuberculosis, WHO = World Health Organization, XDR-TB = extensively drug-resistant tuberculosis.

Keywords: a teenager, pediatrics, tonsillitis, tuberculosis

Editor: Maya Saranathan.

Ethics Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of "St. Mary" Children Emergency Hospital, lasi, Romania 17251/15.06.2021.

Consent for publication: Written informed consent was obtained from the patient's parents for publication of the case details.

The authors have no conflicts of interest and funding information to disclose. Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Department of Mother and Child Medicine – Pediatrics, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania.

* Correspondence: Vasile Valeriu Lupu, str. Universitatii, nr. 16, lasi, 700115, Romania (e-mail: valeriulupu@yahoo.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Moisa SM, Miron I, Adam-Raileanu A, Lupu W, Lupu A, Tarca E. Primary tonsillar tuberculosis in a pediatric patient: Case report and literature review. Medicine 2021;100:44(e27616).

Received: 3 July 2021 / Received in final form: 4 October 2021 / Accepted: 13 October 2021

http://dx.doi.org/10.1097/MD.0000000000027616

1. Introduction

Tuberculosis (TB) is an infectious malady frequently caused by Mycobacterium tuberculosis bacteria. Although it usually affects the lungs (90%), other organs can be involved, causing extrapulmonary tuberculosis. ^[1] The most common extrapulmonary site of tuberculosis is represented by the lymph nodes, the nasopharynx and oropharynx, having a less than 5% incidence. ^[2] Tonsils seem to acquire even in a smaller percentage of the disease due to the thickness of the protective epithelial covering of the oropharyngeal mucosa, to the oral cavity's saprophytes action or because of the antiseptic effect and cleansing action of the saliva. ^[3] The right diagnosis and the accurate treatment are vital for peoples' health, not ignoring the devastating social and economic impact, including poverty, stigma, and discrimination.

The most recent reports of the World Health Organization (WHO) show that 10 million people fell ill with TB in 2019, tuberculosis killing 5000 people every day. TB treatment saved about 58 million lives globally between 2000 and 2018, but important diagnostic and treatment gaps persist. Vaccination, pasteurization of milk to anti-TB treatments plays their role, but somehow the poor nutrition, low personal hygiene, immunode-

ficiency diseases and the increasing rates of multiple drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) seem to frustrate the efforts of the healthcare providers. [4] Pediatric tuberculosis in particular can be troublesome to discover and treat because often in everyday practice this diagnostic is overlooked. Another ugly truth of our days is that due to the current epidemiological context of "Sars-Cov-2 infection" the access to medical care tends to be more difficult and Mycobacterium tuberculosis tends to be forgotten, fact that inevitable leads to a delay in diagnosis and treatment.

In this study, we report a primary form of tonsillar tuberculosis, a rare medical condition, in a 14-year-old female accompanied by the medical literature.

2. Case report

We present the case of a 14-year-old female teenager, presented to our Pediatric Service with a 14-day history of dysphagia, odynophagia and left reflex otalgia associated with a 5 kg weight loss. During this time, the patient was treated with antibiotics (Amoxicillin/Clavulanate, Cefixime) and anti-inflammatory drugs, with no clinical improvement. There was no relevant personal or familial background of tuberculosis or other infectious. Immunized to date according to the national immunization scheme (BCG included).

On clinical examination, there was tender bilateral laterocervical adenopathy (\sim 25/20 mm-right side, \sim 30/25mm-left side), painful, mobile and nonadherent to the deep planes; mild posterior pharyngeal wall erythema, marked enlargement of the left tonsil infiltrating the lateral pharyngeal wall and the uvula, moderate trismus. No other abnormal findings were found on the detailed examination.

Initial laboratory tests showed normal complete blood count (CBC), a mildly elevated erythrocyte sedimentation rate (ESR) at 57 mm/1 h and serum C-reactive protein (CRP): 7.79 mg/L, normal liver, and renal function, quantitative immunoglobulins, and urinalysis. Negative pharyngeal swab.

Immunology evaluation identified high levels of Epstein–Barr antibodies to viral capsid antigen (VCA) IgG-66.58 S/CO, and Epstein–Barr nuclear antigen (EBNA) IgG-24.13 S/CO, elevated Cytomegalovirus IgM-1.4 and IgG antibodies >250 AU/mL.

To dispel the suspicion of either malignancy, either a rare infectious disease (Tuberculosis, Actinomycosis) a CT scan of the head and neck was needed, followed by a local biopsy—not possible due to the refusal of the patient's legal relatives. Biopsy was postponed. Instead, a soft tissue and abdominal ultrasound was performed: bilateral latero-cervical inflammatory lymph nodes, mesenteric adenitis, right inguinal inflammatory lymph node.

Positive interferon-gamma release assay (QuantiFERON-TB gold). Mantoux test reading was 16 mm. There were no acid-fast bacilli (AFB) detected from his morning gastric lavage fluid analysis, negative GeneXpert. Normal Chest X-ray excluded pulmonary involvement.

Craniocerebral and cervical magnetic resonance imaging (MRI): chronic bilateral maxillary sinusitis, bilateral ethmoiditis; inflammatory aspect at the level of bilateral palatine tonsils and adenoid vegetation; multiple bilateral upper and middle jugular lymphadenopathy.

