



Case report

The occurrence of a multidrug-resistant tuberculous retropharyngeal abscess in an immunocompetent patient: A case report



N. Tiresse^{d,1}, S. Oucharqui^{b,1}, E. Benaissa^{a,b,*}, B. Badri^d, F. Bssaibis^b, A. Maleb^c, M. Elouennass^{a,b}

^a Epidemiology and bacterial resistance research team/BIO-INNOVA Centre, Faculty of Medicine and Pharmacy (University Mohammed V), Rabat, Morocco

^b Department of Bacteriology, Mohammed V Military Teaching Hospital / Faculty of Medicine and Pharmacy (University Mohammed V), Rabat, Morocco

^c Laboratory of Microbiology, Mohammed VI University Hospital / Faculty of Medicine and Pharmacy (University Mohammed the first), Oujda, Morocco

^d Department of pneumology, Mohammed V Military Teaching Hospital / Faculty of Medicine and Pharmacy (University Mohammed V), Rabat, Morocco

ARTICLE INFO

Article history:

Received 6 July 2021

Received in revised form 2 September 2021

Accepted 2 September 2021

Available online xxxx

Keywords:

Multidrug-resistant
Retropharyngeal abscess
GeneXpert MTB/RIF
GenoType MTBDRplus
GenoType MTBDRsl

ABSTRACT

Retropharyngeal abscess is an uncommon location of tuberculosis (TB). In this report, we describe a multidrug-resistant tuberculous retropharyngeal abscess in a 21-year-old female patient who was treated for lymph node TB for one year. CT scan revealed a large retropharyngeal abscess that was aspirated intraorally under local anesthesia. The diagnosis of TB was retained by molecular and histological study. GeneXpert MTB/RIF (Cepheid, Sunnyvale, CA, USA), performed on the pus, showed rifampicin resistance and a first- and second-line drug resistance test using GenoType MTBDRplus VER.2 and MTBDRsl VER.1 (Hain Lifescience GmbH, Nehren, Germany) showed TB highly resistant to rifampicin, isoniazid, and aminoglycosides. Treatment is primarily medical as it combines specific antituberculous antibiotics, and aspiration for drainage of the abscess. Our patient was put on long-term 2nd line anti-TB treatment.

© 2021 The Authors. Published by Elsevier Ltd.
CC_BY_NC_ND_4.0

Introduction

Tuberculous retropharyngeal abscess is not frequently reported in the literature and pre-extensive tuberculous retropharyngeal abscess is even less frequently reported [1]. Early recognition of this condition is essential to prevent serious complications. The diagnosis is difficult and relies on a combination of clinical, radiological and biological arguments. We report a case of multidrug resistant (MDR) tuberculous retropharyngeal abscess in a 21-year-old female patient treated for lymph node tuberculosis (TB) for one year and discuss the different diagnostic and therapeutic elements of this pathology, highlighting the contribution of molecular biology in the effective management of MDR extra-pulmonary TB.

* Corresponding author at: Epidemiology and bacterial resistance research team/BIO-INNOVA Centre, Faculty of Medicine and Pharmacy (University Mohammed V), Rabat, Morocco.

E-mail addresses: nabil.tiresse1@gmail.com (N. Tiresse), oucharqui@gmail.com (S. Oucharqui), benaissaelmostafa2@gmail.com (E. Benaissa), bouchra.ba04@gmail.com (B. Badri), bssaibisfatna@yahoo.fr (F. Bssaibis), maleb.adil@gmail.com (A. Maleb), elouennassm@yahoo.fr (M. Elouennass).

¹ Oucharqui sara and Tiresse nabil have contributed equally in the elaboration of the work.

Case report

This is a 21-year-old female with a history of chronic headache for several years with Chiari decompression surgery performed in 2017 and latero-cervical adenopathy diagnosed as lymph node TB on bacteriological, molecular and histological arguments in 2019. GeneXpert MTB/RIF performed on the cervical lymph node came back positive for TB, without resistance to rifampicin. She was then treated at another institution according to the national protocol which includes quadritherapy with isoniazid, rifampicin, ethambutol and pyrazinamide for 2 months followed by bitherapy with isoniazid and rifampicin for 10 months (2RHZE/10RH). The evolution was then marked by the disappearance of the lymph nodes after one year of treatment. Six months after the end of treatment, the patient presented to the emergency room with severe headaches.

