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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/24398
DOI URL: <http://dx.doi.org/10.21474/IJAR01/24398>



RESEARCH ARTICLE

A CHALLENGING CASE OF HODGKIN LYMPHOMA MIMICKING TUBERCULOSIS IN A YOUNG FEMALE PATIENT: A CASE REPORT

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Manuscript Info

Manuscript History

Received: 12 August 2026

Final Accepted: 14 September 2026

Published: October 2026

Key words:-

Hodgkin lymphoma; gigantocellular epithelioid granuloma; caseous necrosis; lymphadenopathy; anatomopathological study; chemotherapy.

Abstract

Hodgkin lymphoma (HL) is a rare malignancy. Distinguishing between Hodgkin lymphoma and tuberculosis (TB) is challenging. A 22-year-old patient had been undergoing treatment for lymph node tuberculosis (TB) for 18 months based on the histological examination of cervical lymphadenopathy. The patient presented with neurological signs suggestive of spinal cord compression, prompting MRI and CT of the chest, abdomen, and pelvis (CT CAP) to investigate a potential neoplastic origin. The CT CAP scan revealed infiltration of the left supraclavicular and lateral cervical regions. An ultrasound-guided biopsy of the infiltrated area was performed, and the histological and immunohistochemical findings were consistent with stage IV classic Hodgkin lymphoma. Epithelioid granulomas with caseous necrosis are not exclusive to TB; lymphoma should also be considered in this context, and immunohistochemical analysis should be performed for an accurate diagnosis.

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Introduction:-

Hodgkin lymphoma is a rare malignancy characterized histologically by the presence of Reed-Sternberg cells. It accounts for 15% of lymphomas [1]. According to the latest global data analysis, the incidence of HL is 0.98 per 100,000 people and is still on the rise, particularly among females and young individuals [2]. The most common manifestation is asymptomatic lymphadenopathy in the cervical and supraclavicular regions [3]. This may mimic TB, as its most prevalent extrapulmonary site of involvement is the cervical lymph nodes. Alongside the similar and overlapping clinical presentations, this poses a diagnostic challenge in distinguishing between the two pathologies, leading to misdiagnosis [4].

Case Presentation:-

We present the case of a 22-year-old patient who first presented four years ago with cervical lymphadenopathy, which was diagnosed as lymph node tuberculosis based on histological evidence. The patient subsequently received prolonged antituberculous treatment for a total of 18 months. However, due to a lack of improvement, with an increase in lymph node size, surgical excision of the lymph node was indicated. The histopathological examination

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of the latter revealed a giant-cell epithelioid granuloma with caseous necrosis and a negative GeneXpert result. The clinical course was subsequently complicated by neurological signs suggestive of spinal cord compression, prompting spinal magnetic resonance imaging (MRI). The scan revealed a lesion in the left paravertebral soft tissues involving the left pedicle and partially extending into the vertebral body of D2. This led to compression of the vertebral body and invasion of the spinal canal. Spinal cord compression resulted from this process, and the findings were suggestive of Pott's disease or metastatic disease (Figure 1).



Figure 1. Sagittal MRI section of the spine showing a lesion affecting the left pedicle and partially extending into the vertebral body of D2 (yellow arrow).

The clinical examination revealed a patient in a generally stable clinical condition with a WHO performance status of 2. She was eupneic, with an oxygen saturation of 97% on room air, and had a normal cardiopulmonary examination. Upon inspection and palpation, the sites of the previous bilateral lymph node excisions showed scars, with no palpable lymphadenopathy. Neurological examination revealed signs of pyramidal irritation, including a positive Babinski sign and brisk osteotendinous reflexes in all four limbs. As part of the staging evaluation, computed tomography of the chest, abdomen, and pelvis (CT CAP) was performed, revealing an excavated mass in the left lower lobe, with spiculated margins, heterogeneous contrast enhancement, and extension into the fissure and parietal pleura. Additionally, the scan revealed parenchymal consolidation at the pulmonary apex, associated with bronchiectasis (Figure 2). The scan also showed extensive mixed discovertebral involvement from C3 to D4, with vertebral body compression, opposing erosions, prevertebral infiltration without fluid collection, as well as epidural inflammation. Furthermore, infiltration of the left supraclavicular and lateral cervical regions was observed, involving the sternocleidomastoid muscle and subcutaneous fat.