During hospitalization, the patient received Clindamycin and Gentamicin for 3 days i.v., with discrete relief of symptoms and inflammatory markers. On the 4th day of hospitalization,

treatment with Imipenem/Cilastin is started for 7 days in microperfusion, with tonsil hypertrophy decrease in size and favorable clinical evolution.

The case was diagnosed as a form of primary tonsillar tuberculosis. At discharge, the patient was given a 6-month course of anti-tuberculous drug.

3. Literature review methodology

A literature search was conducted using PubMed and Scopus to search case reports, clinical trials and case series published from January 1960 through September 2020 for the following keywords (tuberculosis or Mycobacterium tuberculosis) and tonsil. Scientific articles were selected and reviewed to assess the epidemiology, presentation, diagnosis and treatment of tonsillar tuberculosis. Studies reporting the simultaneous presence of tonsillar tuberculosis and tuberculosis of another site or oral malignancy in the same lesion site were also included. We excluded reports available only as abstracts or published in other language than English or Romanian.

The literature search identified 177 studies, of which 17 were not in English or Romanian, 45 concerned other sites of primary or secondary tuberculosis, and 52 were available only as abstracts. The remaining 63 studies consisted of 46 unique case reports and 17 case series, leaving 86 patients included in the analysis (Table 1).

4. Discussion

Tonsillar tuberculosis is a rare medical condition, both in children and adults. In addition to the general immunesuppressing conditions known to influence the incidence of TB in its pulmonary form, poor oral hygiene, periodontitis, dental extraction and leukoplakia seem to be predisposing factors for tuberculous tonsillitis. [5] Its primary form is presented only as a tonsillar involvement without pulmonary touch. [6] Medical history and clinical examination may raise the suspicion of tuberculosis. TST and IGRA provide evidence for infection but for confirmation, histological examination, Ziehl Neelsen staining, and mycobacterial culture must be done. Treatment of primary tonsillar tuberculosis consists of antituberculous therapy, 6 months of standard anti-tuberculous regimen. [4,6] Although due to the atypical clinical appearance there is a delay in treatment initiation, there is a general good outcome when treated.^[7] Unlike its pulmonary form, tonsillar tuberculosis is a multidrug-resistant TB strain free, no case being reported in the literature.^[8]

Related to our literature search, of the 63 included studies, 66.67% were conducted in Asia, 22.22% in Europe, 5.56% USA, 3.7% in Africa, and 1.85% in Australia, leaving Asia in a front position in TB incidence and total number of cases, just as WHO reports described. Asia had 44% of the new cases diagnosed in 2019, with the highest incidence of 4.34. The age varied from 3 to 80 years with a mean age of 34.9. Most tonsillar tuberculosis cases were identified among 20 to 50 years old adults: 62.74%, with a preponderance of male cases—67.25%, while women represented 37.25%. The male sex seemed predominant as well in the pediatric population (15.6% children < 18 years), were was identified only 1 case of secondary tonsillar tuberculosis. [9] Findings are similar to WHO's distribution of cases reported in 2019: 56% men \geq 15 years old, 32% women \geq 15 years old, 12% children <15 years old. [4]

Nain	characteristic	s and r	esuits o	tue e	Main characteristics and results of the eligible studies.											
Year	Author	Number of cases	er Age es (years)	s) Sex	ex Clinical symptoms	Tonsil affected	Latero-cervical adenopathy	AFB	Culture	Mantoux	Chest X-ray	Tonsilectomy		Anti-TB treatment HIV	Tb concomitent V involvment	Comorbidities
1964	Mohindra et al ^[20]	4	NA	AN	frequent low fever	3 left tonsil	Yes	sod	NA	1 poz	NA	Yes	AN A	NA	A Adenoids	NA
1966	Sanford et al [47]	-	30	-	hoarseness difficulty in swallowing	bilateral	Yes	sod	sod	NA	sod	FNAC	Yes	beu	g Lungs	No
1972	Cowan et al [44]	-	48	E	sore throat persistent sore throat right otalgia dysphagia weight loss	bilateral	Yes	sod	sod	zod	sod	FNAC	Yes	beu	g Lungs	ON N
1979	Raman et al ^[32]	-	41	Ε	occasional night sweats left side pain	left	No	sod	beu	NA	sod	FNAC	Yes	N A	A Lungs	Left tonsilar
1987	Plesiss et al ^[9]	-	9	—	difficulty swalowing sore throat fever	bilateral	Yes	sod	neg	non reactive	sod	FNAC	Yes	neg	g Lungs, larynx, mesenteric TB	carcinoma No
1988	Park et al [55]	-	20	4	anorexia left otalgia sore throat	left	No	sod	beu	AN	sod	FNAC	Yes	beu		No
1989 1	Pedrol et al ^[36] Adiego et al ^[54]		22 58	EE	noarsness progressive odynophagia odynophagia	bilateral left	No Yes	sod	NA pos	sod	sod	Yes FNAC	Yes	beu	Klaney g Lungs, pharynx g Lungs, Brain	0 N 0 O
1995	Selimoglu et al ^[18] Sutbeyaz et al ^[56]		67 48	EE	oyspraga hyporexia weight loss sore throat Hoarseness difficulty in swallowing	left left	No No	bod	NA pos	sod	sod beu	Yes FNAC	Yes	neg	g – g Lungs, larynx	N N N N
2000	Naik et al [29]	-	18	—	sore throat recurrent throat pain	bilateral	No	neg	NA	beu	neg	Yes	Yes	beu	- D	No
2000	Kardon et al ^[52]	က	29, 34, 41	41 m	tever sore throat dysphagia	bilateral	NA	sod	beu	neg	1 pos/2 neg	Yes	Yes	beu	g Lungs	No No
2000	Fortún et al ^[28] Al-Serhani et al ^[63]	5 -1	o NA	МA	NA	bilateral bilateral	NA 2 Yes	pos NA	neg NA	N N A	neg 1 pos/4 neg	Yes NA	Yes	NA neg	A – g 1 lungs	0 0 N
2001	Awad et al [58]	2	16-81	NA	SOL	2 left tonsil/ 3 bilateral	/3 No 3 Yes /2 No	sod	beu	2 pos	Deu	FNAC	Yes	neg	- D	No O
, 2002	Yamamoto et al ^[57]	-	23	-	odynophagia sore throat hoarseness	bilateral	No	sod	neg	neg	sod	Yes	Yes	neg	g Lungs, larynx	No
2002	Srirompotong et al [16]	9	20-72	3m	SOF.	NA	NA	5 pos/	NA	NA	4 pos/2 neg	Yes	Yes	neg	g 4 lungs	No
2003	Jana et al [42] Srirompotona	- 9	NA 20	E Z	persistent sore throat dysphagia cough dry	bilateral NA	Yes NA	sod V	sod A	A A	sod V	FNAC NA	Yes	neg NA	g Lungs A 1 nasopharvnx	0
	et al ^[66] Efde et al ^[61]	-	61	E	SOL	left	No	Sod	neg	sod	sod	Yes	Yes	beu		Rheumatoid arthritis
2005	Nakayama et al ^[48] Krishnappa et al ^[43]		30	∓ E	weight loss NA	left left	Yes Yes	sod s	Sod	sod	neg Dos	Yes	Yes	neg	9 – G	N o

