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Case Series

Two are more dangerous than one-review of cases of coexisting tuberculosis and hodgkins lymphoma

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ABSTRACT

Background: The coexistence of tuberculosis (TB) and Hodgkin's lymphoma (HL) is a clinically challenging condition that poses considerable diagnostic and treatment challenges. TB is a contagious bacterial infection primarily affecting the lungs, while HL is cancer that originates in the bone marrow and lymphatics. Despite their subtle differences, the clinical and radiological manifestations of TB and HL overlap considerably, posing a diagnostic dilemma. While coexisting cases have been reported in literature, the myriad overlap between clinical manifestations and radiological findings of both diseases makes an accurate diagnosis difficult in such cases.

Case Report: A 23-year-old male from Badlapur, Maharashtra, India, presented with persistent cough, low-grade fever, breathlessness, chest pain, weight loss, and neck swelling for 3months. Imaging revealed cavitatory consolidation in the lungs and necrotic lymphadenopathy on HRCT findings. Bronchoscopic lavage confirmed Mycobacterium tuberculosis (TB) infection by CBNAAT. 4 months later he presented with bilateral chylothorax and large cervical lymphadenopathy, and further evaluation revealed coexisting Hodgkin's lymphoma on neck node tissue biopsy. PET-CT (Positron Emission Tomography and Computed Tomography)scan confirmed increased metabolic activity in lymph nodes and lungs.(increased metabolic activity in bilateral cervical, mediastinal, axillary, and cardiophrenic? lymph nodes. There was also increased metabolic activity in the soft tissue involving muscles of the left side of the neck and anterior mediastinum. Additionally, increased metabolic activity was noted in the regions of consolidation with surrounding nodules in both lungs, confirming the coexistence of TB and Hodgkin's lymphoma) Chemotherapy was commenced for Hodgkin's lymphoma ABVD Regimen(Adriamycin, Bleomycin, Vinblastine, Dacarbazine) and TB treatment with a 4-drug all-oral fixed-dose weight-adjusted regimen of HRZE (Isoniazid, Rifampicin, Pyrazinamide, Ethambutol).The patient received a total of 8 cycles of chemotherapy and after 8 cycles of chemotherpy repeat PET CT revealed complete resolution of cervical lymphadenopathy and chylothorax.

Conclusion: The coexistence of TB and Hodgkin's lymphoma is an uncommon but clinically challenging condition requiring a high index of suspicion index and prompt and thorough evaluation, so that timely treatment can be commenced to achieve absolute cure, in the coexistence of two conditions which are otherwise fatal. Diagnosis and management of such cases often requires a multidisciplinary approach, and timely initiation of appropriate treatment for both TB and Hodgkin's lymphoma is essential for optimal patient outcomes. Microbiology, biopsy and immunohistochemistry are crucial for accurate diagnosis.

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1. Introduction

Tuberculosis (TB) and Hodgkin's lymphoma (HL) are two diseases that affect young patients differently. Tuberculosis

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is a contagious bacterial infection caused by Mycobacterium tuberculosis, primarily affecting the lungs but can also involve other organs.[1] Conversely, Hodgkin's lymphoma is a type of cancer originating in the lymphatic system, conventionally characterized by the presence of Reed-Sternberg cells in biopsy specimens. While these two conditions may seem unrelated, there have been cases where they coexist, posing diagnostic and treatment challenges for healthcare providers.[2]

The overlapping clinical manifestations and radiological findings of TB and HL makes accurate diagnosis challenging, and delays in appropriate treatment can lead to serious consequences. Using established diagnostic tools, such as imaging, biopsy, microbial and molecular testing, along with a thorough clinical evaluation, is crucial to identify and differentiate between the two conditions and guide appropriate treatment decisions.[3]

