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"DIAGNOSTIC CHALLENGES IN A YOUNG FEMALE: MILIARY TUBERCULOSIS WITH CYSTIC LUNG CHANGES AND PNEUMOTHORAX"

Respiratory Medicine

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KEYWORDS

CASE REPORT:
The patient, a 25-year-old female with an unremarkable medical history, presented to KIMS hospital complaining of fever, night sweats, weight loss, and a non-productive cough persisting for a month. Following initial evaluations including clinical assessment, hematological tests, and radiological examinations, a diagnosis of military tuberculosis (TB) affecting the lungs was made, prompting initiation of anti-tubercular treatment (ATT). However, subsequent follow-up revealed non-response to treatment, accompanied by the development of cystic changes in the lung and pneumothorax. Further diagnostic exploration ensued, including consideration of alternative diagnoses such as lymphangioleiomyomatosis (LAM), ultimately leading to a conclusive diagnosis of granulomatous inflammation likely due to tuberculosis. Treatment was adjusted accordingly, leading to symptomatic relief and eventual discharge.

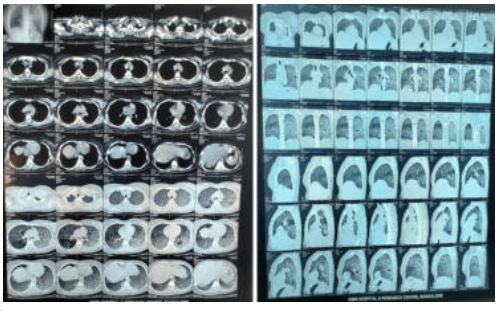
Demographic Data:
The patient, identified as XYZ, a 26-year-old female homemaker residing in Bangalore, presented on 11/03/2023, with readmission occurring on 12/05/2023. Her presenting symptoms and subsequent medical history were meticulously recorded, providing crucial insights into her condition.

Chief Complaints:
The patient's complaints were consistent with a deteriorating respiratory condition, including worsening dyspnea, persistent cough with expectoration, and right-sided chest pain. Furthermore, she reported recurrent pneumothorax over the past three months, alongside weight loss and dyspnea on exertion.

History:
The patient's medical journey began with symptoms of fever, night sweats, and weight loss leading to her initial admission to the Respiratory Intensive Care Unit (RICU). Radiological investigations, including CT scans, revealed findings indicative of miliary tuberculosis with concurrent minimal right pneumothorax, prompting the initiation of ATT. However, subsequent clinical deterioration and pneumothorax recurrence raised concerns regarding treatment efficacy and led to further diagnostic exploration.

Radiology - CXR:
The chest X-ray (CXR) revealed diffuse bilateral micro nodular opacities consistent with a miliary pattern, suggesting hematogenous dissemination of an infectious or neoplastic process. The distribution and characteristics of these nodules aligned with the clinical suspicion of tuberculosis, prompting further investigation and treatment initiation. The frontal radiograph demonstrated diffuse bilateral micro nodular opacities, indicative of a miliary pattern resulting from hematogenous dissemination. This pattern typically arises from infectious or neoplastic processes, with tuberculosis being a primary consideration based on the patient's risk factors. Additionally, the CXR showed a random distribution of pulmonary micro nodules, further supporting the diagnosis of miliary tuberculosis.

CT Findings:
Computed tomography (CT) scans highlighted extensive cystic changes in the lungs, particularly notable in the right upper lobe and left lower lobe, along with miliary nodules scattered throughout the lung fields. These cystic changes were observed in all segments of the right upper lobe and apical segments of the left lower lobe. A subpleural large cyst was also noted, contributing to the patient's respiratory symptoms. Furthermore, the presence of miliary nodules throughout the lung fields and calcified modules in the apical segment of the right lower lobe provided additional evidence supporting the diagnosis of tuberculosis.



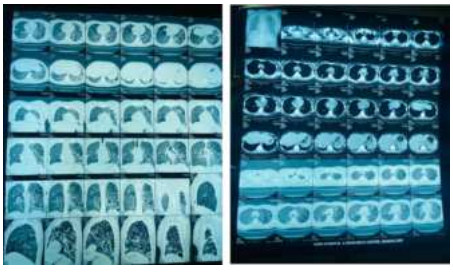
Lab Parameters:
Laboratory investigations unveiled abnormalities consistent with an underlying infectious process, including elevated inflammatory markers such as ESR (69 mm/hr) and CRP (3.88 mg/L). Hematological parameters were indicative of ongoing infection, with a hemoglobin level of 10.5 g/dL, TLC of 11790/cumm, RBC count of 4.39 lac/cumm, and PLT count of 4.44 lac. Additionally, liver and kidney function tests revealed no significant abnormalities, suggesting primarily pulmonary involvement.

