Indonesian Journal of Rheumatology
Journal Homepage: https://journalrheumatology.or.id/index.php/IJR

Behcet Disease: When Laryngeal Tuberculosis Unforeseably Strikes

Chaïmaâ Zeroual[1]*, Leïla Barakat[1], Mina Moudatir[1], Khadija Echchilali[1], Safaâ Mourabit[1], Hassan El Kabli[1]

[1]Department of Internal Medicine, Ibn Rochd University Hospital, Faculty of Medicine and Pharmacy of Casablanca, Casablanca, Morocco

ARTICLE INFO

Keywords:
Laryngeal tuberculosis
Subclinical pulmonary tuberculosis
Behçet disease
Immunosuppressant
Azathioprine

***Corresponding author:**
Chaïmaâ Zeroual

E-mail address:
chaimaazeroual42@gmail.com

All authors have reviewed and approved the final version of the manuscript.

A B S T R A C T

Behçet disease (BD) is a chronic vasculitis that can affect all organs, particularly the skin, mucous membranes, eyes and joints. It can lead to severe complications requiring immunosuppressive therapy (IS). Although the prescription of IS is indisputable and life-saving, they carry a significant risk of opportunistic infections. Tuberculosis is an infectious disease primarily caused by the bacterium Mycobacterium tuberculosis, also known as Koch's bacillus. It predominantly affects the lungs due to airborne transmission and favorable conditions for the bacillus's survival in this area; however, it can also affect other sites to a lesser extent, such as the brain, bones, skin and « ear, nose and throat » (ENT) regions. Laryngeal tuberculosis (LT) is a rare and underdiagnosed localization that often occurs in immunocompromised patients. This article reports the case of a patient with BD under IS who developed LT secondary to subclinical pulmonary tuberculosis. The outcome after discontinuing azathioprine and initiating antituberculous treatment was favorable. The case report aims to shed light on the rare and underrecognized presentation of tuberculosis in BD and in case of immune vulnerability, unraveling the intricate interplay between immunosuppression and opportunistic infections. Its significance lies in underscoring the critical need for heightened clinical vigilance, as LT can masquerade as BD-related manifestations, posing diagnostic dilemmas.

1. Introduction

Rare and unknown, laryngeal tuberculosis (LT) represents an atypical localization of tuberculosis infection. Occurring in the context of immunosuppression due to chronic inflammatory diseases such as Behçet's disease (BD), LT can be potentially fatal in the absence of early management. BD is a systemic vasculitis characterized by symptoms including recurrent oral-genital aphthosis, skin lesions, uveitis, and other severe manifestations necessitating the use of immunosuppressants (IS). However, the immunosuppression induced by these treatments predisposes patients to infections, including tuberculosis. LT, being a specific form of extrapulmonary tuberculosis, can present misleadingly and mimic other pathologies, particularly malignant ones. Dysphonia, dysphagia, or odynophagia are all nonspecific symptoms that may delay diagnosis.[1,2] The treatment for LT is primarily medical, based on antituberculous chemotherapy administered over several months. The association between BD and LT highlights not only the diagnostic challenge but also the therapeutic one due to the need to suspend IS, thus increasing the risk of BD relapse. We describe the case of a patient who developed LT while on azathioprine prescribed for BD. By emphasizing the importance of proactive tuberculosis screening, precise differentiation of symptoms,

and swift therapeutic intervention, this case serves as a compelling reminder of the delicate balance required to navigate life-saving immunosuppression while mitigating infection risks in vulnerable patients.

2. Case Presentation

The patient was a 53-year-old man who had been vaccinated against during childhood and had no significant pathological history, particularly toxic or phthisiological (no exposure or history of tuberculosis). He had been followed in internal medicine since 1993 for severe BD characterized by bipolar aphthosis and revealed by ocular involvement in 1997. In 2017, the patient experienced vascular involvement due to bilateral pulmonary embolism from an intracardiac thrombus in the right ventricle. He received anticoagulation therapy along with 6 boluses of methylprednisolone (1g) and 6 of cyclophosphamide (1g) monthly, followed by oral corticosteroids and azathioprine (150 mg/day). BD was confirmed based on International Criteria for Behcet's Disease (ICBD) with a score of 8 points (Table 1).