Additional and all continued and all contin	1100	(continued).															
Companies of all all all all all all all all all al	Year	Author	Number of cases		Sex	Clinical symptoms	Tonsil affected	Latero-cervical adenopathy		Culture	Mantoux	Chest X-ray	Tonsilectomy	Anti-TB treatment	¥	Tb concomitent involvment	Comorbidities
Dependence at 4						sore throat otalgia											
Reconcision of all 2 44 44 44 44 44 44	2006	Duijnstee et al ^[59]	-	35	E	sore throat difficulty in swallowing	left	Yes	sod	sod	¥	neg	Yes	Yes	- zod	1	HIV positive
Maintenency et at 10 14 1 10 10 10 10 10	2006	Ricciardiello et al ^{[19} .		AM	ΑΝ	weignt loss deteriorating dysphonia	NA	NA	Ą	NA	Ą	sod	NA	Yes		Lungs	No
Although a giant g	2007	Maciaszczyk et al ^{[53}		45	—	pitalyrigodynia sore throat anorexia fever	bilateral	Yes	sod	sod	¥	sod	Yes	Yes		Lungs	NO No
Second Figure F	2007	Al-Sebeih et al ^[33] Chakravarti et al ^[11]		65 22	EE	cough NA sore throat cdynophagia	right bilateral	N N No	sod	NA pos	pos NA	neg neg	Yes FNAC	NA Yes		Adenoids -	N O N
Companies of a 1 2	2008	Belizna et al ^[46]	-	40	Ε	occasional lever malaise sore throat	bilateral	Yes	sod	sod	¥	sod	Yes	Yes		Lungs	No
Becomplexe et al 131 1 7 1 Cohynologiage left of couple 1 Prophologiage left of couple Prophologiage Prophologiage <t< td=""><td>2008</td><td>Kant et al [31]</td><td>-</td><td>55</td><td>E</td><td>dysphagia sore throat difficulty in swallowing</td><td>left</td><td>N N</td><td>neg</td><td>sod</td><td>sod</td><td>neg</td><td>FNAC</td><td>Yes</td><td></td><td>ı</td><td>No</td></t<>	2008	Kant et al [31]	-	55	E	dysphagia sore throat difficulty in swallowing	left	N N	neg	sod	sod	neg	FNAC	Yes		ı	No
Benotie et al	2010	Ghatak et al ^[41]	-	7	—	solid food odynophagia cough	left	Yes	neg	NA	neg	neg	FNAC	Yes		ı	No No
Modificate et al ¹⁷³ 1 6 m despite total source of a count, pain in throat right No pos neg 1 m despite total source of a count point in throat right No pos neg 1 m despite total condition and somethies at al ¹⁷³ 1 6 m despite total condition and another at al ¹⁷³ 1 10 m despite total count point in throat right No pos neg 1 m despite total count point in throat right No pos neg 1 m despite total count point in throat right No pos neg 1 m despite total count point No pos neg 1	2010	Barouta et al ^[38] Cherkaoui et al ^[30]	- _C	67 15-42	m 3m /2f	dys dys	right bilateral	NA Yes 2	poz	pos NA	poz poz 3	neg poz 2	FNAC 3 FNAC	Yes		2 lungs	rheumatoid arthritis No
Babasubramarian 1 53 m soverthroad among better of adjustment and thought and appealite best of weight	2011	McAllister et al ^[17] Sood et al ^[13]		16 58	Ε ↓	weight loss dysphagia stifness of mouth pain in throat	bilateral right	Yes No	sod	NA neg	₹\$	NA neg	Yes Yes	NA Yes		1.1	NA No
Prasad et al ^[23] 1 10 m Fever officially in swallowing and a cough. bitateral officially in swallowing and a cough. Ves or a proper officially in swallowing and a cough. Ves or a proper officially in swallowing and a cough. Proper officially in swallowing and a cough. <td>2012</td> <td>Balasubramanian et al ^[39]</td> <td>-</td> <td>53</td> <td>E</td> <td>breamy from oral carry sore throat odynophagia loss of weight and appetite otalgia.</td> <td>right</td> <td>Yes</td> <td>Deu</td> <td>sod</td> <td>A</td> <td>sod</td> <td>FNAC</td> <td>Yes</td> <td></td> <td>Lungs</td> <td>o N</td>	2012	Balasubramanian et al ^[39]	-	53	E	breamy from oral carry sore throat odynophagia loss of weight and appetite otalgia.	right	Yes	Deu	sod	A	sod	FNAC	Yes		Lungs	o N
Bagga et al ^[63] 1 31 m soveralization in an adiating pain non radiating pain non radiating pain cough non radiating pain cough non radiating pain page page page page page page page page	2012	Prasad et al [23]	-	10	Ε	cough Fever	bilateral	Yes	sod	sod	sod	neg	Yes	Yes	- Beu	1	No
Cobay et al 12 1	2012	Bagga et al ^[63]	-	31	E	omrcury in swallowing severe burning non radiating pain cough	bilateral	Yes	neg	sod	N A	sod	FNAC	Yes		rnngs	tongue cancer
Barman et al [55] 1 48 m sort troat fever right Yes pos NA NA neg FNAC Yes neg Cervical lymphadenitis Ceylan et al [65] 1 56 m sore throat of sophagia faitigue left Yes pos NA NA pos FNAC Yes neg Larynx, lungs Ozbay et al [69] 1 NA	2013	Lukšić et al ^[12]	-	23	E	loss of appetite fever	bilateral	Yes	sod	neg	beu	neg	Yes	Yes		ı	No
Ceylan et al ⁽⁶⁵⁾ 1 56 m Soin indiales 1 (64) Yes pos pos NA pos FNAC Yes neg Larynx, lungs obsphagea fattigue night sweats loss of weight Ozbay et al ⁽⁶⁹⁾ 1 NA	2014	Barman et al [25]	-	48	E	sore throat fever	right	Yes	sod	NA	¥	neg	FNAC	Yes		Cervical lymphadenitis	No
Ozbay et al ⁽⁶⁹⁾ 1 NA NA NA Diateral NA pos NA NA Yes NA NA -	2014	Ceylan et al ^[65]	-	26	E	sore throat dysphagia fatigue night sweats	left	Yes	sod	sod	NA	sod	FNAC	Yes		Larynx, lungs	ON.
	2014	Ozbay et al [69]	1	NA	NA	ioss of weignt NA	bilateral	NA	sod	NA	NA	NA	Yes	NA			NA