Otherwise, no cough, chest pain, fever, or loss of appetite was reported. The patient noted no signs of trismus or difficulty breathing. She reported no known allergies and had no history of smoking or drinking alcohol. On admission, physical examination revealed a body temperature of 36.6 °C, a heart rate of 90 beats/min, and a blood pressure of 117/75 mmHg. Palpation of both sides of the neck revealed no tenderness and no lymph nodes were noted. Examination of the oral cavity revealed no pathological findings, and



Fig. 1. Sagittal CT scan revealed a peripherally enhanced collection in the retropharyngeal area after injection of contrast medium.

no posterior pharyngeal wall projections were observed. The lungs were clear on auscultation and no neurologic deficits were noted on initial clinical examination.

The biological workup showed hemoglobin at 12.6 g/l; white blood cell count at 4.8 G/l; and C-reactive protein at 0.8 mg/l. In addition, serologies for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C were negative.

A cerebral CT scan performed as part of the etiological diagnosis fortuitously revealed a peripherally enhanced collection in the retropharyngeal area after injection of contrast medium measuring 19 × 21 mm, associated with an adjacent necrotic adenopathy measuring 10 × 06 mm. (Fig. 1).

A cervical MRI was realized later and confirmed the presence of the retropharyngeal collection. (Fig. 2).

The abscess was drained under local anesthesia. 02 milliliters of pus were aspirated. The specimen was sent for bacteriological analysis for *Mycobacterium tuberculosis* complex (MTC) and banal germs as well as for pathological study. A molecular study using GeneXpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) resulted in detection of MTC with detection of rifampicin resistance in less than 2 h. In response to this rifampicin resistance, we performed other molecular tests, including GenoType MTBDRplus VER. 2 and GenoType MTBDRsl VER.1 (Hain Lifescience GmbH, Nehren, Germany) on the pus to confirm rifampicin resistance and also to investigate resistance to other anti-TB drugs. It should be noted that this technique is not validated on extrapulmonary specimens directly, although many studies have showed a good correlation with the usual resistance screening methods. The MTBDRplus VER. 2 showed resistance to both rifampicin and isoniazid, while MTBDRsl VER.1 showed resistance only to aminoglycosides.

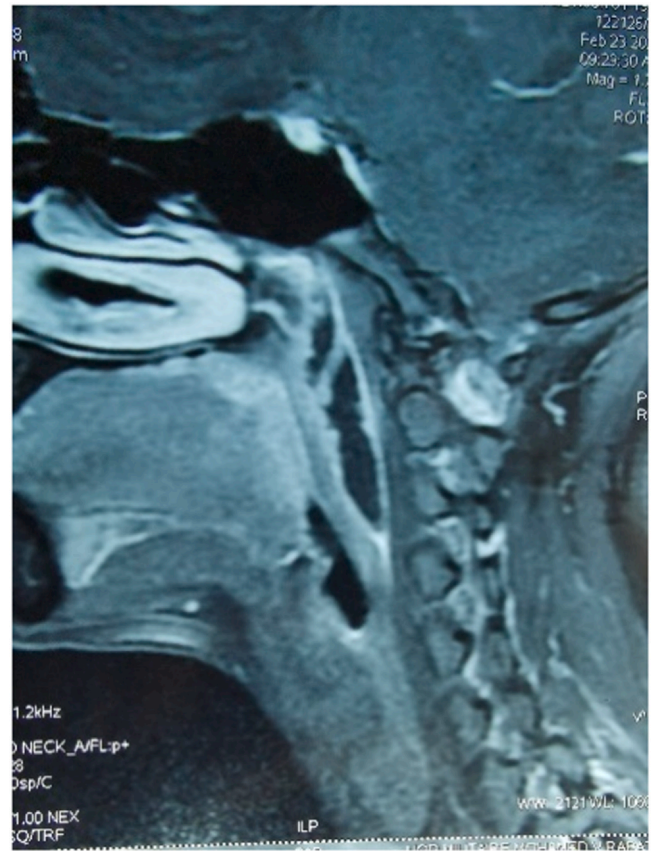


Fig. 2. Sagittal MRI revealed the presence of the retropharyngeal collection.

Direct examination after special Ziehl-Nielsen staining was positive and cultures on Lowenstein-Jensen® (LJ) solid medium and Mycobacteria Growth Indicator Tube (MGIT®) liquid medium were positive after 32 days and 12 days respectively, thus confirming the molecular diagnosis.

