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Combating drug-resistant tuberculosis: A case study of successful treatment and the importance of adherence

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Abstract
This case study presents a 23-year-old female with cervical lymphadenopathy, initially treated with anti-tuberculosis medication. Subsequent histopathological and molecular testing confirmed multidrug-resistant tuberculosis (MDR-TB) with rifampicin and isoniazid resistance, as well as resistance to fluoroquinolones, indicating extensive drug-resistant tuberculosis (XDR-TB). The patient responded well to a tailored treatment regimen consisting of Bedaquiline, moxifloxacin, linezolid, clofazimine, and cycloserine, with regression of all lymph nodes observed on ultrasound monitoring. The case underscores the importance of comprehensive diagnostics, individualized treatment, and close monitoring in managing drug-resistant tuberculosis effectively. It emphasizes the need for early detection, appropriate treatment, and patient adherence to combat drug-resistant TB and improve outcomes.

Keywords: Cervical lymphadenopathy, drug resistance

Introduction

Tuberculosis causative agent is discovered by Sir Robert Koch in 1882, it is an airborne infectious disease caused by Mycobacterium tuberculosis complex organism. TB continues to be a major cause of morbidity and mortality, primarily in low-income and middle-income countries [1]. The two types of clinical manifestation of tuberculosis (TB) are pulmonary TB (PTB) and extrapulmonary TB (EPTB). The former is most common. EPTB refers to TB involving organs other than the lungs (e.g., pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, or meninges [2].

Patients with tuberculosis (TB) are classified as either having latent TB infection (LTBI), which is an asymptomatic and non-transmissible condition, useful in clinical and health point of view or active TB disease, which is transmissible in the case of active pulmonary TB. Diagnostic methods such as culture-based or molecular techniques are employed for confirmation. Individuals with active TB may exhibit general symptoms like fever, fatigue, decreased appetite, and weight loss. Those with pulmonary involvement might manifest a persistent cough and hemoptysis in advanced stages. However, some as having subclinical TB [3, 4].

Mycobacterial lymphadenitis, known historically as "scrofula" or "King's evil," has afflicted humanity for centuries. Since ancient times, mycobacterial lymphadenitis, also referred to as "scrofula" or "King's evil," has been a persistent issue. "Scrofula," an ancient term denoting mycobacterial lymphadenitis, has been synonymous with glandular swelling and "King's evil" throughout history. Throughout history, mycobacterial lymphadenitis, often termed "scrofula" or "King's evil," has been a common affliction characterized by glandular swelling [5, 6, 7].

Mycobacterial lymphadenitis exhibits significant geographic diversity. In less developed nations, tuberculosis lymphadenitis remains prevalent, while non-tuberculous mycobacterial lymphadenitis is rare. Multiple research studies in India have consistently identified Mycobacterium tuberculosis as the predominant pathogen responsible for mycobacterial lymphadenitis, comprising nearly all reported cases [7, 8, 9, 10].

In a survey conducted door-to-door within a population of 23,229 residing in 35 adjacent villages in the rural area of Wardha district, Maharashtra State, Central India, spanning from May 1993 to May 1994 and from March 1995 to February 1996, it was documented that the occurrence of lymph node tuberculosis was recorded at a rate of 4.43 per 1000 children [11, 12].

Pathogenesis of Tuberculosis lymphadenopathy: "Mycobacterium tuberculosis typically enters the body through the respiratory tract and spreads via hematogenous and lymphatic routes. The initial lymphoid tissues encountered during this spread from the lung parenchyma are the hilar and mediastinal lymph nodes. This dissemination can happen during primary infection or later in life due to reactivation of latent infection. Additionally, the tonsils serve as another significant entry point. From there, the infection can progress through the lymphatic system to the nearest cervical lymph nodes [13].

In the early stages, the affected lymph nodes may appear discrete clinically. However, Periadenitis can lead to the clustering and immobility of the lymph nodes. Eventually, these nodes merge and deteriorate, forming caseous pus. This pus may breach the deep fascia, resulting in a swollen area on the skin surface known as a collar-stud abscess. The skin above this area becomes hardened, breaks down, and forms a sinus. If left untreated, this sinus may persist for years without healing. Healing can occur at any of the three stages, often resulting in calcification or scarring [13]."