(continued)

	Author	Number of cases	Age (years)	Sex	Clinical symptoms	Tonsil affected	Latero-cervical adenopathy	AFB	Culture	Mantoux	Chest X-ray	Tonsilectomy	Anti-TB treatment	AH #	Tb concomitent involvment	Comorbidities
2014 Brı	Bruzgielewicz et al ^[62]	7	49-71	NA	sore throat fever malasse	N A	Yes	sod	NA	3 pos	3 pos	3 FNAC/4 tonsilectomies	NA	NA	3 lungs	1 planoepithelial carcinoma
2015 Da	Das et al ^[3]	-	92	E	weight loss sore throat reccurent tossilitis	bilateral	Yes	sod	beu	NA	neg	FNAC and tonsilectomy	Yes	neg	1	No
2015 Ka	Kamath et al ^[34]	-	20	-	sore throat fever	bilateral	Yes	sod	neg	NA	neg	FNAC and tonsilectomy	Yes	neg	Nasopharynx (adenoids)	No
2016 Kıl	Kılıç et al ^[40]	-	56	E	progressive dyspriagramer fever pain throat difficulty swalling	bilateral	No N	sod	sod	NA	sod	Yes	Yes	neg	Lungs	No N
2016 An	Amit et al ^[15]	-	17	—	fever	bilateral	No	NA	beu	NA	neg	Yes	Yes	neg		No
2016 An	Amaya-Tapia et al [37]	-	46	Ε	dysphagia	bilateral	Yes	sod	beu	sod	neg	FNAC	Yes	neg	Mesenteric	No
2017 Fel	Ferreira et al ^[60]	-	32	—	odynophagia fever	left	Yes	sod	beu	NA	sod	FNAC	Yes	neg	Lungs	Behçet's syndrome
2017 Se	Sellami et al [27]	-	36	—	Sore throat	right	Yes	sod	beu	sod	beu	FNAC	Yes	neg	ı	No
2017 Sri	Sriram et al [35]	-	NA	NA	progressive dyspriagla fever eviallowing of the pack	NA	Yes	NA	NA	NA	NA	FNAC	NA A	A	Adenoids	No
2018 Su 2018 Erc	Subramani et al ^[7] Eroğlu et al ^[24]		22 51	- -	sore throat throat pain dysphagia	left left	Yes Yes	sod sod	NA pos	pos NA	NA neg	FNAC	Yes	neg	1.1	No No
2018 Sa	Sasikumar et al ^[22]	-	22	-	loss of appetite post partum odynophagia	left	Yes	sod	neg	sod	neg	Yes	Yes	neg	ı	0 <u>V</u>
2019 Ba	Balica et al ^[21]	-	44	E	loss of weight intense odynophagia referred otalgia anterior uveitis	left	O _N	sod	beu	реп	Беи	FNAC	Yes	neg	ı	Conjunctival-palpebral Kaposi's sarcoma glaucoma anterior ischemic
2019 Mc	Motahari et al ^[5]	-	18	-	sore throat fever	bilateral	Yes	sod	neg	beu	neg	Yes	Yes	neg		optic neuropathy No
2019 Lim	m et al ^[2]	-	9	E	loss of weight recurrent sore throat associated with	bilateral	Yes	sod	neg	zod	neg	Yes	Yes	beu	Adenoids	No
2020 Ha	Hassan et al ^[26]	-	21	E	snoring sore throat difficulty swaling	bilateral	Yes	sod	NA	NA	beu	Yes	Yes	neg	ı	No
2020 Dh	Dhanasekar T et al ^[1]	-	10	Ε	throat pain snoring snoring	bilateral	No	sod	neg+gene xpert	AN	neg	Yes	Yes	neg	1	No
2020 Tis	Tisekar et al ^[6]	-	55	Ε	change in voice sore throat difficulty in swallowing	left	Yes	sod	NA	NA	neg	Yes	Yes	neg	ı	No
2020 Na	Naserrudin et al [10]	-	26	Ε	recurrent sore throat	bilateral	NA	sod	N A	NA	beu	Yes	Yes	neg	1	No
2020 Ka	Kayabasi et al ^[14]	1	NA	ţ	spisouss NA	unilateral	NA	sod	NA	NA	neg	Yes	NA	NA		No