Personal History:
The patient's personal history revealed no significant habits or familial predispositions. However, dietary changes, reduced appetite, and disturbed sleep patterns were noted, potentially reflecting the impact of her medical condition on daily life. Despite her young age, the patient exhibited signs of nutritional deficiency, warranting further evaluation and management.

General Physical Examination:
Upon examination, the patient appeared poorly nourished with evidence of pallor but lacked significant findings suggestive of other systemic abnormalities. The absence of cyanosis, clubbing, lymphadenopathy, or edema indicated a primarily respiratory pathology. Vital signs were within normal limits, aside from tachycardia indicative of the patient's underlying condition.

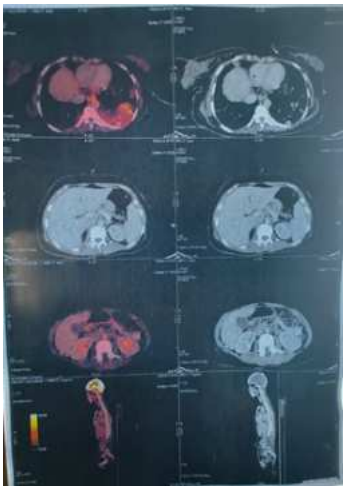
Systemic Examination:
Detailed examination of the upper and lower respiratory tracts revealed localized findings such as absent breath sounds and reduced vocal resonance, consistent with the radiological and clinical presentation of the disease. Hyperresonant notes were auscultated in the right mammary, infrascapular, and infraaxillary areas, reflecting underlying pulmonary pathology. Additionally, reduced breath sounds were noted in these areas, suggestive of airspace consolidation or pleural effusion.

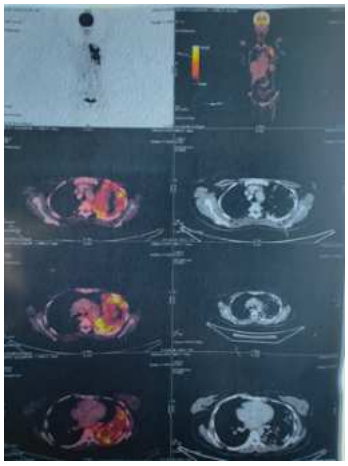
High-Resolution Computed Tomography of Thorax Findings:
CT scans elucidated the extent of lung involvement, highlighting cystic changes, pneumothorax, and miliary nodules throughout the lung fields. These findings were consistent with the clinical suspicion of tuberculosis and provided valuable information for treatment planning. Furthermore, the presence of pleural effusions and interlobular septal thickening suggested concomitant inflammatory changes in the lungs, warranting close monitoring and management.



Bronchoscopy:
Flexible bronchoscopy with bronchoalveolar lavage (BAL) was performed to obtain samples for analysis, including CBNAAT testing. Despite negative results, the procedure provided valuable insights into the disease process and ruled out alternative diagnoses. The bronchoscopy revealed no significant abnormalities in the airway architecture, ruling out obstructive lesions or endobronchial masses. However, bronchoalveolar lavage (BAL) fluid analysis yielded inconclusive results, necessitating further diagnostic evaluation.

PET CT:
Positron emission tomography-computed tomography (PET-CT) scans revealed increased metabolic activity along the distribution of micronodules, indicative of an infectious pathology, further strengthening the suspicion of tuberculosis. The PET-CT demonstrated increased 18FDG activity along the distribution of micronodules, indicating heightened metabolic activity consistent with an inflammatory or infectious process. This finding correlated well with the patient's clinical presentation and radiological findings, supporting the diagnosis of tuberculosis.





Lung Biopsy:
A CT-guided lung biopsy was pursued to obtain tissue samples for histopathological analysis. Microscopic examination revealed evidence of granulomatous inflammation, confirming the diagnosis of tuberculosis and guiding subsequent treatment decisions. The biopsy specimen exhibited caseating granulomas comprising epithelioid cells and multinucleated giant cells, characteristic of tuberculosis. Additionally, acid-fast staining revealed the presence of acid-fast bacilli, confirming active mycobacterial infection.

Approach to CXR with Miliary shadows:
The miliary pattern observed on CXR prompted consideration of various differential diagnoses, including infectious, neoplastic, and inflammatory etiologies. Given the patient's clinical presentation and risk factors, tuberculosis remained a primary consideration. Differential diagnoses included fungal infections, metastatic malignancies, sarcoidosis, and other granulomatous diseases. However, the characteristic distribution and appearance of the nodules were highly suggestive of tuberculosis, necessitating further evaluation and treatment initiation.

