

A Case of Hodgkin's Lymphoma Mimicking Tuberculosis in 9-Year-Old Boy

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Abstract: *Concomitant presentation of TB and lymphoma is a rare entity. We described a 9-year-old boy with multiple lymphadenopathy on neck and armpits that initially diagnosed with clinical tuberculosis. Diagnostic workup by lymph node biopsy was in accordance with tuberculous lymphadenitis. Antituberculosis medication was given for 9 months without improvement of clinical manifestation. Biopsy examination was done for evaluation of therapy and revealed mixed cellularity Hodgkin lymphoma. Chest multi sliced computed tomography scan with contrast revealed paraesophageal lymphoma. Patient's condition was deteriorated due to self-decline of chemotherapy. Patient was planned to initiate chemotherapy after the condition stabilized.*

Keywords: children, Hodgkin's lymphoma, lymphadenopathy, tuberculosis.

1. Introduction

Of all the paediatric malignancies, lymphomas account for about 10-15% of the cases with half of them diagnosed as Hodgkin's lymphoma. Remarkably, this malignancy has a high cure rate with a 5-year survival rate approaching 95%. Hodgkin's lymphoma has an overall incidence rate of 14 per 100,000 under 15 years of age. It has a typical bimodal distribution with respect to age. In developed countries, the peak incidence is seen in the young adults and elderly. While, in developing countries the incidence is higher among children and young adults with a male preponderance. Histologically, mixed cellularity subtype of classical Hodgkin's lymphoma occurs commonly in the children and in developing countries.[1]

Hodgkin's lymphoma has similar clinical presentation with tuberculosis (TB). However, concomitant presentation of TB and lymphoma is a rare entity. Very few case reports of such a presentation are published till date. A primary malignancy like Hodgkin's lymphoma may cause a suppression of the cell-mediated immunity which predisposes to a concomitant TB infection. Tuberculosis and Hodgkin's lymphoma have similar signs and symptoms like cough, fever, loss of appetite, loss of weight, night sweats, hepatosplenomegaly and mediastinal adenopathy, therefore misdiagnose or delay in diagnosis of both TB and Hodgkin's lymphoma may occur. [2]

2. Case Report

A 9-year-old boy complained of painless lumps on both sides of neck and armpits that appeared since 15 months prior to admission. The lumps were noticed on November 2019 with the size of a peanut, without sign of inflammation. Patient also complained of intermitten fever since 1 month before admission, without any respiratory symptoms. Patient's weight had decreased for 2 kg since last

1 month, not accompanied by night sweating. Patient had contact with relative that diagnosed with confirmed tuberculosis, and still underwent antituberculosis therapy. Initial ultrasonography examination found multiple hypoechoic nodular lesion with fine border, regular surface, with largest diameter of 1.34 x 0.80 x 2.12 cm at right cervical and 1.33 x 0.46 x 0.91 cm at left cervical. Chest x-ray examination found hilar lymphadenopathy. Initial cervical lymph node biopsy result in accordance with tuberculous lymphadenitis. Evaluation of tuberculosis scoring was 6, consist of tuberculosis contact (3), prolong fever (1), moderate malnutrition (1), and lymphadenopathy (1), therefore patient was diagnosed with clinical tuberculosis and got antituberculosis medication. After 6 months of antituberculosis therapy, the cervical lymph nodes were enlarged with largest diameter of 3 cm. Acid-fast stain of gastric lavage found negative result, however the antituberculosis medication were continued.

Follow up after 9 months of therapy found persisted lymphadenopathy. Patient also looked pale since the prior three weeks, accompanied with decreased body weight, night sweat, and occasional back pain. There was no fever and respiratory symptoms. Reevaluation of biopsy examination of left cervical lymph node found unclear lymphoid follicle structure, consists of lymphocytic cells with same nucleus as mature lymphocytes, Dutta Reed Steinberg cells with prominent nucleolus and multiple nucleoli, in accordance with mixed cellularity Hodgkin lymphoma. Multi sliced computed tomography (MSCT) scan of thorax with contrast revealed isodense lesion with fine and irregular border, with diameter of 3.76 x 4.38 x 3.14 cm at superior mediastinum-right lateral esophagus, no calcification and bone destruction, in accordance with paraesophageal lymphoma. Examination of lumbosacral MSCT found no abnormality. Patient was planned for chemotherapy, but the family refused to start the therapy.

3. Current Admission

Patient came to our center two months after diagnosed with Hodgkin Lymphoma, with chief complaint shortness of breath since 3 days before admitted to hospital. It also accompanied by abdominal swelling. Patient complained of intermitten fever since 3 months. The body weight was significantly decreased and he also had night sweating. Physical examination found dullness on both hemithorax with decreased vesicular breathing sound. Multiple firm and nontender lymphadenopathy at cervical and axillary region were found, with no sign of inflammation. Abdominal examination found splenomegaly of Schuffner III, flat surface without tenderness; and ascites. Chest x-ray examination found bilateral pleural efusion with upper border at third intercostal space (Figure 1). Abdominal ultrasonography (USG) found splenomegaly and ascites. Cervical USG found multiple hypoechoic nodular lesion with fine border, regular surface, with largest diameter of 1.12 x 0.64 x 1.97 cm at right cervical and 1.04 x 0.37 x 0.71 cm at left cervical, without calcification (Figure 1). Laboratory examination found leukocytes $3.1 \times 10^3/\mu\text{L}$ (neutrophils 84.6%, lymphocytes 9.4%), hemoglobin 2.9 g/dL (mean corpuscular volume 106 fL, mean corpuscular hemoglobin 32.2 pg), hematocrit 9.5%, thrombocytes $64 \times 10^3/\mu\text{L}$, albumin 3 g/dL, with normal renal and liver function test.