AFB=acid fast bacili, f=female, FNAC=fine needle aspiration cytology, m=male, NA=not available, neg=negative, pos=positive.

The commonest presentation of TB tonsil was sore throat (59%) just as Nadia Syafeera Naserrudin et al^[10] also observed. 15.11% of tonsils infected with TB appear to have ulceration, masses and white patches. In 46% of cases, both tonsils were involved, although a similar percentage of 41.2% of left tonsil lesions was found. Latero-cervical adenopathies were identified in 61.5% of patients. Isolated palatine tonsil lesions are acquired by inhalation and many times are related to pure oral hygiene or are seen in patients with a low immune status. [11] Our review of literature identified only 7% of immunocompromised patients, most of the tonsillar tuberculosis cases being free of comorbidities, just as the presented patient.

All patients had diagnostic based on histopathological examination (54.4% tonsil-lectomy, 45.6% fine needle aspiration biopsy) with 95.58% positive results. Only 40 of them had their sputum examined with 42.5% positive direct smear microscopy. A tuberculosis skin test (TST) was conducted in 33 patients with 60.60% positive results. Forty-one percent of patients had pulmonary form of tuberculosis was confirmed by a positive chest X-ray, only 1 patient confirmed by CT-scan after initial negative X-ray assessment.

Primary tuberculosis of tonsils in the absence of pulmonary involvement is a rare entity with an incidence of <5%, although our literature review identified more cases of primary tonsillar tuberculosis than secondary forms (59% vs 41%): primary tonsillar tuberculosis was found in 59% of patients, 39.4% of them presenting tonsils as unique tuberculosis site^[3,10,12–31] while the rest of 9.6% of them had simultaneous tuberculosis and epithelial squamous cell carcinoma of the tonsil—1 case,^[32] 4 cases of tuberculosis of tonsil and adenoids,^[2,30–35] 3 cases of tonsillar and pharyngeal tuberculosis,^[9,20,36] 1 case of tonsillar and cervical lymphadenitis related to tuberculosis,^[25] 2 cases of tuberculosis involving the tonsils, cervical and mesenteric lymphadenitis,^[9,37] and 1 case of tonsillar tuberculosis developed under anti-TNF alfa inhibitors and Methotrexate treatment.^[38]

The percentage of patients with concomitant pulmonary involvement was 41, [10,16,39–53] among them identifying 1 case of simultaneous pulmonary, tonsillar and cerebral tuberculosis, [54] 1 case of simultaneous pulmonary, tonsillar and renal involvement, [55] 3 cases of pulmonary, tonsillar and larynx tuberculosis, [56–58] and 5 immunocompromised patients: 1 case of HIV infection associated with pulmonary and tonsillar tuberculosis, [59] 2 patients developing pulmonary and tonsillar tuberculosis under anti TNF alpha inhibitors treatment, [60,61] and 2 cases of epithelial squamous cell carcinoma of the tonsil [62] or tongue [63] coexisting with pulmonary and tonsillar tuberculosis.

