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Navigating complexity: Disseminated tuberculosis in an immunocompromised female patient

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Abstract
Disseminated tuberculosis (TB) poses a significant challenge in diagnosis and management, particularly in immunocompromised individuals. This case study presents a 45-year-old immunocompromised female patient with no prior TB history, exhibiting constitutional symptoms, chest wall lesion, and lymphadenopathy. Diagnostic evaluations confirmed disseminated TB with multisystem involvement, exacerbated by concurrent hepatitis B infection. Treatment involved a tailored multidrug regimen, emphasizing the importance of prompt diagnosis and comprehensive care in such cases. This study underscores the complexities of disseminated TB and highlights the need for heightened awareness, early detection, and multidisciplinary management to optimize outcomes, especially in vulnerable populations. Efforts toward TB prevention, improved diagnostics, and enhanced healthcare infrastructure are essential to address the global TB burden effectively.

Keywords: Disseminated TB, miliary TB, TB in immunocompromised

Introduction

TB remains a significant global health challenge. According to the World Health Organization (WHO) Global Tuberculosis Report 2022, there were an estimated 10.4 million new TB cases worldwide in 2020, resulting in 1.67 million TB-related deaths [1]. India plays a crucial role in the TB burden. It accounts for more than one-quarter of the global TB burden, with an estimated 2.7 million new TB cases and over 400,000 TB-related deaths in 2017 [2].

Disseminated TB is a life-threatening condition, especially if the diagnosis and treatment are delayed [3]. The diagnosis is difficult because of its nonspecific clinical picture and the paucity of tools available for confirmatory laboratory diagnosis, such as low sensitivity of acid-fast bacilli (AFB) smear, time-consuming cultures, and the inability to easily detect Miliary changes in chest X-ray.

Disseminated tuberculosis (TB) is defined as the presence of two or more noncontiguous sites resulting from hematogenous dissemination of Mycobacterium tuberculosis, occurring as a result of progressive primary infection, reactivation of a latent focus with subsequent spread [3], "Miliary TB, also known as disseminated tuberculosis, involves the widespread dissemination of the disease throughout the body via the bloodstream, even in the absence of typical pathological or radiological indicators [3, 4]."

The diagnosis is difficult because of its nonspecific clinical picture and the paucity of tools available for confirmatory laboratory diagnosis, such as low sensitivity of acid-fast bacilli (AFB) smear, time-consuming cultures, and the inability to easily detect Miliary changes in chest X-ray [3].

Miliary and disseminated TB continue to be a diagnostic problem even in areas endemic to TB, where clinical suspicion is very high. Mortality from MTB disease has remained high despite effective therapy being available. In patients with human immunodeficiency virus [HIV] infection acquired immunodeficiency syndrome [AIDS] DTB and MTB are particularly common [3, 5].

Pathology, Pathophysiology, and Pathogenesis of disseminated tuberculosis in a patient who is Hepatitis B positive.

Pathology: Disseminated tuberculosis, also known as Miliary tuberculosis, occurs when Mycobacterium tuberculosis (the bacterium causing TB) spreads throughout the body via the bloodstream. Tiny tubercle bacilli enter the bloodstream and are carried to various organs, where they multiply and cause widespread infection. Clinical manifestations are nonspecific and can vary depending on the predominant site of involvement. Common symptoms include fever, night sweats, anorexia, and weight loss. Physical findings may include hepatomegaly (enlarged liver), splenomegaly (enlarged spleen), and lymphadenopathy (swollen lymph nodes) [7]

Pathophysiology: The pathophysiology of disseminated TB involves the following steps: Hematogenous spread: Tubercle bacilli enter the bloodstream from the primary site of infection (usually the lungs) Systemic dissemination: The bacilli are carried to distant organs, including the liver, spleen, bone marrow, and lymph nodes. Inflammatory response: The immune system responds by activating macrophages and other immune cells to contain the infection. Granuloma formation: Granulomas (small nodules) form around the infected areas, attempting to wall off the bacilli. Caseous necrosis.: Within granulomas, central areas undergo caseous necrosis (a type of tissue death). Spread to other organs: The bacilli continue to multiply and spread, leading to widespread organ involvement [6].

Pathogenesis: The pathogenesis of disseminated TB involves the following key factors: Immunosuppression: Patients with conditions like HIV/AIDS or Hepatitis B are at higher risk due to compromised immune responses. Bacteremia: Tubercle bacilli enter the bloodstream, leading to systemic infection. Organ-specific manifestations: The bacilli can affect various organs, causing specific symptoms

and complications. Severity: Disseminated TB can be severe and life-threatening if not promptly diagnosed and treated. Treatment: Antitubercular medications are essential to control the infection and prevent further dissemination [8].

