

A challenging case of Hodgkin lymphoma mimicking tuberculosis in a young female patient: A case report.

Abstract:

Hodgkin lymphoma (HL) is a rare malignancy. Distinguishing between Hodgkin's Lymphoma and tuberculosis is challenging. A 22-year-old patient has been undergoing treatment for lymph node tuberculosis (TB) for 18 months based on histological study of cervical lymphadenopathy. The patient showed neurological signs indicating spinal cord compression, for which she underwent a (MRI) and a (CCTAP) to explore a potential tumor origin. The CCTAP 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 analysis arguments were in favor of a typical stage IV Hodgkin's lymphoma. Giant epithelioid granuloma with caseous necrosis is not exclusive to TB, the possibility of a lymphoma should be considered in this context, and immunohistochemical analysis should be performed for an accurate diagnosis

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

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 individuals of young age [2]. The most common manifestation is asymptomatic lymphadenopathy in the cervical and supraclavicular regions [3]. This may mimic TB as its most prevalent extrapulmonary localization is in the cervical region. And alongside the similar and overlapping clinical presentations, this poses the challenge of distinguishing between the two pathologies, leading to misdiagnosis [4].

CASE PRESENTATION:

We present the case of a 22-year-old patient who presented four years ago with a cervical lymphadenopathy diagnosed as lymph node tuberculosis based on histological evidence. Regarding this the patient underwent prolonged antibacillary treatment for a total of 18 months. However, due to the non-improvement marked by the lymphadenopathy size increase, a ganglion cleanse was indicated. The anatomopathological examination of the latter revealed a gigantocellular epithelioid granuloma with caseous necrosis and a negative GeneXpert.

The evolution was marked by the appearance of neurological signs indicative of spinal cord compression, for which the patient underwent a spinal cord magnetic resonance imaging (MRI). The scan revealed a lesion in the left paravertebral soft tissues affecting the left pedicle and partially extending into the vertebral body of D2. This led to a compression of latter and the invasion of the dorsal canal. Spinal cord compression was a result of this process and the findings were suggestive of Pott's disease or metastases (figure1.)



Figure 1. Sagittal spinal cord MRI section showing a lesional process affecting the left pedicle and partially extending to the vertebral body of D2 (yellow arrow.)

The clinical examination revealed a patient in a generally stable condition with a WHO performance status of 2. She was eupneic, with an oxygen saturation of 97% in ambient air with a normal pleuro-pulmonary examination. Upon inspection and palpation, the location of the bilateral ganglion cleanse shows scars without palpable lymphadenopathies. Neurological examination revealed signs of pyramidal irritation comprised of a positive Babinski sign and brisk osteotendinous reflexes in all four limbs.

As a part of the staging evaluation, a computed tomography of the chest, abdomen and pelvis (CCTAP) was performed, revealing an excavated lower-left lobar pulmonary mass with spiculate contours, showing a heterogeneous enhancement with contrast and extending into the fissure and parietal pleura. Additionally, the scan revealed the presence of a parenchymatous consolidation at the pulmonary apex with bronchiectasis (Figure 2.) The scan also showed extensive mixed disco-vertebral involvement from C3 to D4, with vertebral body compressions, mirror erosions, prevertebral infiltration without fluid collection, as well as epiduritis. Furthermore, there was also an infiltration of the left supraclavicular and lateral cervical regions, which included sternocleidomastoid muscle and subcutaneous fat.

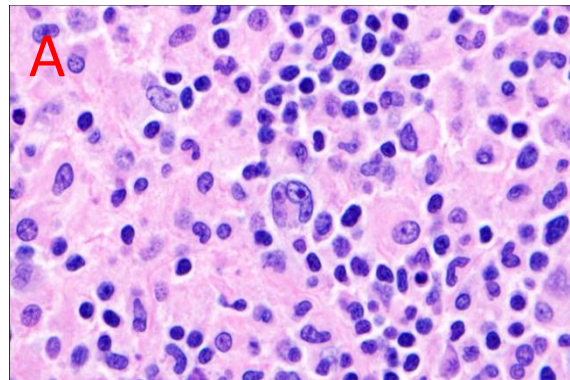
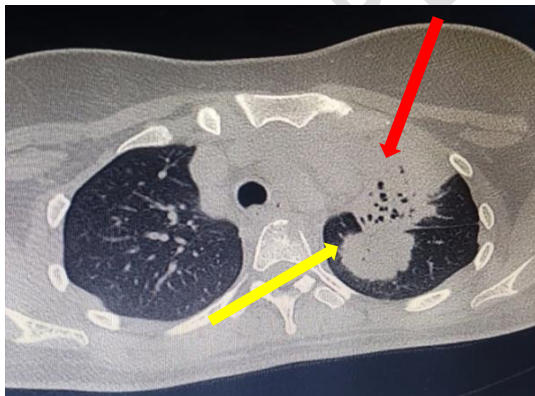


Figure 2. Axial parenchymal section of a thoracic CT showing condensation of the pulmonary apex containing bronchiectasis (red arrow), with left lower lobar pulmonary process (yellow arrow.)