All patients received anti TB treatment, just as our presented case. Almost a quarter of them (26.7%) received anterior antibiotic treatment without any clinical improvement, exactly as our 14 old patient who took both betalactam antibiotics and cephalosporins at home, and lincosamide associated with an aminoglycoside during hospital admission, responding only to imipenem/cilastin, a 5th category of antituberculosis drug. [64–69]

Regarding our case report, we must admit that we had some limitations and the patient's medical management was not the one initially desired. We had a strong clinical suspicion of either malignancy, either infectious disease but despite explaining the patient's relatives the risks that inadequate treatment could expose the patient to, we faced their refusal for a CT scan, forward making a biopsy impossible to obtain. We had no other option than to wait and see the evolution under antibiotic treatment. After a MRI scan was performed, its result with the

local clinical remission no longer recommended a local biopsy, leaving us no other way than establishing a diagnosis based only on a positive TST and QuantiFERON-TB gold result.

While both the patient's and doctor's autonomy are a dynamic interface influencing decision making, we faced the ethical dilemma of respecting patient's legal tutors right to refuse investigation knowing the risks that the patient could be exposed to. Unfortunately, an increasing number of patients tend to make an abuse of their legal rights because of present media propaganda, finally leading only to longer admission duration, higher costs and of course, more severe medical cases.^[70,71]

The purpose of the present paper, a precise analysis of previous presented cases is to come as a support for the medical practitioners' global efforts of reducing the TB medical, social and economic burden.

5. Conclusion

Primary tonsillar tuberculosis is a rare condition, especially in the pediatric age but must be considered when facing a persistent tonsillitis in countries with a high prevalence of tuberculosis. Histopathological findings and bacteriological confirmation are ideal for establishing a positive diagnosis and immediate initiation of adequate treatment. The particularity of this case is represented by the rarity of primary tuberculosis of tonsils in children, with unilateral involvement, displaying at the same time a common issue encountered in the current practice: the limitations and the difficult course of setting the diagnosis due to the involvement of relatives in the medical act.

Acknowledgments

All authors have equally contributed in preparing this manuscript.

We like to thank the Radiology and Laboratory Department for their help in managing this patient.

Author contributions

Conceptualization: Stefana Maria Moisa, Ingrith Miron, Anca Adam Raileanu, Vasile Valeriu Lupu, Ancuta Lupu, Elena Tarca. Investigation: Stefana Maria Moisa, Ingrith Miron, Anca Adam Raileanu, Vasile Valeriu Lupu, Ancuta Lupu, Elena Tarca.

Methodology: Stefana Maria Moisa, Ingrith Miron, Anca Adam Raileanu, Vasile Valeriu Lupu, Ancuta Lupu, Elena Tarca.

Writing – original draft: Stefana Maria Moisa, Ingrith Miron, Anca Adam Raileanu, Vasile Valeriu Lupu, Ancuta Lupu, Elena Tarca.

Writing – review & editing: Stefana Maria Moisa, Ingrith Miron, Anca Adam Raileanu, Vasile Valeriu Lupu, Ancuta Lupu, Elena Tarca.

References

- Dhanasekar T, Inba Shyamala R, Majeed Arshad A, et al. An interesting case of tonsillar tuberculosis in a 10-year-old boy. J Clin Tuberc Other Mycobact Dis 2020;20:100162.
- [2] Lim CC, Misron K, Loong SP, et al. Primary adenotonsillar tuberculosis in an immunocompetent child—a case report. Iran J Otorhinolaryngol 2019;31:319–22.
- [3] Das Á, Das SK, Pandit S, et al. Tonsillar tuberculosis: a forgotten clinical entity. J Family Med Prim Care 2015;4:124–6.
- [4] World Health Organization. Global Tuberculosis Report 2020. Available at: https://www.who.int/teams/global-tuberculosis-programme/global-report-2020. Accessed February 24, 2021.