Figure 2. Axial CT image of the lung parenchyma showing consolidation at the pulmonary apex with bronchiectasis (red arrow) and a left lower lobe pulmonary lesion (yellow arrow).

The patient underwent bronchofibroscopy, which revealed a normal macroscopic appearance. Investigations for acid-fast bacilli, including direct examination and culture, as well as GeneXpert MTB/RIF Ultra, GeneXpert MTB-XDR, and post-bronchoscopy sputum examination for *Mycobacterium tuberculosis*, all returned negative results. Consequently, an ultrasound-guided biopsy of the infiltrated area was performed. The histological and immunohistochemical findings were consistent with classic Hodgkin lymphoma (Figure 3).

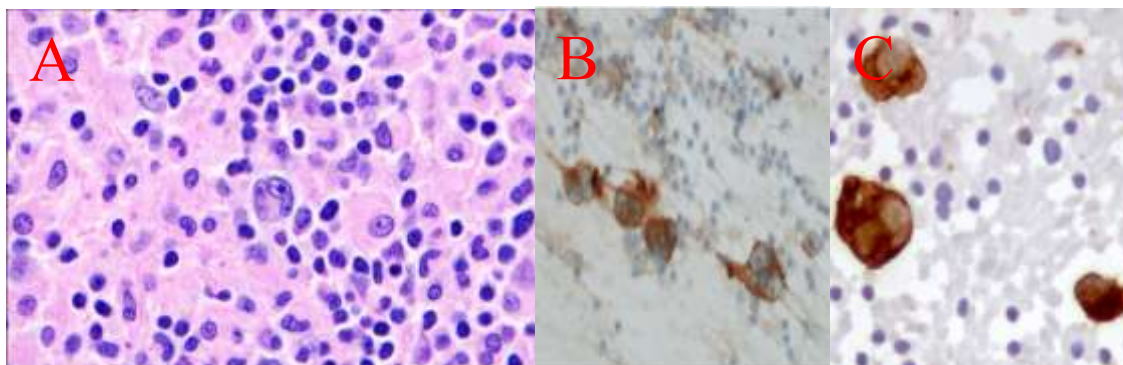


Figure 3. Histological findings in the patient, showing:

A. Large binucleated Reed–Sternberg cells with prominent nucleoli in the biopsy specimen from the left supraclavicular infiltrative lesion;

B. Positive CD15 staining in Reed–Sternberg cells on immunohistochemistry

C. Positive CD30 staining in Reed–Sternberg cells on immunohistochemistry.

The investigations were completed with positron emission tomography (PET), which revealed a cervicomedastinal hypermetabolic pathological process involving the trachea and esophagus below the larynx, with lateral extension into the lungs. Additionally, there was posterior extension to the spine from C4 to D4, with several vertebral lytic lesions and spinal canal involvement. The scan also revealed parenchymal consolidation with sequelae-like bronchiectasis at the left pulmonary apex. Bilateral hypermetabolic foci were also observed in the cervical and mediastinal lymph nodes (Figure 4).