A treatment was initiated on the basis of molecular data. The histopathological study confirmed the molecular diagnosis by showing epithelioid and gigantocellular granulomas with caseous necrosis, without histological evidence of malignancy.

Subsequently, the patient was put on a long-term protocol consisting of 6 months of bedaquiline, levofloxacin, linezolid, clofazimine, and cycloserine and 12–14 months of levofloxacin, linezolid, clofazimine, and cycloserine.

After 1 month of treatment, the antibacillary drugs appear to be well tolerated, and the patient is still being monitored.

Discussion

TB remains a major public health problem in the world, mainly affecting developing countries [2]. Its incidence has also increased in developed countries, partly due to co-infection with HIV [2], the latter being more frequent in extra-pulmonary forms [3].

The 2019 WHO report estimates the number of new cases at 10 million and the number of deaths at 1.5 million [4]. TB usually affects the lungs (pulmonary) or sometimes other organs (extrapulmonary). Excluding laryngeal TB, TB of the head and neck is rare and constitutes 2–6% of extrapulmonary TB and 0.1–1% of all forms of TB [5]. Retropharyngeal localization is rare [1].

Infection of the retropharyngeal space and subsequent abscess formation are mainly due to acute bacterial infections of the head and neck region, especially in children, injury to the posterior pharyngeal wall, and forward spread of spinal TB [6].

Spread to the retropharyngeal space occurs via lymphatics involving persistent retropharyngeal nodes or by hematogenous spread from pulmonary or extrapulmonary sites [5]. In our patient, the retropharyngeal abscess was probably due to lymphatic dissemination from lymph node TB because radiological exploration revealed a centimetric adenopathy with a necrotic center adjacent to the retropharyngeal abscess and there was no evidence of any distant involvement that could support hematogenous, pulmonary, or other dissemination. Tuberculous retropharyngeal abscess in an immunocompetent adult is rare [6].

Drug-resistant TB represents a major challenge to national, regional and global TB control programs. Some MDR strains have developed additional resistance mechanisms to second-line antibacterials, namely fluoroquinolones and aminoglycosides [7]. Each year, 500,000 cases of MDR-TB or rifampicin-resistant TB (RR-TB) and nearly 200,000 deaths are reported worldwide.

In 2019, the reported treatment success rate was 56% for MDR and extensively drug-resistant (XDR) TB cases and 39% for XDR-TB [4]. In Morocco, where TB remains endemic, the 2014 National TB Drug Resistance Survey found a low prevalence of MDR/XDR-TB (1% MDR-TB among new cases and 8.7% among previously treated cases) [4].

In 2019, 235 cases of drug-resistant TB were treated in Morocco, and 1500 cumulative cases have been reported since 2012 [4]. MDR extrapulmonary localizations have rarely been described in the literature [3,7,8]. An Indian study published in 2014 reported 3 cases, including 2 lymph node localizations and 1 cervical cold abscess [3].

MDR extrapulmonary forms are more frequent in young female subjects with a history of TB [8]. This is in accordance with our case. Another Moroccan study published in 2018 presented 7 cases of MDR extrapulmonary TB, of which 6 patients had a history of TB and 1 patient had a therapeutic failure [7]. 4 of these 7 patients had additional resistance to second-line anti-TB drugs [7].

The diagnosis of MDR in extrapulmonary forms should be made by tissue or biological fluid sampling, but this is sometimes difficult [3]. Tuberculous retropharyngeal abscess can present with variable manifestations, ranging from asymptomatic to subtle features such as odynophagia alone and neck pain, due to early stage and lesser severity of the disease, to life-threatening respiratory obstruction [6]. Our patient had only chronic headache that can be attributed to her Chiari malformation. In addition, the general condition was preserved. On throat examination, swelling due to tuberculous retropharyngeal abscess is usually located in the midline [6].

Radiologic imaging plays an important role in demonstrating the extent of the abscess and the involvement of surrounding structures [2,5]. CT has an accuracy of 89% and MRI is even more accurate, as it allows for better soft tissue analysis and allows for the assessment of vascular complications, including internal jugular vein thrombosis [2,5]. Both CT and MRI in our patient showed the retropharyngeal abscess.

TB was first diagnosed by direct microscopic examination and the discovery of acid-fast bacilli in the abscess aspirate using Ziehl-Neelsen stain, and then confirmed by culture, which remains the gold standard method [2].