Epidemiology

Miliary TB accounts for less than 2% of all cases of TB and up to 20% of all TB cases in various clinical studies in immunocompetent individuals; the corresponding figures in autopsy studies have been higher. Caution must be exercised while comparing these epidemiological data as these studies are hospital based or autopsy studies.

The emergence of the HIV/AIDS pandemic and widespread use of immunosuppressive drugs have changed the epidemiology of MTB. Since its first description by John Jacob Manget, the clinical presentation of MTB has changed dramatically. Especially its occurrence as a complication of childhood infection is diminishing and the "cryptic form" in a much older group is emerging [37-39]. The modulating effect of Bacilli Calmette-Guerin [BCG] vaccination resulting in substantial reduction in MTB and TB meningitis among young vaccinees, increasing use of computed tomography [CT], and wider application of invasive diagnostic methods could also have contributed to the demographic shift [4].

Clinical Manifestation

The clinical manifestation of Disseminated tuberculosis can manifest with diverse symptoms, typically featuring prolonged or gradual onset constitutional signs like fever, loss of weight, and nocturnal perspiration. Additionally, presentations may span from reduced appetite and unexplained fever to even systemic organ dysfunction indicative of the affected organ's involvement [3].

The duration of symptoms before the diagnosis is variable. Patients may experience progressive symptoms and signs over days to weeks or occasionally over several months. Therefore, the diagnosis of this disease is generally difficult and more than 50% of patients usually delay in seeking medical help for >1 month [9]. Adults more commonly have symptoms and signs of anorexia, fatigue, dyspnea, night sweats, fever, abdominal pain, hemoptysis, headache, mental changes, pleural effusion, ascites, and lymphadenopathy than child patients, whereas diarrhea, vomiting, seizures, hepatomegaly, splenomegaly, jaundice, and meningism are more common in children.

Investigations

Abnormal results of several investigations have been described, most of which are diagnostically insignificant as they provide nonspecific results.

Laboratory workup

Hematological abnormalities include anemia of different types, pancytopenia, and leukopenia mainly lymphopenia, leukemoid reaction, high Erythrocyte sedimentation rate, dissemination intravascular coagulation, and rarely myelofibrosis [1, 10]. Abnormal liver function tests usually with moderate elevations in transaminases, alkaline phosphatase, and bilirubin

Imaging modalities

Imaging studies alone are insufficient for the making of a conclusive diagnosis as they lack sensitivity and specificity. However, they are important adjuncts in the diagnostic evaluation of disseminated TB as they can help determine the sites involved and guide technicians to obtain appropriate specimens for diagnosis [11].

Chest radiograph

Chest radiography is usually the initial and most cost-effective tool, which plays an important role in the early diagnosis of disseminated TB. The classic Miliary pattern is seen in 85%–90% of cases. However, these findings are not specific for disseminated TB as they can be mimicked by histoplasmosis, sarcoidosis, pneumoconiosis, metastasis, bronchoalveolar carcinoma, and pulmonary siderosis [12, 13].

High-resolution computed tomography

High-resolution computed tomography (CT) may show findings not visible on chest X-rays such as Miliary nodules, ground-glass opacities, and interlobular septal thickening [13].

Pulmonary Functions, Gas Exchange Abnormalities

Miliary TB is associated with abnormalities of pulmonary functions typical of diffuse interstitial disease of the lungs [14]. The impairment of diffusion has been the most frequent and severe abnormality encountered [14]. Sharma *et al* [97] studied the pulmonary functions [n = 31] and gas exchange abnormalities on arterial blood gas analysis [n = 13] in patients with MTB. They found a mild restrictive ventilatory defect, impairment of diffusing capacity and hypoxemia due to widening of alveolar arterial oxygen gradient. A mild reduction in the flow rates suggestive of peripheral airways involvement was also observed.

Treatment

Untreated, DTB/MTB is uniformly fatal within one year [15, 16]. Delay in confirmation of the diagnosis often leads to delay in the institution of specific anti-TB treatment and significantly contributes to the mortality. A high clinical suspicion and efforts towards confirming the diagnosis by demonstrating Mycobacterium TB early in the disease are imperative.

There is no consensus regarding the optimum duration of treatment in patients with DTB/MTB [Table 29. [15, 16, 17]. According to the World Health Organization [WHO] guidelines [15] patients with MTB receive six months of standard antiTB treatment. The WHO guidelines [15] mention that some experts recommend 9-12 months of treatment for TB meningitis and indicate 9 months of treatment when bone and joint TB is also present.