The patient underwent a bronchofibroscopy, revealing a normal macroscopic appearance. The investigation for the existence of acid-fast bacilli, including direct examination and culture, as well as geneXpert MTB-RIF ultra, gene Xpert MTB-XDR and post-bronchoscopy sputum examination for Mycobacterium tuberculosis all

returned negative. Consequently, an ultrasound-guided biopsy of the infiltrated area was performed. The histological and immunohistochemical studies came back in favor of a classic Hodgkin lymphoma (figure 3.)

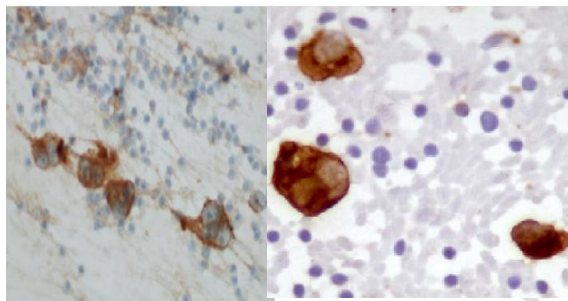


Figure 3. Histological findings of the patient showcasing:

A. Large binucleated reed-sternberg cells with prominent nucleoli in the left supraclavicular infiltration biopsy;

B. positive marking of CD 15 of Reed-sternbeg cells under immunohistochemistry;

C. positive marking of CD 30 of Reed-sternbeg cells under immunohistochemistry.

The investigations were completed with a positron emission tomography, which revealed a cervical-mediastinal hypermetabolic pathological tissue process affecting the trachea and the esophagus below the larynx, and invading the lungs laterally. Additionally, there was a posterior invasion of the spine between C4 and D4, with several vertebral lyses and spinal canal infiltration. Additionally, there was a parenchymatous consolidation containing sequellal-like bronchiectasis at the left pulmonary apex. The scan equally showed bilateral hypermetabolic pathological foci in the cervical and mediastinal lymph nodes (figure 4.)

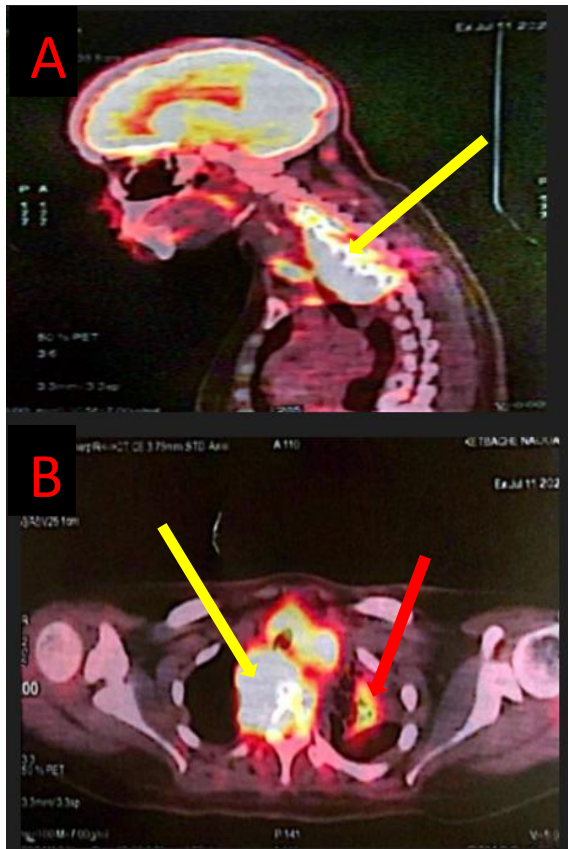


Figure 4. Fluorodeoxyglucose positron emission tomography – computed tomography (FDG-PET-CT) scan images pre-chemotherapy.

A. FDG-PET-CT sagittal section demonstrating metabolically active pathological cervical-mediastinal tissue process including the trachea and the esophagus with invasion of the spine between C4 and D4, in addition to vertebral lyses and spinal canal infiltration (yellow arrow.)

B. FDG-PET-CT axial section at the mid-thoracic level showing parenchymatous consolidation containing bronchiectasis at the left pulmonary apex (red arrow,) along with a tissue process invading lungs laterally (yellow arrow.)

For treatment, given the potential neurological risks, spinal surgery was not considered. Chemotherapy of the Hodgkin's Lymphoma was proposed leading to good clinical and radiological improvement (figure 5.)



Figure 5. Post-treatment axial image of FDG-PET-CT at the mid-thoracic level shows near complete resolution of the previously noted locally-advanced lung lesion, with a minimal remaining right paravertebral thickening at the level of D2-D3.