Classification of Diffuse Cystic Lung Diseases with Pneumothorax:
The presence of cystic lung changes and pneumothorax necessitated consideration of various etiologies, including neoplastic, genetic, developmental, and congenital causes. Among these, lymphangioleiomyomatosis (LAM) emerged as a significant differential diagnosis. LAM, characterized by cystic lung lesions and abdominal angiomyolipomas, was thoroughly evaluated given its relevance to the clinical presentation. Understanding the pathophysiological mechanisms underlying LAM facilitated diagnostic interpretation and therapeutic decision-making.

Approach to Cystic Lung Disease:
LAM, characterized by cystic lung lesions and abdominal angiomyolipomas, was thoroughly evaluated given its relevance to the clinical presentation. Understanding the pathophysiological mechanisms underlying LAM facilitated diagnostic interpretation and therapeutic decision-making. Differential diagnoses included pulmonary Langerhans cell histiocytosis (PLCH), lymphocytic interstitial pneumonia (LIP), and Birt-Hogg-Dubé syndrome (BHDS), among others. However, the absence of characteristic features such as smoking history, lymphocytic infiltrates, or skin manifestations made these less likely.

Role of Estrogen in LAM:
The influence of estrogen in LAM pathogenesis was explored, emphasizing its role in disease progression and potential therapeutic targets. Estrogen's impact on cellular proliferation, matrix remodeling, and metastatic properties underscored its significance in LAM management. Elevated estrogen levels promote the proliferation of smooth muscle-like cells, leading to the development of cystic lung lesions and angiomyolipomas. Targeting estrogen signaling pathways has emerged as a promising therapeutic approach in LAM management, aiming to halt disease progression and improve outcomes.

Clinical Presentation and Complications of LAM:

The heterogeneity of LAM presentation, including respiratory symptoms, chylothorax, and abdominal manifestations, highlighted the complexity of the disease process. Awareness of potential complications guided comprehensive patient care and management strategies. Complications such as chylothorax, renal angiomyolipomas, and lymphangioleiomyomas may arise, necessitating multidisciplinary management involving respiratory, surgical, and medical specialties. Moreover, extrapulmonary manifestations such as lymphatic involvement and renal angiomyolipomas require vigilant monitoring and intervention to prevent disease progression and improve quality of life.

Radiological Findings and Diagnostic Workup in LAM:

Radiological investigations, including HRCT, played a pivotal role in diagnosing LAM by identifying characteristic cystic changes in the lungs. Additional diagnostic modalities, such as serum biomarkers and histopathological analysis, contributed to diagnostic confirmation. HRCT findings typically include multiple thin-walled cysts, predominantly in the lung bases, with sparing of the costophrenic angles. These cysts may vary in size and distribution, often demonstrating a diffuse, bilateral pattern. Serum biomarkers such as VEGF-D levels may aid in the diagnosis and monitoring of LAM, although their utility remains limited in isolation. Histopathological examination of tissue samples obtained via biopsy or surgical resection provides definitive diagnostic confirmation, revealing characteristic smooth muscle proliferation and cystic changes consistent with LAM.

DISCUSSION:

The case of the 25-year-old female patient presented several diagnostic and therapeutic challenges, highlighting the importance of a systematic approach to complex clinical presentations. Initially diagnosed with military tuberculosis based on clinical, radiological, and laboratory findings, the patient's subsequent clinical course underscored the need for vigilant reassessment and consideration of alternative diagnoses. The development of cystic lung changes and pneumothorax raised concerns regarding treatment response and necessitated further investigation.

The differential diagnosis expanded to include conditions such as lymphangioleiomyomatosis (LAM), given the patient's clinical and radiological features. LAM, characterized by cystic lung lesions and angiomyolipomas, shares overlapping clinical manifestations with tuberculosis, making it a pertinent consideration in this case. Diagnostic modalities such as PET-CT and lung biopsy played crucial roles in elucidating the underlying pathology, ultimately confirming granulomatous inflammation consistent with tuberculosis.

The role of estrogen in LAM pathogenesis emerged as a significant point of discussion, highlighting potential therapeutic avenues for disease management. Understanding the molecular mechanisms underlying estrogen's effects on cellular proliferation and matrix remodeling offers insight into targeted therapies for LAM. Additionally, the clinical implications of LAM complications, such as chylothorax and renal angiomyolipomas, underscore the importance of comprehensive multidisciplinary care in optimizing patient outcomes.

CONCLUSION:

In conclusion, the presented case underscores the diagnostic and therapeutic challenges inherent in complex respiratory presentations. A multidisciplinary approach integrating clinical evaluation, radiological imaging, and histopathological analysis is essential for accurate diagnosis and tailored management. While tuberculosis remains a significant global health concern, conditions such as lymphangioleiomyomatosis pose diagnostic dilemmas due to overlapping clinical features. Vigilant reassessment and consideration of alternative diagnoses are imperative in cases of treatment non-response or atypical disease progression. Future research exploring novel diagnostic modalities and targeted therapies holds promise for improving outcomes in patients with complex respiratory conditions.

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