Complications and Prognosis: Disseminated tuberculosis (TB) occurs when the bacteria spread beyond the lungs to other parts of the body. Complications can vary depending on the organs affected. They may include meningitis, bone and joint infections, abdominal TB, and TB in the lymph nodes, among others. Prognosis can be serious, especially if not promptly treated, but early detection and appropriate treatment can significantly improve outcomes.

Observational and Retrospective type of Case Study

Case Study

Age 45 years, Female, Diagnosis: PTB with EPTB disseminated Kochs. Patient has no history of PTB, No history of TB contact. Pt c/o weight loss, loss of appetite, dyspnea on exertion and fever, consulted a Private doctor

who on examination found chest wall lesion and left supraclavicular lymph node.

On examination: Left chest wall lesion 2.5× 2.5 cm for 8 months, ulcerative lesion, scar +, left axillary lymph nodes 3×3 cm, left supraclavicular 1.5× 1 cm, multiple other cervical nodes both right and left supraclavicular region. Left chest wall lesion biopsy sent, Supraclavicular LN biopsy histopathology and GeneXpert sent.

Biopsy report: Nature of Material: Edge web biopsy from chest wall lesion

Clinical Details: 47 years-female presented with chest wall lesion for 8 months

Macroscopic Appearance: Received multiple grey-white soft tissue measuring 0.6x0.3x0.3 cm, entire soft tissue submitted in one paraffin

Specimen Type: Biopsy from chest wall lesion

Microscopic Appearance: The section studied shows vascularized fibro collagenous tissue with dense inflammatory granulation issue comprising of mixed inflammatory infiltrate predominantly lymphocytes and plasma cells, Foci of ill-formed 7.00PM epithelloid cell granuloma with multinucleated giant cells. No necrosis was seen. No atypical large mononucleus cells were seen. Negative for metastases/malignancy. Special stains for AFB, PAS and GMS do not highlight any micro-organisms.

Impression: Edge web biopsy from chest wall lesion: Chronic granulomatous inflammation. Negative for malignancy.
Blood reports dated have Australia Antigen (HBsAg) Reactive.

Urine Routine and Microscopic: Urine albumin ++, occult blood ++, epithelial cells ++, Pus cells ++ Urine ketones fasting absent

Histopathology Report: Specimen: Left Supraclavicular Lymph Node

Gross Examination: Received two grey white tissue bits aggregating to 1 x 0.5 x 0.4 cm. Submitted entirely.

Microscopic Examination

- Necrotizing granulomatous inflammation of mycobacterial etiology.
- Z-N stain has revealed acid fast bacilli.
- GeneXpert MTB RIF Ultra report dated 21/02/24 shows MTB detected low, Rifampicin sensitive.
- CT findings show.
- -Innumerable randomly distributed nodules scattered in bilateral lung parenchyma of them are coalescing to form denser nodules.
- -Well defined heterogenous enhancing soft tissue noted in the right paravertebral region causing erosion of adjacent fourth rib.
- -Necrotic cervical, mediastinal, abdominal and bilateral axillary lymphadenopathy.
- Visualized sections of the abdomen reveals infective granulomas in the liver as well as spleen.
- There is ill-defined heterogeneously enhancing soft tissue noted involving the left sternoclavicular joint and bilateral sternocostal joints causing underlying bony erosions
- of the medial end of left clavicle. Superior end of the sternum and adjacent ribs. There is peripherally enhancing collection noted in this region which is reaching up to the skin surface and measures 2 cm in maximum thickness.
- -Above findings are suggestive of disseminated Koch's.

Discussion

The presented case depicts a challenging scenario of disseminated tuberculosis (TB) in an immunocompromised female patient with no previous history of TB or known TB contact. Disseminated TB refers to the spread of Mycobacterium tuberculosis (MTB) beyond the lungs to involve multiple organs, leading to systemic symptoms and complications.

Key findings in this case include

Clinical Presentation: The patient presented with constitutional symptoms such as weight loss, loss of appetite, dyspnea on exertion, and fever. Additionally, the presence of a chest wall lesion and left supraclavicular lymphadenopathy raised suspicion for disseminated TB.

Biopsy Results: Histopathological examination of the chest wall lesion revealed chronic granulomatous inflammation without evidence of malignancy. Similarly, the supraclavicular lymph node biopsy showed necrotizing granulomatous inflammation of mycobacterial etiology, with acid-fast bacilli detected on Ziehl-Neelsen (Z-N) stain.