The burden of coexisting TB and HL lies in the challenges of accurate diagnosis, as TB and HL share similar constitutional symptoms such as fever, night sweats, fatigue, appetite and weight loss, and pulmonary symptoms such as cough, hemoptysis, dyspnoea and chest pain making it difficult to differentiate between the two conditions based on clinical presentation alone. Additionally, radiological findings, such as lymphadenopathy, can be present in both TB and HL, further complicating the diagnostic process. Misdiagnosis or delayed diagnosis can lead to delays in treatment initiation, resulting in disease progression and poor outcomes.[4]

Prevalence of TB in India is 41% and Hodgkins in India 2.5 per 100000 people, and separate prevalence in young. HL has bimodal peak at ages 15 and 35.The prevalence may be underreported due to challenges in accurate diagnosis and limited data availability. Further research and surveillance are needed to understand better the true prevalence and burden of coexisting TB and HL worldwide.[5] On a global scale, its prevalence may vary depending on the epidemiological profile of TB and HL in different regions. According to a study, coexisting TB and HL prevalence was 1.1% among lymphoma patients in a tertiary care centre in Saudi Arabia and around 1.9% in South Africa.[6] These findings suggest that the coexistence of TB and HL is not limited to India but is also observed in other countries with varying prevalence rates, with a prevalence of 2.2% of coexisting TB and HL among lymphoma patients in North India.[7] A prevalence of 1.6% of coexisting TB and HL among lymphoma patients in South India. These studies highlight that TB and HL coexistence is uncommon in India.

2. Case Presentation

2.1. Case 1

A 23-year-old male from Badlapur , Maharashtra,mechanic by occupation presented to the hospital with a persistent cough and low-grade fever lasting the past 3 months. He also complained of breathlessness (modified Medical Research Council III) for the past 15 days, dull aching chest pain, along with loss of appetite and weight. Additionally, he noticed hard, painless swellings on both sides of his neck for the past 1 year, which were not associated with any pain, discharge or inflammation. There was no history of night sweats, hemoptysis, or recent travel to TB-endemic areas, or close contact with a diagnosed case of TB, or familial history of TB or cancer.

Vitals on initial admission were normal

Chest Examination – Increased tactile vocal fremitus, Increased vocal resonance

Similarly – Abdomen – Splenomegaly found

The past medical and surgical history was insignificant. Blood investigations, including complete blood count, liver and kidney function tests were within normal limits and serology for human immunodeficiency virus (HIV), was negative. Chest X-ray film showed cavitatory consolidation in bilateral lungs. High-resolution computed tomography (HRCT) of the thorax revealed bilateral partially necrotic lymphadenopathy with cavitatory consolidation. Bronchoscopic lavage was performed, and the samples were positive for Mycobacterium tuberculosis (MTB) sensitive to first-line anti-TB drugs, including isoniazid and rifampicin, by line probe assay (LPA). Based on the clinical and imaging findings, the patient was diagnosed with pulmonary tuberculosis and mediastinal lymphadenopathy.

During the second admission which occurred after 4 months, the patient developed acute onset breathlessness, tachypnea, tachycardia, and fever. Repeat imaging with HRCT of the thorax revealed bilateral pleural effusion, for which ultrasound guided thoracocentesis was performed twice after informed consent, under all aseptic precautions and local anasethesia, the procedure being uneventful-both effusions were milky suggesting a chylothorax. Ether test was performed by addition of 2 ml of ethyl ether to the milky chylous fluid to differentiate between chylothorax and pseudo chylothorax, it was negative, confirming chylothorax.

Further evaluation was done with an excision biopsy of the right cervical lymph node, which showed an extensively necrotic lymph node with preserved areas showing a fair number of large atypical lymphoid cells and smaller lymphocytes in a sclerotic background. Immunohistochemistry of the large atypical cells showed positivity for CD30, CD15, Pax-5, and BOB-1, confirming the diagnosis of Hodgkin's lymphoma.(Figures 1, 2, 3, 4, 5,