- [5] Motahari SJ, Afshar P, Ghasemi M, et al. Primary tonsillar tuberculosis: a forgotten clinical identity. Iran J Microbiol 2019;11:542–5.
- [6] Tisekar O, Bhaskar M, Biraris P, et al. Primary tonsillar tuberculosis masquerading as carcinoma of the tonsil. Indian J Tuberc 2020;67: 386–8
- [7] Subramani S, Saravanam PK, Rajendran R. Extrapulmonary tuberculosis: atypical presentation in otorhinolaryngology, BMJ Case Rep Published Online First: 2018.doi:10.1136/bcr-2018-224802.
- [8] Kakisi OK, Kechagia AS, Kakisis IK, et al. Tuberculosis of the oral cavity: a systematic review. Eur J Oral Sci 2010;118:103–9.
- [9] Plesiss A, Hussey G. Laryngeal tuberculosis in childhood. Pediatric Infect Dis J 1987;6:678–80.
- [10] Naserrudin NS, Indumathi H. Primary tonsillar tuberculosis: a case report & review of literature. Int Med J 1994;27:235–6.
- [11] Chakravarti A, Pal S, Sahni JK. Primary tuberculosis of tonsil and posterior oropharyngeal wall. Indian J Tuberc 2008;55:48–50.
- [12] Lukšić B, Kljajić Z, Roje Z, et al. Direct molecular detection of Mycobacterium tuberculosis suspected to be the specific infection in a case of recurrent tonsillitis. J Infect Chemother 2013;19:1185–7.
- [13] Sood A, Bhardwaj B, Gill J. Primary tuberculosis of the tonsil. Nepalese J ENT Head Neck Surg 2012;2:17–8.
- [14] Kayabasi S, Hizli O, Cayir S, et al. A comprehensive analysis of histopathologic examination results of tonsillectomy specimens. 2020 Cureus 12(1): e6655.
- [15] Amit S, Vikas S, Sudhamani B, et al. A rare site for primary tuberculosis of tonsils. Int J Integrated Med Res 2012;3:53–5.
- [16] Srirompotong S, Yimtae K, Srirompotong S. Clinical aspects of tonsillar tuberculosis. Southeast Asian J Trop Med Public Health 2002;33: 147–50.
- [17] McAllister KA, MacGregor FB. Diagnosis of tuberculosis in the head and neck. J Laryngol Otol 2011;125:603–7.
- [18] Selimoğlu E, Sütbeyaz Y, Çiftçioğlu MA, et al. Primary tonsillar tuberculosis: a case report. J Laryngol Otol 1995;109:880–2.
- [19] Ricciardiello F, Martufi S, Cardone M, et al. Otorhinolaryngologyrelated tuberculosis. Acta Otorhinolaryngol Ital 2006;26:38–42.
- [20] Mohindra tonsillar tuberculosis. Indian J Otolaryngol 1964;16: 136–41.
- [21] Balica NC, Poenaru M, Preda MA, et al. Primary tonsillar tuberculosis—case report. Rom J Morphol Embryol 2019;60:267–71.
- [22] Sasikumar S, Ayub II, Kannan S, et al. Primary tonsillar tuberculosis. BMJ Case Rep 2018;2018:bcr2017223634.
- [23] Prasad P, Bhardwaj M. Primary tuberculosis of tonsils: a case report. Case Rep Med 2012;120382.
- [24] Eroğlu O, Yağmahan MS, Artaş G, et al. Primary tuberculosis of tonsils: a case report. Eur J Rhinol Allergy 2018;1:76–8.
- [25] Barman S, Khaund G. Primary tuberculosis of upper airway: case report of 3 rare presentation. Indian J Otolaryngol Head Neck Surg 2014;66: 208, 11
- [26] Hassan MJ, Panhotra S, Mohroo RN, et al. Tonsillar Tuberculosis: Report of a common infection at a rare location. IP J Diagn Pathol Oncol 2020;5:336–8.
- [27] Sellami M, Mnejja M, Charfi S, et al. Tuberculosis of the tonsil simulating a cancer. Lancet Infect Dis 2017;17:1317.
- [28] Fortún J, Barros C, Melcon E, et al. Ex-tra-laryngeal head and neck tuberculosis. Clin Microbiol Infect 2000;6:644–8.
- [29] Naik MA, Dhulia KD. Primary tubercular infection of tonsil: a case
- report. Indian J Otolaryngol Head Neck Surg 2000;52:397–8. [30] Cherkaoui A, Hajjij A, Ouatassi N, et al. La tuberculose des amygdales
- palatines [Tuberculosis of the tonsils]. Pan Afr Med J 2010;4:1.
 [31] Kant S, Sanjay Verma SK. Isolated tonsil tuberculosis. Lung India Off
- Organ Indian Chest Soc 2008;25:e163–4.
 [32] Raman R, Kuruvilla A, Bakthaviziam A. Carcinoma of the palatine tonsil
- co-existing with tuberculosis. J Laryngol Otol 1979;93:927–31.
- [33] Al-Sebeih K, Katchy K. Adenotonsillar granuloma: histopathological correlation. Med Princ Pract 2007;16:450–3.
- [34] Kamath PM, Shenoy VS, Nirupama M, et al. Tuberculosis of waldeyer's ring with an atypical presentation as chronic adeno-tonsilitis. J Clin Diagn Res 2015;9:MD01–2.
- [35] Sriram R, Bhojwani KM. Manifestations of tuberculosis in otorhinolaryngology practice: a retrospective study con-ducted in a Coastal city of South India. Indian J Otolaryngol Head Neck Surg 2017;210–5.
- [36] Pedrol E, Estruch R, Barceló J, et al. Tonsillar and pharyngeal tuberculosis in a patient without HIV antibodies. J Infect Dis 1989; 159:598.