Table 1. The criteria used to retain the bD in the patient according to *ICBD*

-Oral aphthosis	2 points
-Genital aphthosis	2 points
-Skin lesions of the necrotizing pseudofolliculitis type	1 point
-Ocular involvement of the panuveitis type in the left eye	2 points
-Vascular involvement of the pulmonary artery thrombosis type	1 point

He was admitted to our facility for the progressive evolution over 4 months of a condition characterized by dysphonia with odynophagia, occurring in the context of a deterioration in general health without night sweats. He had no respiratory symptoms, particularly cough or dyspnea. Upon admission, he was afebrile at 36.9°C, eupneic at 19 breaths per minute, normocardiac at 67 beats per minute, normotensive at 11/7 cmHg, with a Fatigue Severity Scale (FSS) score of 6 and a Body Mass Index (BMI) of 17. The ENT examination revealed complete filling and involvement of both valleculae by an ulcerative-budding process extending to the epiglottis. The glottis and supraglottis appeared whitish and edematous. Furthermore, other examinations including pleuropulmonary, lymphatic, joint, and abdominal assessments were unremarkable. A cervical-thoracic CT scan was performed, showing a likely infectious pneumonia (Figure 1) with thickening and infiltration of both vocal cords, the epiglottis and even the aryepiglottic folds.

The laryngeal biopsy showed tuberculoid granulomatous inflammation associated with large areas of suppurative necrosis at the level of the epiglottis and vocal cords (Figure 2 (a) & (b)). Additionally, the *Quantiferon-TB Gold Plus* test was positive, and during three induced sputum samples for acid-fast bacilli (AFB), the result of the first day was positive on direct examination and *Ziehl-Neelsen* staining. Serologies for The

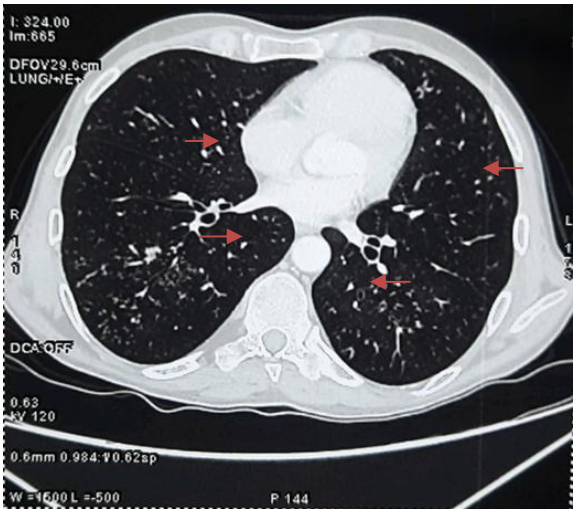

Figure 1. Cross sectional view of the chest computed tomography (CT). Red arrow show nodules scatterd throughout the lungs.

human immunodeficiency viruses (HIV1/2), hepatitis B and C were negative. Given the bacillary nature of the patient and thus the significant risk of contamination, he was initially isolated. After discontinuing azathioprine, he was placed on anti-bacillary treatment for 9 months according to the standard regimen for tuberculosis. The evolution was favorable, marked by regression of symptoms and improvement in general health.

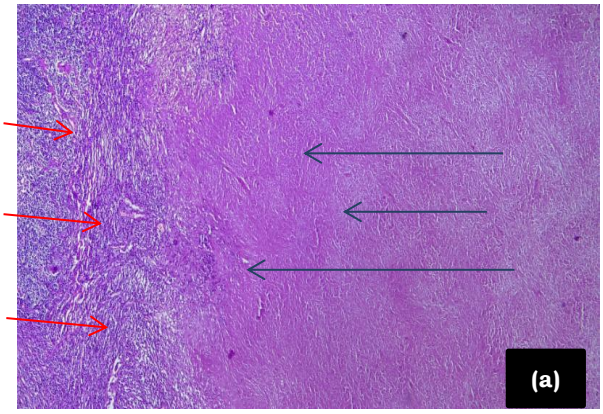

Figure 2a. Hematoxylin-eosin (H&E) staining (x100): Microscopic appearance of laryngeal biopsy characteristic of tuberculosis

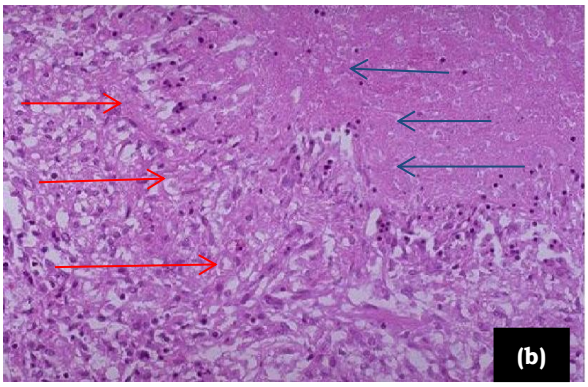

Figure 2b. Hematoxylin-eosin (H&E) staining (x100): Microscopic appearance of laryngeal biopsy characteristic of tuberculosis

The red arrows indicate granulomas (composed of epithelioid cells and Langhans-type giant cells, surrounded by a dense lymphocytic infiltrate).
The blue arrows show the caseous necrosis (also known as suppurative necrosis indicating an intense inflammatory process often secondary to a bacterial superinfection).