Diagnostic Tests: GeneXpert MTB RIF Ultra report confirmed MTB detection with rifampicin sensitivity, supporting the diagnosis of TB. Additionally, CT findings demonstrated extensive involvement, including pulmonary nodules, soft tissue lesions with bony erosions, and lymphadenopathy in various regions.

Laboratory Findings: Blood reports revealed positivity for Australia Antigen (HBsAg), indicating concurrent hepatitis B infection. Urine analysis showed abnormalities suggestive of renal involvement, which can occur in disseminated TB.

Immunocompromised State: The patient's immunocompromised state, likely due to factors such as age and underlying conditions, contributed to the dissemination of TB and increased susceptibility to opportunistic infections like hepatitis B.

Multisystem Involvement: Disseminated TB manifested with involvement of multiple organ systems, including the lungs, lymph nodes, liver, spleen, and bones. This widespread dissemination underscores the severity of the disease and the need for prompt diagnosis and management.

Treatment Implications: Given the disseminated nature of the disease and the patient's immunocompromised status, treatment should involve a multidrug regimen tailored to TB sensitivity patterns, with close monitoring for treatment response and potential drug interactions.

In short, this case highlights the challenges in diagnosing and managing disseminated TB, particularly in immunocompromised individuals. A comprehensive approach involving clinical evaluation, diagnostic tests, and multidisciplinary care is essential for achieving optimal outcomes in such cases

Conclusion

In conclusion, the presented case underscores the complexity and severity of disseminated tuberculosis (TB) in an immunocompromised female patient with no prior history of TB or known TB contact. The patient's clinical presentation, including constitutional symptoms, chest wall lesion, and lymphadenopathy, prompted investigation leading to the diagnosis of disseminated TB.

Histopathological examination and diagnostic tests confirmed the presence of Mycobacterium tuberculosis, with multisystem involvement evident on imaging studies. The patient's immunocompromised state, likely influenced by age and concurrent hepatitis B infection, contributed to the dissemination and severity of TB.

This case emphasizes the importance of a thorough clinical evaluation, including consideration of TB in the differential diagnosis of systemic symptoms, especially in immunocompromised individuals. Prompt diagnosis and initiation of appropriate multidrug TB treatment are crucial for preventing disease progression and complications in such cases.

Moving forward, close monitoring of treatment response, management of comorbidities, and multidisciplinary care are essential for optimizing outcomes and preventing disease recurrence in immunocompromised patients with disseminated TB. Additionally, efforts to address underlying immunocompromising conditions and promote TB prevention strategies remain imperative in managing similar cases in the future.

Summary

This case study describes a 45-year-old immunocompromised female patient presenting with constitutional symptoms, chest wall lesion, and lymphadenopathy. Despite no history of tuberculosis (TB) or known TB contact, diagnostic evaluations including histopathology, genexpert testing, and imaging confirmed disseminated TB with multisystem involvement.

The patient's immunocompromised state, likely influenced by age and concurrent hepatitis B infection, contributed to the severity and dissemination of TB. Treatment involved a multidrug regimen tailored to TB sensitivity patterns, with close monitoring for treatment response and potential drug interactions.

In conclusion, this case highlights the challenges in diagnosing and managing disseminated TB in immunocompromised individuals. A comprehensive approach involving clinical evaluation, diagnostic tests, and multidisciplinary care is essential for achieving optimal outcomes in such cases.

Message

Social Message: It is crucial to raise awareness about tuberculosis (TB) and its impact on vulnerable populations, including immunocompromised individuals. Communities should be educated about TB transmission, prevention, and the importance of seeking timely medical care. Support systems and resources should be made available to help individuals navigate the challenges of TB diagnosis and treatment, especially in marginalized or underserved populations.

Clinical Message: Healthcare providers need to maintain a high index of suspicion for TB, particularly in immunocompromised patients presenting with nonspecific symptoms or unusual clinical manifestations. Comprehensive evaluation, including appropriate diagnostic tests and imaging studies, should be conducted promptly to facilitate early diagnosis and initiation of appropriate treatment. Close monitoring and multidisciplinary management are essential to address the complexities of disseminated TB and associated comorbidities.

Prospective/Way Forward: To combat the burden of TB, efforts should focus on strengthening healthcare systems to improve access to diagnostic tools, medications, and specialized care for TB patients, especially those who are immunocompromised. Research and development initiatives should continue to advance TB diagnostics, therapeutics, and vaccines. Additionally, collaborative efforts involving healthcare providers, policymakers, and community stakeholders are essential to implement comprehensive TB control strategies and achieve the goal of TB elimination.

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