Differential Diagnosis of lymphadenopathy: Peripheral lymphadenopathy can arise from various causes, such as reactive lymphadenitis due to viral or bacterial infections, tuberculosis, lymphoma, sarcoidosis, secondary carcinoma, and less common factors like fungal infections, toxoplasmosis, and diseases affecting the reticuloendothelial system. Features aiding in the diagnosis of TB lymphadenitis include multiplicity, matting, and caseation. In lymphoma patients, lymph nodes typically feel rubbery and are not matted. Conversely, in cases of secondary deposits in lymph nodes, often from a primary source in the drainage area, the nodes tend to be hard and may be adherent to surrounding structures [13]."

Treatment: Presently, it is generally agreed that anti-TB treatment alone is sufficient for majority of the cases and surgical intervention is required only in selected cases for specific situations. In India, patients with lymph node TB receive daily treatment.

"Some patients with tuberculosis affecting the lymph nodes may necessitate extended treatment periods. Although the response to tuberculosis treatment might be slower in cases of lymph node tuberculosis, it is customary for medical practitioners and surgeons to diagnose these patients with multidrug-resistant tuberculosis (MDR-TB) lymphadenitis prematurely. However, it's crucial to recognize that MDR-TB is a diagnosis made through laboratory testing, wherein the bacteria must be cultivated and shown to resist rifampicin and isoniazid *in vitro*. Given that lymphadenitis typically involves low levels of bacteria, cultivating Mycobacterium tuberculosis in cultures can be challenging in many cases. Hence, the designation of MDR-TB lymphadenitis should be applied cautiously. Whenever feasible, initial phenotypic and genotypic drug susceptibility testing (DST) should be conducted on the lymph node tissue [13]."

Studies have demonstrated that lymph nodes can increase in size during treatment for tuberculosis (TB), or new nodes may emerge during or after treatment. The emergence of new lymph node enlargement during treatment may indicate an immunological response, often referred to as the "paradoxical reaction." This reaction is typically temporary, and the nodes generally diminish in size over time [14].

Case Study: It is an Observation Retrospective Case Study

23years old female presents with swelling on Right side of neck. Multiple enlarged, matted, painless lymph nodes. Patient gives history of swelling 3 years back and taken AKT for 1 year. After biopsy histopathological report shows Granuloma with caseating in the middle, GenXpert test done on specimen shows MTB detected with Rifampicin resistance, LPA 1st line shows MTB detected with Rifampicin and Isoniazid resistance, LPA 2nd line shows resistance to Fluoroquinolones drugs and Resistance not detected with Second line injectable. She was started on All oral longer regime BDQ Mfx(h) Lnz Cs and Cfx, Bedaquiline (BDQ), moxifloxacin (Mfx), linezolid (Lnz), clofazimine (Cs), and cycloserine (Cfx). patient responded to treatment and treatment was completed in 18 months USG neck shows regression of all lymph nodes. Patient's AKT was stopped after giving her 3 months extension.

Discussion

The case presents a 23-year-old female with a history of neck swelling and painless enlarged lymph nodes, initially treated with AKT (anti-tuberculosis treatment) due to suspicion of tuberculosis (TB). Histopathological examination of a lymph node biopsy revealed granulomas with caseation, a hallmark of TB infection. Further testing using the GeneXpert assay confirmed the presence of Mycobacterium tuberculosis (MTB) with rifampicin resistance, indicating multidrug-resistant tuberculosis (MDR-TB).

Subsequent testing with line probe assay (LPA) revealed resistance not only to rifampicin and isoniazid (first-line drugs) but also to fluoroquinolones (second-line drugs), while resistance was not detected for second-line injectables. This pattern suggests extensive drug-resistant tuberculosis (XDR-TB), which is resistant to both first- and second-line anti-TB drugs except for a few.