Molecular biology has demonstrated its effectiveness even on pauci-bacillary specimens by allowing the identification and detection of resistance to anti-TB drugs through several studies. GeneXpert MTB/RIF is a rapid, automated, World Health Organization (WHO)-recommended nucleic acid amplification test that is widely used for the simultaneous detection of MTC and rifampicin resistance in pulmonary and extrapulmonary specimens. It has a sensitivity of more than 80% in cerebral spine fluid, pus and biopsy fragments [7]. In our study, GeneXpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) allowed identification of MTC and detection of rifampicin resistance.

In addition to the GeneXpert MTB/RIF, there are the MTBDRplus and MTBDRsl genotype tests which allow the identification of MTC from pulmonary clinical specimens or cultivated samples. The MTBDRplus test is used to identify resistance to rifampicin and isoniazid [7]. The MTBDRsl test is designed to detect resistance to the second-line antibacterial drugs, namely aminoglycosides on the *gyrA* gene, fluoroquinolones on the *rrs* gene, and ethambutol on the *embB* gene [7]. The MTBDRplus test and the MTBDRsl test have a sensitivity greater than 80% for the detection of resistance to rifampicin, isoniazid, fluoroquinolones, and aminoglycosides [7]. The discovery of an additional aminoglycoside resistance makes the choice of treatment even more difficult. These tests have been shown to be effective in detecting resistance to anti-TB drugs from extrapulmonary samples, even though they are not validated on these samples. This has been reported in some studies [9,10].

In our case, the aspiration was positive by GeneXpert MTB/RIF with a detection of rifampicin resistance. The MTBDRplus test confirmed resistance to rifampicin and isoniazid and the MTBDRsl test showed additional resistance to aminoglycosides. Later on, mycobacterial culture on solid and liquid media both became positive after 32 days and 12 days respectively. Pre-ultraresistant TB (pre-XDR TB) is defined as MDR/RR-TB in addition to resistance to any fluoroquinolones (levofloxacin and moxifloxacin).

Antibacterial drug resistance can be primary or secondary, primary drug resistance is defined as resistance in a patient who has never been treated for TB. Treatment with anti-TB drugs exerts selective pressure on the *Mycobacterium tuberculosis* population, resulting in a decrease in susceptible bacilli, an increase in drug-resistant mutants, and the emergence of drug resistance (acquired resistance). Given her previously treated lymph node TB, it seems safe to assume that our patient has acquired drug resistance.

In recent years, significant progress has been made in the rapid diagnosis of TB and drug resistance, as well as in treatment: new drugs, reduction of the age of indication for certain drugs as well as modification of the classification of drugs used to treat MDR-TB.

For MDR-TB of all forms, the WHO recommends a short regimen of 9–11 months, which includes a 4–6 month loading phase with high dose amikacin, moxifloxacin, etonamide, clofazimine, pyrazinamide, ethambutol and high dose of isoniazid. In the maintenance phase, patients are put on moxifloxacin, clofazimine, pyrazinamide and ethambutol [11]. Another recent WHO review in 2020 updated the recommendations eliminating short regimens containing injectables, replacing them with a short regimen containing bedaquiline [4]. Another WHO trial approved by the FDA in 2019 recommends the combination of bedaquiline, linezolid, and pretomanide for ultraresistant TB or XDR-TB for 9 months if the three molecules have not been taken previously [4,11].

In Morocco, the short regimen has been adapted for some cases, but the old long regimen is still widely prescribed. This long regimen is based on 6 months of initial treatment with bedaquiline combined with levofloxacin, linezolid, clofazimine and cycloserine, followed by cessation of bedaquiline and maintenance of the remainder for 12–14 months if there is no resistance to group A and B molecules [4]. Our patient was put on a standard regimen by replacing aminoglycosides with bedaquiline. The simultaneous medical and surgical approach seems to be the best strategy for the management of tuberculous retropharyngeal abscess [3,5].

As with any abscess, the mainstay of management of retropharyngeal tubercular abscess is drainage of the pus. Therapeutic aspiration only has been used successfully and can be repeated if necessary [2]. Anti-TB drug therapy and conservative neck stabilization should be the initial treatment if a retropharyngeal abscess is due to an extension from cervical spine TB, with a stable spine and without any neurological deficit or with minimal neurological signs [6]. If left untreated, internal jugular vein thrombosis, mediastinitis and airway obstruction are potential complications [1,2].