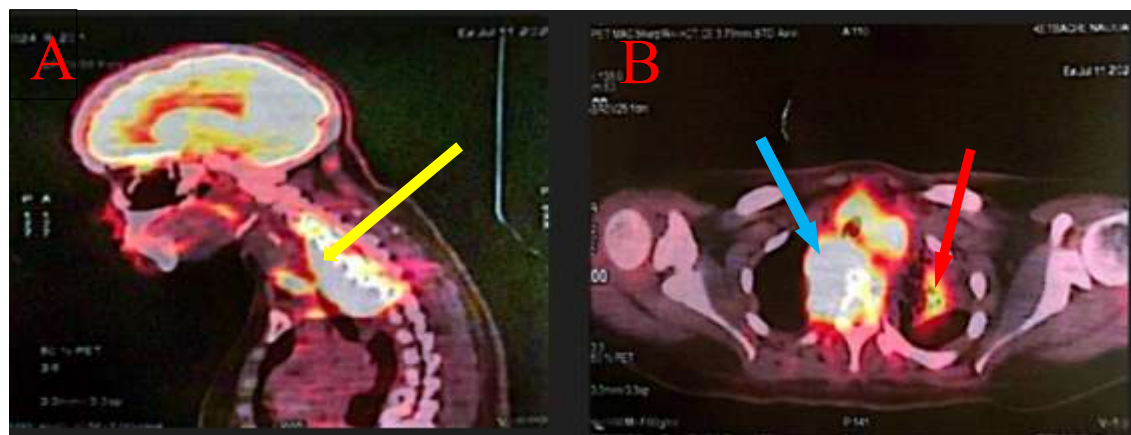


Figure 4. Pre-chemotherapy fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) images:

A. Sagittal FDG-PET/CT image showing a metabolically active pathological tissue process extending from the cervical to mediastinal regions, involving the trachea and esophagus and invading the spine between C4 and D4. Vertebral lytic lesions and spinal canal infiltration are also present (yellow arrow).

B. Axial FDG-PET/CT image at the mid-thoracic level showing parenchymal consolidation with bronchiectasis at the left pulmonary apex (red arrow), along with a pathological tissue process extending laterally into the lungs (blue arrow).

Given the potential neurological risks, spinal surgery was not considered. The patient was therefore treated with chemotherapy for Hodgkin lymphoma, which led to good clinical and radiological improvement (Figure 5).



Figure 5. Post-treatment axial FDG-PET/CT image at the mid-thoracic level showing near-complete resolution of the previously identified locally advanced lung lesion, with minimal residual right paravertebral thickening at the level of D2–D3.

Discussion:-

Cervical lymphadenopathy is a recurring symptom in various pathologies, notably TB and lymphoma [5]. This could explain the confusion and misdiagnosis in the present case. While the typical clinical presentation of HL involves palpable enlarged lymph nodes, mostly in the cervical region [6], lymphomas may also manifest with a variety of presentations, especially in early-stage disease, resulting in diagnostic delay [7]. Such presentations include symptoms of spinal cord compression, which occurs in approximately 5% of patients with solid tumors and accounts for up to 5% of presentations involving spinal cord compression [8]. Histologically, the presence of epithelioid granulomas is a strong argument in favor of a TB diagnosis. Central caseous necrosis is not always present; however, when present, it is considered strong but non-specific evidence of TB. Similarly, giant-cell epithelioid granulomas are not specific to TB, as they may also be found in sarcoidosis, brucellosis, leprosy, and lymphoma, among other conditions [15].

One of the potential differential diagnoses of HL is TB [5]. This was the case with our patient, whose cervical lymphadenopathies, apical parenchymal consolidation, granulomatous lesion with caseous necrosis on the first biopsy, and lesions mimicking Pott's disease with spondylodiscitis on imaging all led to the suspicion of multifocal TB. When TB is suspected, multiple investigations can be useful to confirm the diagnosis. These include the isolation of *Mycobacterium tuberculosis* from bodily fluids or tissues. Other techniques include culture, acid-fast bacilli (AFB) smear microscopy, and rapid nucleic acid amplification tests, such as GeneXpert® [9, 10]. These tests were used to assess the possibility of TB in our patient. However, all yielded negative results before treatment was initiated. Similarly, the mycobacterial cultures, whose results became available six weeks later, were negative for TB. When drug resistance is suspected, especially in the absence of clinical improvement, the use of GeneXpert MTB-XDR may be useful in detecting resistance [10].