3. Discussion

BD is a complex condition characterized by its clinical polymorphism. It is ubiquitous, more common in regions corresponding to the historical "Silk Road," notably in the Middle East, Japan, and Turkey.[3] According to the revised

Chapel Hill classification from 2012, it is included among systemic vasculitides that can affect various blood vessels of all calibers.[4] In cases of severe manifestations (neurological, vascular, cardiac, etc.), treatment relies on immunosuppressants such as high-dose corticosteroids and azathioprine. Vascular involvement during BD, grouped under the term angio-Behçet, has a prevalence of 37.8% and can compromise both functional and even vital prognosis.[5] Angio-Behçet preferentially affects the male sex and is characterized by high morbidity and mortality, justifying the administration of immunosuppressants and long-term monitoring. These treatments increase susceptibility to opportunistic infections, particularly tuberculosis.[6]

The latter remains endemic in Morocco, with an incidence rate of 92 cases per 100,000 people as of 2023 according to Trading Economics (2025).[7] Certain regions, such as the northwestern Mediterranean area (Tangier and Tetouan), report higher prevalence rates compared to the national average.[8] While Morocco has made progress in reducing tuberculosis incidence, the disease persists as a significant public health concern, exacerbated by challenges like delayed diagnosis and healthcare access disparities.

On the other hand, Indonesia is one of the highest tuberculosis-burden countries globally, ranking second after India. The estimated incidence rate is 312–349 per 100,000 people, with significant regional variations.[9] For example, Sumatra has a prevalence of 913 per 100,000 people, while Java-Bali reports lower rates at 593 per 100,000. Tuberculosis is endemic across the country, with urban areas generally experiencing higher prevalence than rural ones.[10]

LT represents less than 1% of tuberculosis cases and primarily occurs in adults aged 40 to 60 years.[11] Symptoms include dysphonia (80-100% of cases), odynophagia (50-67%), dyspnea and dysphagia in advanced cases.[11,12] In patients with BD who are taking IS, manifestations may be atypical and delayed. Risk factors associated with any form of tuberculosis include the absence of The Bacillus Calmette–Guérin (BCG) vaccination, a history of pulmonary tuberculosis, malnutrition, close living conditions and immunosuppression. LT can be primary, manifesting directly in the larynx, or secondary to a pre-existing pulmonary infection.[13,14,15,16] In our patient, LT followed an infraclinical but bacillary pulmonary tuberculosis, which poses a significant diagnostic challenge. Unusually, pulmonary tuberculosis can be asymptomatic, but pulmonary lesions may be present and active without the patient's awareness. The diagnosis of LT relies on paraclinical arguments. Laryngoscopy may reveal erythematous or whitish lesions. Additionally, ulcerations or vegetations may be present on the vocal cords. Histologically, it often shows epithelioid granulomas with caseous necrosis in typical forms. However, the absence of caseation does not exclude the diagnosis. Microbiologically, Mycobacterium tuberculosis is visualized through Ziehl-Neelsen staining and cultured on Löwenstein medium.[17,18]

Early diagnosis of LT and appropriate treatment generally allow for complete resolution of symptoms. In contrast, any diagnostic delay can lead to damage such as irreversible destruction of laryngeal tissue or systemic dissemination.

Regarding the suspension of IS following tuberculosis treatment, there is currently no literature determining the duration. However, it is crucial to assess the patient's condition after completing antituberculous chemotherapy and before reintroducing any IS. It would be prudent to wait at least six months after the end of

anti-bacillary treatment. During this period, close monitoring is essential to detect any reactivation of tuberculosis. Maintaining the quiescence of BD without IS remains a significant challenge. A multidisciplinary approach is desirable for the simultaneous management of BD and LT while minimizing risks associated with immunosuppression in the context of an active infection.