Given the complexity of drug resistance, the patient was started on a longer regimen consisting of all oral drugs: Bedaquiline (BDQ), moxifloxacin (Mfx), linezolid (Lnz), clofazimine (Cs), and cycloserine (Cfx). This regimen is tailored for cases of MDR-TB and XDR-TB and typically involves a combination of newer drugs to which the bacteria may still be susceptible.

The treatment duration extended to 18 months, longer than the standard TB treatment duration, reflecting the challenges posed by drug resistance. Monitoring via ultrasound (USG) showed regression of all lymph nodes, indicating a favorable response to treatment.

Overall, this case underscores the importance of thorough diagnostic evaluation, including histopathological and molecular testing, in suspected cases of drug-resistant TB. It also highlights the need for individualized treatment regimens involving newer drugs to effectively manage MDR-TB and XDR-TB cases. Regular monitoring is crucial to assess treatment response and adjust therapy as needed.

Conclusion

The conclusion of the case study highlights the successful management of a young female patient with multidrug-resistant tuberculosis (MDR-TB) and extensive drug-resistant tuberculosis (XDR-TB). Through a comprehensive diagnostic approach involving histopathological examination and molecular testing, the patient's drug resistance profile was accurately identified. This facilitated the initiation of a tailored treatment regimen consisting of newer oral drugs.

The patient's positive response to treatment, as evidenced by the regression of all lymph nodes on ultrasound monitoring, demonstrates the efficacy of the chosen regimen. The case underscores the importance of personalized treatment strategies and the utilization of newer anti-TB drugs in combating drug-resistant forms of tuberculosis.

Additionally, the successful outcome emphasizes the significance of close monitoring and prolonged treatment duration in managing complex cases of MDR-TB and XDR-TB. Overall, the case serves as a testament to the importance of early detection, appropriate treatment selection, and diligent follow-up in achieving favorable outcomes in drug-resistant tuberculosis patients.

Summary

Summary: A 23-year-old female presented with swelling on the right side of her neck and painless enlarged lymph nodes.

History revealed a previous episode of swelling, for which she underwent anti-tuberculosis treatment (AKT) for a year.
Biopsy showed granulomas with caseation, indicative of tuberculosis (TB), confirmed by GeneXpert test revealing Mycobacterium tuberculosis (MTB) with rifampicin resistance.
Line probe assay (LPA) revealed resistance to rifampicin, isoniazid, and fluoroquinolones, suggesting multidrug-resistant tuberculosis (MDR-TB) and extensive drug-resistant tuberculosis (XDR-TB).
Treatment included a longer regimen of all oral drugs: Bedaquiline, moxifloxacin, linezolid, clofazimine, and cycloserine.
Treatment duration extended to 18 months, with ultrasound showing regression of all lymph nodes, indicating a positive response.
The case highlights the importance of comprehensive diagnostics, individualized treatment, and close monitoring in managing drug-resistant TB effectively.

Message

Social Message: This case highlights the critical importance of early detection, appropriate treatment, and patient adherence in combating drug-resistant tuberculosis (TB). By effectively managing the disease with a tailored treatment regimen and ensuring patient compliance, we can prevent its spread and improve individual outcomes. Increased awareness and access to comprehensive TB care are essential in addressing this global health challenge.

Clinical Message: The presented case underscores the significance of a comprehensive diagnostic approach, including histopathological examination and molecular testing, in identifying drug-resistant TB. Tailoring treatment regimens based on drug susceptibility testing results, such as utilizing all oral longer regimes, can lead to successful outcomes, as evidenced by the regression of lymph nodes observed in this patient. Clinicians should remain vigilant for TB recurrence and monitor patient response closely throughout the treatment course.

Prospective Message: Moving forward, further research into novel TB treatment strategies and improved diagnostic tools is imperative to effectively combat drug-resistant TB. Additionally, efforts should be directed towards enhancing public health initiatives aimed at early detection, treatment adherence, and reducing TB stigma. By addressing these challenges comprehensively, we can work towards achieving better outcomes for TB patients and ultimately reducing the global burden of this disease.

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