DISCUSSION:

Cervical lymphadenopathy is a reoccurring symptom in various pathologies notably TB and lymphoma [5]. This could explain the confusion and the misdiagnosis in the case in our hands. While the typical clinical presentation of HL involves palpable swollen 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 medullar compression symptoms, with a prevalence of about 5% of the total number of solid tumors, which also constitute up to 5% of the medullar compression presentations [8].

Histologically, the presence of epithelioid granulomas is a strong argument in favor of a TB diagnosis. The central caseous necrosis is not always present. However, when it is, it is considered strong evidence of TB, albeit non-specific. Similarly, gigantocellular epithelioid granuloma is not specific to TB as it may also be found in sarcoidosis, brucellosis, leprosy, and lymphoma, amongst other conditions [15].

One of the potential differentials for HL is TB [5]. This was the case with our patient whose cervical lymphadenopathies, apical parenchymatous consolidation, granulomatous lesion featuring caseous necrosis on the first biopsy, and the lesions simulating Pott's disease with spondylodiscitis under imaging, all directed the diagnosis process towards a potential multifocal TB.

When TB is suspected, multiple exams and tests could be useful to confirm the diagnosis. This includes the isolation of Mycobacterium Tuberculosis off bodily fluids or tissues, other techniques used include cultures, smear tests for AFB, and/or rapid nucleic acid amplification tests like GeneXpert® [9, 10]. These tests were used to assess a potential TB diagnosis in our patient's case. However, all of them returned negative prior to the initiation of treatment. In a similar fashion, TB culture results that came 6 weeks later also showed no evidence of the existence of TB. When resistance to treatment is suspected, especially following non-amelioration, the usage of MTX-XDR could be useful to reveal if the suspicion is correct [10].

Inflammation and medullar lymphocyte proliferation alongside the existence of TB may contribute to the transformation of lymphocytes into CD5+ CD20+ CD23+ tumor lymphocytes. Conversely, the onset of TB, occurring following immunosuppression, could have been a secondary result to the development of B-cell tumor clone [11, 12]. Despite the aforementioned association, TB has not been kept as a final diagnosis due to the non-amelioration and the worsening of clinical and radiological signs, even though the patient underwent anti-TB treatment and had a good therapeutic adherence. Repeated TB-specific tests all returned negative, and ultimately, the diagnosis of HL was confirmed following biopsy of the left supraclavicular infiltration.

Regarding antibacillary treatment, the period required to complete the treatment could lead to a delayed diagnosis of lymphoma, such is the case with our patient. The long therapeutic duration alongside the lack of a regular follow-up during this period, are likely to lead to the deteriorated general condition of the patients when the lymphoma diagnosis is made [13].

The question to be asked is at which point should an alternative diagnosis be considered in the work-up for TB and when should we consider performing a biopsy and immunohistochemistry—the definitive diagnostic test which can identify both TB and lymphoma.

The current National Institute for Health and Care Excellence (NICE) guidelines for TB do not specifically mention the situations where alternative diagnoses should be considered. These guidelines also do not specify which clinical or ancillary elements could be useful in making the difference between the condition [10, 14]. Possible elements that could suggest other conditions other than TB include: the lack of known exposure to TB or the lack of a prior TB infection, affected supraclavicular lymph nodes, first-line TB work-up with negative results, and the non-amelioration of the condition following antibacillary treatment that lasted for 2 months [15].

The mortality rate regarding HL has been decreasing, likely due to early cancer diagnosis and advancements in treatment. However, HL is still considered an aggressive form of lymphoma and any potential delay in diagnosis and treatment could negatively affect the patient's prognosis. The delayed diagnosis in our patient's case was mainly due to her young age, the existence of cavitary lesions in the lungs, as well as the spinal involvement following the lymphadenopathy, this in addition to the granulomatous lesion observed in the biopsy.

Regarding therapy and prognosis, it was found that patients that were initially treated with antibacillaries got to more advanced stages and worse prognoses compared to those who had received no treatment. Similarly, higher rates of treatment failure and mortality was observed in patients treated as tuberculosis cases than those who were not treated [16].

In our case, following chemotherapy, there was an amelioration in terms of clinical symptoms including the regression of functional impairment. Imaging showed a near-complete disappearance of the consolidation, the pulmonar mass, as well as the cervico-mediastinal process. HL is a potentially treatable condition.

CONCLUSION:

Cervical lymphadenopathies could be the manifestation of multiple underlying etiologies which may pose multiple challenges.

Our report suggests that more discussion should take place amongst clinicians concerning the diagnosis of TB. This is especially required when the initial treatment of TB with antibacterials has failed. Further investigations comprised of biopsy and histopathological examinations may provide great arguments to establish an accurate diagnosis.

Giant epithelioid granulomas with caseous necrosis are not exclusive to TB, the possibility of a lymphoma should also be considered in this context. Biopsy coupled with lymphadenectomy and immunohistochemistry should be systematized in all patients presenting with lymphadenopathies.

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