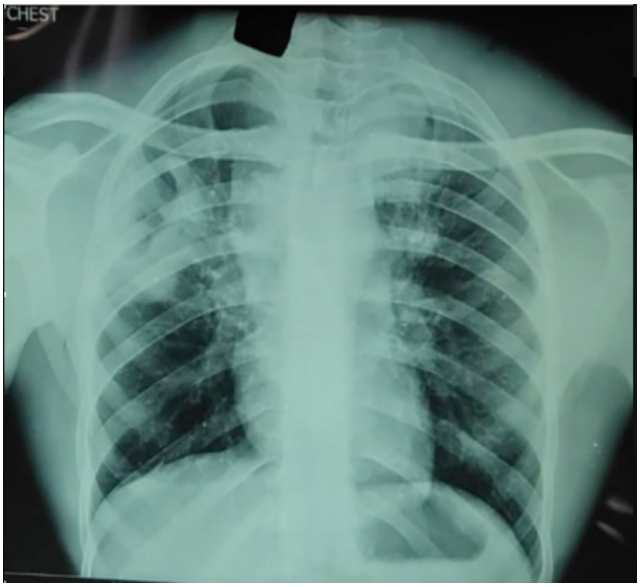


Figure 1:

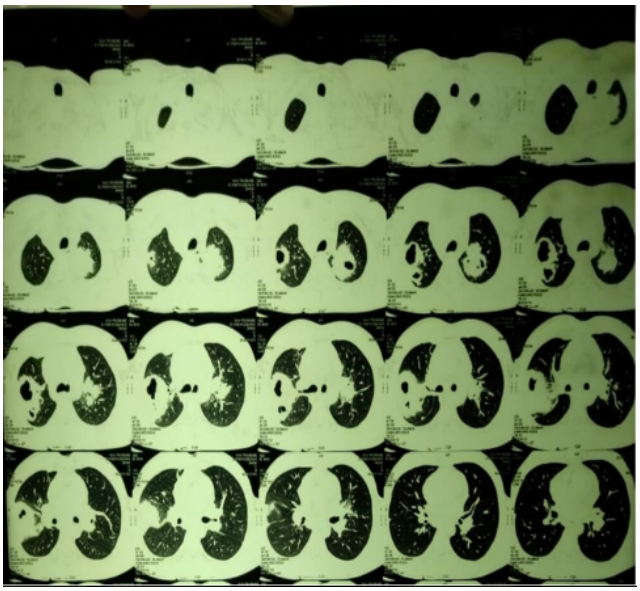


Figure 2: HRCT THORAX

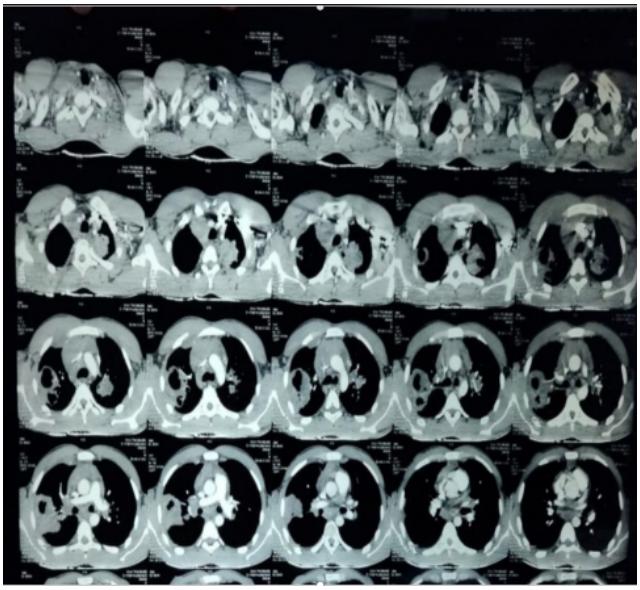


Figure 3: 2nd admission

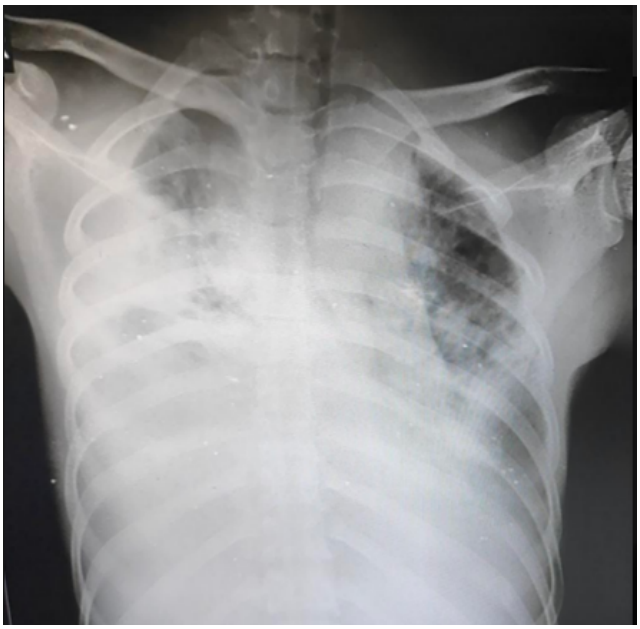


Figure 4:

6, 7 and 8)

To complete the diagnostic workup, a positron emission tomography-computed tomography (PET-CT) scan was performed, which revealed increased metabolic activity in bilateral cervical, mediastinal, axillary, and cardiophrenic lymph nodes. There was also increased metabolic activity in the soft tissue involving muscles of the left side of the neck and anterior mediastinum. Additionally, increased metabolic activity was noted in the