4. Conclusion

This case draw attention to both diagnosis and management of patients with BD developing tuberculosis under IS. Physicians must consider the possibility of LT when evaluating patients presenting with laryngeal symptoms, even in the absence of obvious clinical signs of pulmonary infection. Managing BD and tuberculosis together is a delicate balancing act since treatments for one condition can worsen the other. A precise approach is needed to navigate this complex challenge.

Conflict of Interest

There is no conflict of interest to be disclosed.

Funding

This study was not supported by any institution or company.

References

1. Mahfoudhi M, Khamassi K, Turki S, Kheder A. Difficulté diagnostique d'une tuberculose laryngée isolée chez une femme diabétique [Diagnostic difficulty of isolated laryngeal tuberculosis in a diabetic woman]. Pan Afr Med J. 2015; 21:106.
2. Abbassi IM, El Euch M, Jaziri F, Kefi A, Hamida FB, Turki S, Abdelghani KB, Abdallah TB. Tuberculose laryngée isolée de l'adulte: localisation extra pulmonaire exceptionnelle (à propos d'un cas) [Isolated laryngeal tuberculosis as an uncommon manifestation of extrapulmonary tuberculosis in adults: a case report]. Pan Afr Med J. 2022; 43:9.
3. Mahr A and Maldini C. Epidemiology of Behçet's disease. Rev Médecine Interne 2014;35:81-89.
4. Jennette JC. Overview of the 2012 revised International Chapel Hill Consensus Conference nomenclature of vasculitides. Clin Exp Nephrol 2013; 17:603–6.
5. Boukhris I, Bouzid S, Hamdi MS, Chaabane M, Belhadj L, Cherif E and al. Particularités cliniques de l'angio-Behçet: à propos de 82 cas. La Revue de Médecine Interne 2021; 42: 359-60.
6. Machuca I, Vidal E, de la Torre-Cisneros J, Rivero-Román A. Tuberculosis in immunosuppressed patients. Enferm Infecc Microbiol Clin (Engl Ed). 2018;36(6):366-374.
7. Trading Economics. Morocco - Incidence Of Tuberculosis (per 100,000 People). Retrieved April 8, 2025, from https://tradingeconomics.com/morocco/incidence-of-tuberculosis-per-100-000-people.
8. Ez-Zari A, Farouk L, Mezzoug N et al. Tuberculosis Epidemiology and the Impact of the COVID-19 Pandemic on Tuberculosis Control in Tétouan, Morocco (2015–2022): A Retrospective Descriptive and Analytical Study. Cureus. 2025;17(3): e81467.
9. World Health Organization. Global Tuberculosis Report 2022 [Internet]. Geneva: World Health Organization; 2022. Available from: https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2022.
10. Noviyani A, Nopsopon T, Pongpirul K. Variation of tuberculosis prevalence across diagnostic approaches and geographical areas of Indonesia. PLoS One. 2021;16(10):e0258809.
11. Kurokawa M, Nibu KI, Ichimura KI and Nishino H. Laryngeal tuberculosis: a report of 17 cases. Auris Nasus Larynx 2015; 42(4): 305-310.
12. Rubin F, Jameleddine E, Guiquerro S and Laccourreye O. Laryngeal tuberculosis in the early 21st century. Literature review of clinical, diagnostic and therapeutic data, according to SWiM guidelines. European Annals of Otorhinolaryngology, Head and Neck Diseases 2024; 141(3) :147-152.
13. Bhuyan N, Das AK. Primary laryngeal tuberculosis: a rare cause of chronic laryngitis. International Journal of Advances in Medicine 2014; 1(3): 279-281.
14. Abou-elfadl M, Benzaouia A, Abada R et al. Laryngeal Tuberculosis: About 3 Cases from Morocco. J Otolaryngol Rhinol 2016; 2(4): 1-3.
15. Kamalika PR, Dhruba JD, Srikanth M, Praneeth KK. Tuberculosis of the Larynx: A Review of Two Cases. International Journal of Phonosurgery and Laryngology 2017; 7(1):27-30.
16. D'Aleo Canova GC, Zeroli C, Barberi F, Gorica A et al. Isolated laryngeal tuberculosis complex infection: expect the unexpected. Oxf Med Case Reports. 2024; 2024(3):omae007.
17. Sidibé Y, Samaké D, Haidara AW, Sanogo B et al. Tuberculose laryngée: À propos d'une observation. J. TUN ORL 2022 ;47 :66-9.
18. Teixeira Marques F, Estêvão R, Mota CP, Lousan N. Laryngeal tuberculosis, the great deceiver: A series of 10 cases. Indian J Tuberc. 2024;71(3):238-241.