- [37] Amaya-Tapia G, Rodríguez-Toledo A, Aguilar-Benavides S, et al. Large retropharyngeal abscesses in an immunocompetent adult patient with disseminated tuberculosis. Am J Case Rep 2016;17:690–3.
- [38] Barouta G, Karapetsa M, Kostopoulou E, et al. Oral tuberculosis in a patient with rheumatoid arthritis after long treatment with methotrexate and adalimumab. J Clin Rheumatol 2010;16:330–1.
- [39] Balasubramanian T, Geetha R, Venkatesan U. Secondary tuberculosis of tonsil case report and literature review. Online J Otolaryngol 2012;2: 59–67.
- [40] Kılıç EK, Kılıç C. A pulmonary tuberculosis case presented with tonsillar involvement. Turk Thorac J 2016;17:122–4.
- [41] Ghatak S, Jana T, Bandyopadhyaya S, Biswas SK. Primary oropharyngeal tuberculosis causing destruction of uvula—a rare presentation. Int J Pediatric Otorhinolaryngol Extra 5 (2010): 91–92.
- [42] Jana U, Mukherjee S. Tuberculosis of tonsil—a rare site involvement. Indian J Otolaryngol Head Neck Surg 2003;55:119–20.
- [43] Krishnappa BD. Tuberculosis of tonsil. Indian J Otolaryngol Head Neck Surg 2006;58:210.
- [44] Cowan DL, Jones GR. Tuberculosis of the tonsil: case report and review. Tubercle 1972;53:255–8.
- [45] Golli AL, Niţu MF, Turcu F, et al. Tuberculosis remains a public health problem in Romania. Int J Tuberc Lung Dis 2019;23:226–31.
- [46] Belizna C K, Heron JM, Lévesque F. Tonsillar and lymph node tuberculosis revealing asymptomatic pulmonary tuber-culosis.2008 QJM: monthly. J Assoc Physicians 100: 800–1.
- [47] Sanford DM, Becker GD. Tuberculosis of the tonsil. Extensive pulmonary tuberculosis presenting as a sore throat. Arch Otolaryngol 1966:84:343–5.
- [48] Nakayama R, Sueki H, Iijima H. A case of Phlebitis Tuberculosa Nodosa: Tonsillar tuberculosis was diagnosed from skin lesion. Nishi Nihon Hifuka 2005;67:239–42.
- [49] Menon K, Bem C, Gouldesbrough D, et al. A clinical review of 128 cases of head and neck tuberculosis presenting over a 10-year period in Bradford, UK. J Laryngol Otol 2007;121:362–8.
- [50] Qian X, Albers AE, Nguyen DTM, et al. Head and neck tuberculosis: literature review and meta-analysis. Tuberculosis (Edinb) 2019;116S: S78–88.
- [51] Jindal SK, Jindal A, Agarwal R. Upper respiratory tract tuberculosis. Microbiol Spectr 2016;4:
- [52] Kardon DE, Thompson LD. A clinicopathologic series of 22 cases of tonsillar granulomas. Laryngoscope 2000;110(3 Pt 1):476–81.
- [53] Maciaszczyk K, Wagrowska-Danilewicz M, Pajor A. Wtórna gruźlica migdałków podniebiennychopis przypadku i przeglad piśmiennictwa [Secondary tuberculosis of palatine tonsils-the case report and review of literature]. Otolaryngol Pol 2007;61:1000–3.
- [54] Adiego MI, Millán J, Royo J, et al. Unusual association of secondary tonsillar and cerebral tuberculosis. J Laryngol Otol 1994;108:348–9.
- [55] Park KH, Park SI. Concurrent tuberculosis of the larynx and the tonsil. Yonsei Med J 1988;29:79–83.
- [56] Sutbeyaz YU, Harun K, Riza G. The association of secondary tonsillar and laryngeal tuberculosis: a case report and literature review. Auris nasus larynx 2000;27:371–4.
- [57] Yamamoto K, Iwata F, Nakamura A, et al. Tonsillar tuberculosis associated with pulmonary and laryngeal foci. Intern Med 2002;41: 664-6
- [58] Awad MA, Khalid A. Pharyngeal tuberculosis. Am J Otolaryngol 2001;22:236–40.
- [59] Duijnstee MB. Tonsillar tuberculosis and HIV coinfection. J Otolaryngol 2006;35:205–6.
- [60] Ferreira S, Vaz-Marques P. Tuberculous tonsillitis in a patient treated with an anti-TNF agent. EJCRIM 2017;4.
- [61] Efde MN, Houtman PM, Spoorenberg JP, et al. Tonsillar tuberculosis in a rheumatoid arthritis patient receiving anti-TNFalpha (adalimumab) treatment. Neth J Med 2005;63:112–4.
- [62] Bruzgielewicz A, Rzepakowska A, Osuch-Wójcikewicz E, et al. Tuberculosis of the head and neck—epidemiological and clinical presentation. Arch Med Sci 2014;10:1160–6.
- [63] Bagga P, Dewan A, Agarwal P, et al. Oral tuberculosis following successful treatment of oral malignancy. J Cancer Res Ther 2012;8: 650–1.
- [64] Al-Serhani AM. Mycobacterial infection of the head and neck: presentation and diagnosis. Laryngoscope 2001;111(11 Pt 1):2012–6.
- [65] Ceylan E, Soyalic H, San I. Co-existence of pulmonary, tonsillar and laryngeal tuberculosis. Eastern J Med 2014;19:150–3.

- [66] Srirompotong S, Yimtae K, Srirompotong S. Tuberculosis in the upper aerodigestive tract and human immunodeficiency virus coinfections. J Otolaryngol 2003;32:230–3.
- [67] Stewart CJ, Dixon JM, Curtis BA. Isolation of mycobacteria from tonsils, naso-pharyngeal secretions and lymph nodes in East Anglia. Tubercle 1970;51:178–83.
- [68] Belal A. Latent tuberculosis in tonsils and adenoids; a study of 127 cases. J Laryngol Otol 1951;65:414–25.
- [69] Özbay I, Gençoğlu M, Balıkçı HH, et al. Histopathological analysis of tonsillectomy specimens: a report from Southeastern Anatolia. Kulak Burun Bogaz Ihtis Derg 2014;24:254–8.
- [70] Scheunemann LP, White DB. The ethics and reality of rationing in medicine. Chest 2011;140:1625–32.
- [71] Wancata LM, Hinshaw DB. Rethinking autonomy: decision making between patient and surgeon in advanced illnesses. Ann Transl Med 2016;4:77.