regions of consolidation with surrounding nodules in both lungs, confirming the coexistence of TB and Hodgkin's lymphoma. After the diagnosis of Hodgkin's lymphoma was established, he was referred to our oncology department where chemotherapy with Adriamycin, Bleomycin, Vinblastine, and Dacarbazine was advised and commenced. Concurrently, TB treatment was started with HRZE (isoniazid, rifampicin, pyrazinamide, and ethambutol) for TB. Patient completed 6 months of TB treatment in Jan 2023 and after 8 cycles of chemotherapy with ABVD Regimen, repeat PET-CT revealed complete resolution of chylothoraax and cervical Lymphadenopathy.

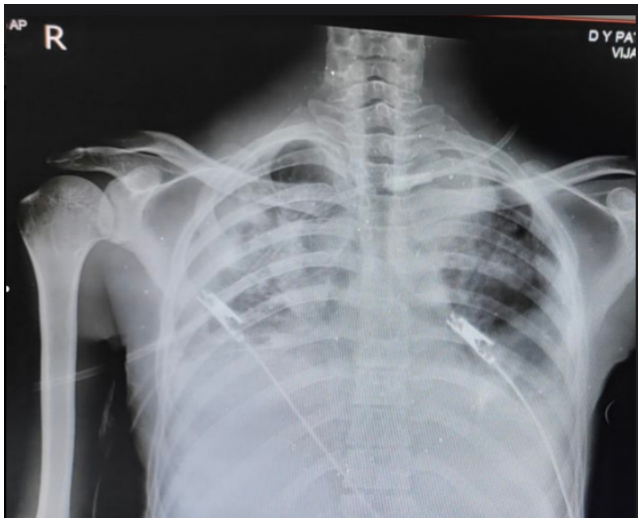


Figure 5:

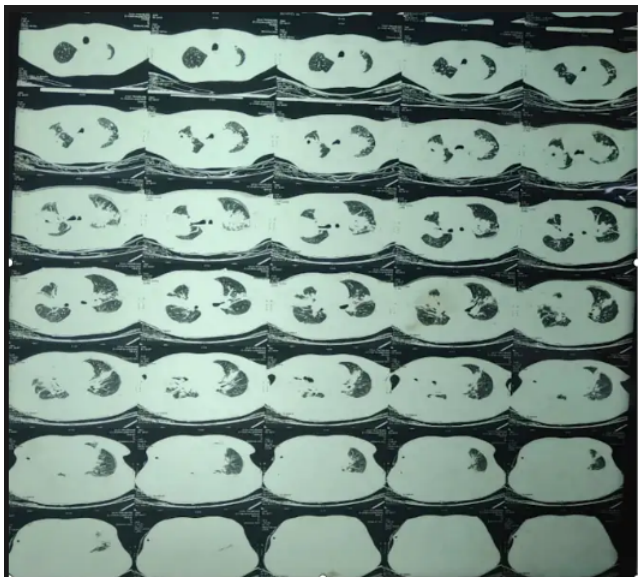


Figure 6: HRCT Thorax

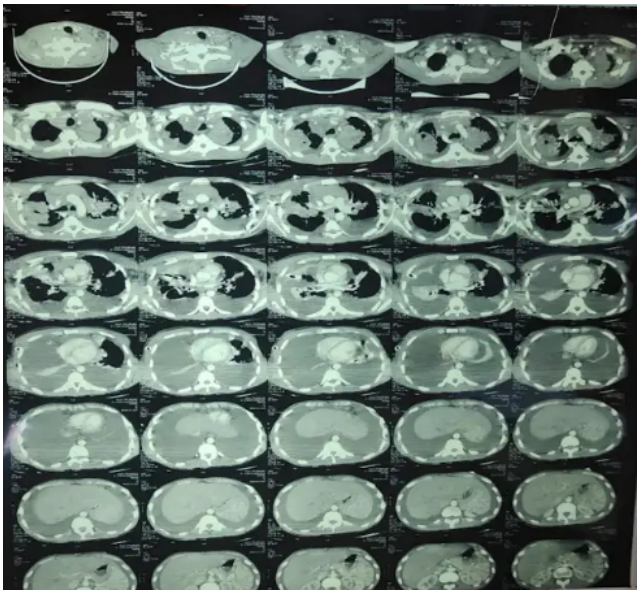


Figure 7:

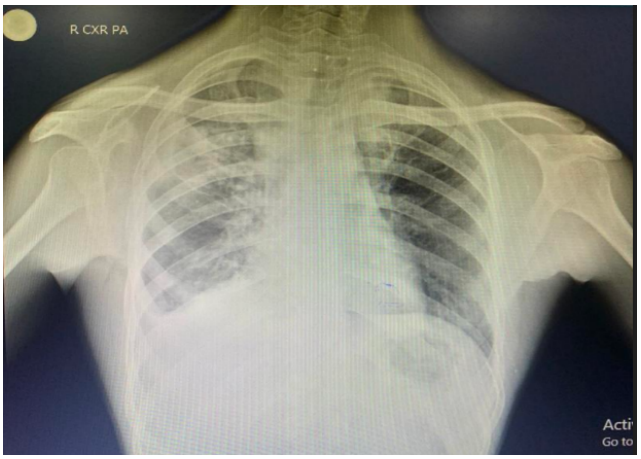


Figure 8: After completion of chemotherapy and ATT

2.2. *Case 2*

A 31-year-old male from Ghansoli, painter by occupation presented to the Outpatient Department (OPD) with complaints of a cough persisting for 1 year, which had worsened over the past 4 days. He also reported chest pain on the right side for the past 10 days, described as dull and aching, aggravated by deep inspiration. Additionally, he had a low-grade fever for 1 month, weight loss amounting to 7 kg over 3 months, decreased appetite over the same duration, and a right parasternal swelling persisting for 3 months. The patient had a history of left tuberculous (TB) pleural effusion in 2018, diagnosed based on pleural fluid reports, and had 800 mL of hemorrhagic fluid tapped. He had undergone antitubercular treatment (AKT) under the Directly Observed Treatment Short-course (DOTS) program for 9 months. He had also been recently diagnosed with hepatitis B virus (HBV) infection. He worked as a painter for 10 years and had a history of alcohol consumption (1 quarter per day) for the past month, smoking (2-3 cigarettes per day) for 12 years, and tobacco chewing (1 packet per day) for 4 years. On further evaluation, a contrast-enhanced computed tomography (CT) scan of the chest on 14/9/22 revealed near total collapse of the left upper lobe with the trachea and mediastinum shifted to the right side. An isodense soft tissue lesion was noted along the medial aspect of the left upper lobe, without air bronchogram, and multiple enlarged lymph nodes were seen in the perivascular, paratracheal, subcarinal, aortopulmonary, and left hilar regions, measuring 0.5 cm