Inflammation and medullary lymphocyte proliferation, alongside the presence of TB, may contribute to the transformation of lymphocytes into CD5+ CD20+ CD23+ neoplastic lymphocytes. Conversely, the onset of TB following immunosuppression could have been a secondary consequence of the development of a B-cell tumor clone [11, 12]. Despite the aforementioned association, TB was not retained as the final diagnosis due to the lack of clinical improvement and the worsening of clinical and radiological findings, even though the patient underwent anti-TB treatment and adhered well to the treatment regimen. Repeated TB-specific tests all returned negative, and ultimately, the diagnosis of HL was confirmed following biopsy of the left supraclavicular lesion. Regarding antituberculous treatment, the time required to complete the treatment course could lead to a delayed diagnosis of lymphoma, as occurred in our patient. The long treatment duration, alongside the lack of regular follow-up during this period, may contribute to deterioration in patients' general condition by the time lymphoma is diagnosed [13].

The key question is when an alternative diagnosis should be considered during the diagnostic work-up for TB, and when a biopsy with immunohistochemical analysis should be performed to establish the diagnosis. The current National Institute for Health and Care Excellence (NICE) guidelines for TB do not specifically address the circumstances in which alternative diagnoses should be considered. They also do not specify which clinical or ancillary findings may help differentiate TB from other conditions [10, 14]. Findings that may suggest a diagnosis other than TB include the absence of known TB exposure or a history of previous TB infection, supraclavicular lymph node involvement, negative results from initial TB investigations, and a lack of clinical improvement after two months of antituberculous treatment [15].

The mortality rate associated with HL has been decreasing, likely due to earlier diagnosis and advances in treatment. However, delays in diagnosis and treatment may adversely affect patient outcomes. In our patient, the diagnosis was delayed in the context of several findings that initially favored TB, including her young age, cavitary lung lesions, spinal involvement, and the granulomatous lesion identified on the initial biopsy. Regarding treatment and prognosis, studies have reported that patients initially treated for presumed TB were more likely to be diagnosed with lymphoma at advanced stages and to have poorer outcomes than those who did not receive antituberculous treatment. Similarly, higher rates of treatment failure and mortality have been reported among patients initially treated for TB than among those who were not treated [16]. These findings suggest that an initial diagnosis of TB may contribute to diagnostic delay, although the association does not necessarily establish a causal relationship. In our case, chemotherapy was followed by clinical improvement, including regression of functional impairment. Follow-up imaging showed near-complete resolution of the pulmonary consolidation, the lung mass, and the cervicomedial process. This case highlights that HL is a potentially treatable malignancy and underscores the importance of reconsidering the diagnosis when presumed TB fails to respond to appropriate treatment.

Conclusion:-

Cervical lymphadenopathy can arise from a variety of underlying conditions, posing diagnostic challenges. Our report suggests that clinicians should reconsider the diagnosis of TB, especially when initial treatment with antituberculous drugs fails. Further investigations, including biopsy and histopathological examination, may help establish an accurate diagnosis. Giant epithelioid granulomas with caseous necrosis are not exclusive to TB. Lymphoma should also be considered in this context. Biopsy with histopathological and, when indicated, immunohistochemical analysis should be considered in patients with persistent or unexplained lymphadenopathy, particularly when the clinical course is inconsistent with TB.

Abbreviations:-

AFB: Acid-fast bacilli

CD: Cluster of differentiation

CT: Computed tomography

CT CAP: Computed tomography of the chest, abdomen, and pelvis

FDG: Fluorodeoxyglucose

HL: Hodgkin lymphoma

MRI: Magnetic resonance imaging

PET/CT: Positron emission tomography/computed tomography

TB: Tuberculosis

WHO: World Health Organization

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