Clinical, bacteriological and radiological surveillance is recommended, as well as monitoring of treatment tolerance [7,11]. The prognosis of MDR pulmonary and extrapulmonary TB has been improved thanks in part to the prescription of new anti-TB drugs such as linezolid and bedaquiline. The success of the treatment is related to the number of effective molecules still available [7]. However, high mortality has been observed in patients with XDR-TB and HIV infection. This could be explained by its synergistic relationship with TB and the emergence of MDR and XDR strains [7]. The HIV serology of our patient is negative which could further improve the prognosis of her disease.

Conclusion

Retropharyngeal abscess is a recognized but rare presentation of TB. Unspecified symptoms and unusual location often lead to delayed diagnosis and treatment. Through this case, we highlight the importance of gene amplification tests in the effective and rapid management of this disease.

Author contributions

OS, TN and BE have been involved in drafting the manuscript, BF, BY, CM, AM have revising the manuscript and ELM have given final approval of the version to be published.

Author statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the IDCases journal.

Competing interest

The authors declare no competing interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.idcr.2021.e01282](https://doi.org/10.1016/j.idcr.2021.e01282).

References

- [1] Kosmidou P, Kosmidou A, Angelis S, Dimitriadou PP, Filippou D. Atypical retropharyngeal abscess of tuberculosis: diagnostic reasoning, management, and treatment. *Cureus* 2020. <https://doi.org/10.7759/cureus.9124>
- [2] Menon E, Baruah P. Tuberculous retropharyngeal abscess revisited. *BMJ Case Rep* 2014;2014. <https://doi.org/10.1136/bcr-2013-202514>
- [3] Mittal N, Bansal P. Multidrug resistant extrapulmonary tuberculosis – three case reports and review of literature. *Intern Med* 2014;2:2. <https://doi.org/10.7243/2052-6954-2-2>
- [4] World Health Organization. *WHO consolidated guidelines on drug-resistant tuberculosis treatment*. Geneva: World Health Organization; 2019.
- [5] Desai L, Shah I, Shaan M. Retropharyngeal abscess as a paradoxical reaction in a child with multi-drug-resistant tuberculosis. *Paediatr Int Child Health* 2019;39:287–9. <https://doi.org/10.1080/20469047.2018.1518054>
- [6] Sinha S, Ekka M. Retropharyngeal abscess as a rare presentation of pulmonary tuberculosis. *Lung India* 2015;32:262–4. <https://doi.org/10.4103/0970-2113.156247>
- [7] Haddaoui H, Mrabet FZ, Aharmim M, Bourkadi J-E. Tuberculose extrapulmonaire multi résistante: à propos de 7 cas. *Pan Afr Med J* 2019;32. <https://doi.org/10.11604/pamj.2019.32.196.17995>
- [8] Mok J, Kang BH, Kim HJ, Lee SJ, Lee T, Lee HK, et al. Drug resistance in extrapulmonary tuberculosis in South Korea: comparison with pulmonary tuberculosis. *Int J Tube Lung Dis* 2019;23(2):151–6. <https://doi.org/10.5588/ijtld.18.0109>
- [9] Mechal Y, Benaissa E, El Mrimar N, Benlahlou Y, Bssaibis F, Zegmout A, et al. Evaluation of GeneXpert MTB/RIF system performances in the diagnosis of extrapulmonary tuberculosis. *BMC Infect Dis* 2019;19(1):1069. <https://doi.org/10.1186/s12879-019-4687-7>. PMID: 31856744; PMCID: PMC6924055.
- [10] Rahman A, Sahrin M, Afrin S, Earley K, Ahmed S, Rahman SM, et al. Comparison of Xpert MTB/RIF assay and GenoType MTBDRplus DNA probes for detection of mutations associated with rifampicin resistance in mycobacterium tuberculosis. *PLoS One* 2016;11(4):0152694. <https://doi.org/10.1371/journal.pone.0152694>
- [11] Migliori GB, Tiberi S, Zumla A, Petersen E, Chakaya JM, Wejse C, et al. MDR/XDR-TB management of patients and contacts: challenges facing the new decade. The 2020 clinical update by the Global Tuberculosis Network. *Int J Infect Dis* 2020;92:S15–25. <https://doi.org/10.1016/j.ijid.2020.01.042>