to 4.7 cm, with the largest measuring 4.7 cm × 3.2 cm. A CT-guided lymph node biopsy on 28/9/22 revealed Classical Hodgkin's lymphoma, with positive findings for Reed-Sternberg cells and positive immunostaining for CD30, CD20, and Pax 6. A gastrology opinion was sought due to the patient's positive HBV status, and he was advised to start on Tenofovir.

Further investigations included a bronchoscopy (BAL) was done the results of which showed a positive first-line line probe assay for Mycobacterium tuberculosis without rifampicin resistance. An oncology opinion was taken subsequently, and CT-guided lung biopsy was advised, which confirmed the diagnosis of Hodgkin's lymphoma, prompting the initiation of chemotherapy with the ABVD (Adriamycin, Bleomycin, Vinblastine, and Dacarbazine) regimen. He was started on anti-TB treatment under NTEP according to the weight-based regimen. 6 cycles of ABVD chemotherapy were recommended, with a repeat PET-CT scan after 3 cycles which showed regression. After completing 5 such cycles of chemotherapy along with anti-TB drugs, he showed significant clinical and radiological improvement; his weight increased from 56 kg to 66 kg in time duration (mention how many months). He is currently asymptomatic and undergoing regular follow-up and monitoring as per his individualized treatment plan.(Figures 9, 10 and 11)

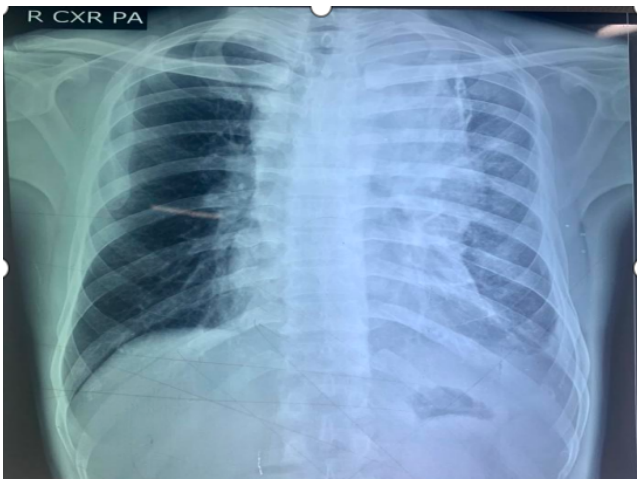


Figure 9:

3. Discussion

The presented cases highlight the coexistence of tuberculosis (TB) and Hodgkin's lymphoma, two distinct diseases with overlapping clinical manifestations. Although TB is a well-known infectious disease caused by Mycobacterium tuberculosis, and Hodgkin's lymphoma is a malignancy of the lymphatic system, the coexistence of these two conditions is rare and poses diagnostic challenges. In the first case, the 23-year-old male presented



Figure 10: HRCT scans

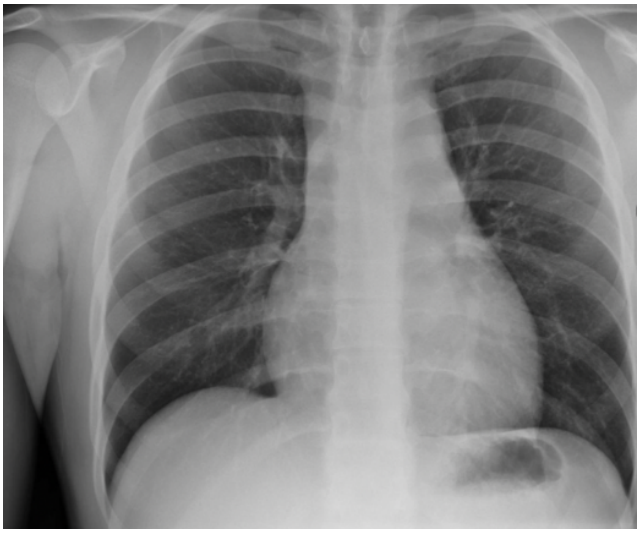


Figure 11: After completion of chemotherapy and ATT

with a persistent cough, low-grade fever, breathlessness, chest pain, loss of appetite, weight loss, and painless swellings on both sides of the neck. Initial imaging with chest X-ray and high-resolution computed tomography (HRCT) of the thorax revealed cavitatory consolidation in bilateral lungs and partially necrotic lymphadenopathy with cavitatory consolidation. Bronchoscopic lavage confirmed the presence of Mycobacterium tuberculosis (MTB) in both patients samples. Subsequent evaluation with an excision biopsy of the right cervical lymph node showed features consistent with Hodgkin's lymphoma. PET-CT scan further confirmed the coexistence of TB and Hodgkin's lymphoma with increased metabolic activity in various lymph nodes and lung lesions.

Similarly, in the second case, the 31-year-old male presented with a chronic cough, chest pain, low-grade fever, weight loss, and a history of previous TB pleural effusion. Contrast-enhanced computed tomography (CT) scan of the chest revealed a collapse of the left upper lobe with a soft tissue lesion and multiple enlarged lymph nodes. CT-guided lymph node biopsy confirmed the diagnosis of Hodgkin's lymphoma with positive findings for Reed-Sternberg cells. The coexistence of TB and Hodgkin's lymphoma can pose diagnostic challenges, as both conditions can present with similar symptoms, such as cough, fever, chest pain, and lymphadenopathy. In both cases, the initial evaluation with blood investigations and imaging was inconclusive, and a definitive diagnosis was made through biopsy and immunohistochemistry. The literature on the coexistence of TB and Hodgkin's lymphoma is limited, and there are only a few reported cases in the literature. However, a study by Badyal et al. reported a case series of five patients with coexistent TB and Hodgkin's lymphoma, highlighting the importance of considering the possibility of dual pathology in patients with similar clinical presentations.[8] Another study by Banerjee et al. reported a case of concurrent pulmonary TB and Hodgkin's lymphoma in a young male, emphasizing the need for a high index of suspicion and thorough evaluation in cases with overlapping clinical features.[9] Managing coexisting TB and Hodgkin's lymphoma requires a multidisciplinary approach involving infectious disease specialists, oncologists, and radiologists. In both cases, the patients received chemotherapy for Hodgkin's lymphoma and anti-TB treatment. In the first case, the patient was started on HRZE (isoniazid, rifampicin, pyrazinamide, and ethambutol) for TB. In contrast, the patient was advised to start on Tenofovir in the second case due to the positive HBV status.[10–12]

4. Conclusion

To summarize, the coexistence of tuberculosis (TB) and Hodgkin's lymphoma is an uncommon yet clinically challenging condition that poses a diagnostic dilemma due to overlapping clinical and imaging manifestations. A high index of suspicion and thorough evaluation is essential for accurate diagnosis. Biopsy and immunohistochemistry are crucial in confirming the presence of TB and Hodgkin's lymphoma in these cases.

Managing coexisting TB and Hodgkin's lymphoma requires a multidisciplinary approach involving pulmonologists, infectious disease specialists, oncologists, pathologists, microbiologists and radiologists. Timely initiation of appropriate treatment for both TB and Hodgkin's lymphoma is crucial to ensure complete cure along with optimal patient outcomes. Chemotherapy for Hodgkin's lymphoma and anti-TB treatment are concurrently required, but may be challenging as it is associated with high drug burden and adverse effects.

It is important to note that the literature on the coexistence of TB and Hodgkin's lymphoma is limited, therefore, clinicians must maintain a high index of suspicion in young patients with overlapping clinical features, such as cough, fever, chest pain, and lymphadenopathy, and consider the possibility of dual pathology.

5. Source of Funding

None.

6. Conflict of Interest

None.

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