Patient had treated by chest tube insertion due to bilateral pleural efusion. A total 1100 of pleural fluid was evacuated, and the production was stopped on fourth day after chest tube insertion. Patient also got packed red cell transfusion due to severe anemia. Evaluation of complete blood count after blood transfusion found increased hemoglobin level to 6.3 g/dL, but decreased thrombocytes level to $51 \times 10^3/\mu\text{L}$. Patient was planned to be referred for chemotherapy after stabilization.

4. Discussion

Hodgkin's lymphoma is a B-cell neoplasm which cripples immune system of the host and promotes opportunistic infections like tuberculosis. Cell mediated immunity plays a pivotal role in the control of mycobacterial infection. Immunosuppression in Hodgkin's lymphoma often leads to Mycobacterial infection in these patients, hence increasing morbidity and mortality. The most common extra pulmonary type of tuberculosis is TB lymphadenitis (TB LAD) accounting for 20% of total TB cases diagnosed annually. Hodgkin's lymphoma (HL) has a low prevalence, with only 2.7 per 100000 cases occurring annually and comprising less than 0.5% of total malignancies discovered, making an association between the two diseases highly unlikely. While the most common malignancies in cervical lymphadenopathies are squamous cell carcinoma, adenocarcinoma, and lymphoma, TB LAD alone accounts for 45% of chronic cervical lymphadenopathies, while HL takes up around 2.5%. [3][11]

WHO classification categorises Hodgkin's lymphoma into classical and nodular lymphocyte-predominant types. Classical Hodgkin's lymphoma is further sub-typed into

nodular sclerosis, lymphocyte-rich, mixed cellularity and lymphocyte-depleted subtypes. [1] Nodular Sclerosis (NS) variant is the most common histopathological type of Hodgkin's disease among those who have mediastinal involvement. It is characterized histopathologically by the presence of classic Reed-Sternberg cells and/or its variants.

In Hodgkin's lymphoma, the neoplastic cells constitute less than 1% in the affected lymph node. Classical Reed-Sternberg cells are relatively infrequent, although cells with a similar phenotype but a varied morphology termed, as Hodgkin/Reed-Sternberg cells are common. Immunophenotypic studies show that these cells are derived from B cells in germinal centre of the lymph node and are CD15; CD30 positive. Interactions between Hodgkin/Reed-Sternberg cells and surrounding inflammatory cells are significant in the pathogenesis of Hodgkin's lymphoma. [1][15]

Paediatric Hodgkin's lymphoma commonly presents with unilateral, painless cervical lymphadenopathy. In 3% of cases, the primary site is subdiaphragmatic. Those with mediastinal involvement present with persistent cough. Rarely, the child may present with splenomegaly; enlarged axillary or inguinal lymph nodes 4. The "B" symptoms include temperature above 38°C , drenching night sweats, and unexplained loss of more than 10% of body weight within the past 6 months occur in about 50% of children from developing countries. [1][8]

Radiological investigations like CT and PET scan helps in localisation of the Hodgkin's lymphoma. The disease extent is evaluated with the Cotswolds' four-stage modification of the Ann Arbor classification. Management of Hodgkin's lymphoma, early-stage unfavourable disease comprises combined chemotherapy and involved-field irradiation. [7]

The most frequent causes of lymph node granulomas may be classified according to their coexistence with an infective agent. Infectious granulomas include two groups of diseases with suppurative and non-suppurative reactions. The second non-infectious granulomatous lymphadenitis may accompany several diseases with different etiopathogenesis, e.g. sarcoidosis, Hodgkin's and non-Hodgkin's lymphomas, sarcoidlike reactions in regional lymph nodes draining neoplasm or Crohn's disease, drug (phenytoin, procainamide, phenylbutazone, chlorpropamide, sulphasalazine, ibuprofen, indomethacin, allopurinol, carbamazepine, amiodarone) or foreign body (berylliosis, talc, anthracosis and silicosis) (Table I). [4][12]

Concomitant presentation of TB and lymphoma is a rare entity. Very few case reports of such a presentation are published till date. A primary malignancy like Hodgkin's lymphoma may cause a suppression of the cell-mediated immunity which predisposes to a concomitant TB infection. Misdiagnose or delay in diagnosis of both TB and Hodgkin's disease may occur because of similar signs and symptoms like cough, fever, loss of appetite, loss of weight, night sweats, hepatosplenomegaly and mediastinal adenopathy. Immunosuppression is the main cause of

Mycobacterial infection in Hodgkin's disease and TB is the main cause of mortality in such cases. [2][6]

Table 1: Frequent cause of lymph node granuloma

Infectious		Non-infectious
Suppurative	Suppurative	
Almost all have central abscesses and necrosis in granulomas induced by Gram-negative bacteria and chlamydia.	Hypersensitivity-type granulomas induced by microorganisms; predominant histiocytes with smaller numbers of T-cells, dendritic cells and peripheral B-cells are recruited for granuloma formation.	Rarely abscesses and necrosis in the centre of granuloma.
Examples		
Tularemia lymphadenitis Cat scratch lymphadenitis Yersinia lymphadenitis Lymphogranuloma venereum Fungal infection	Tuberculous lymphadenitis Atypical mycobacterial infection BCG lymphadenitis Toxoplasma lymphadenitis (Piringer-Kuchinka lymphadenopathy) Leprosy Syphilis Brucellosis Fungal infection Cryptococcus Histoplasma Coccidioidomycosis Pneumocystis	Sarcoidosis Hodgkin lymphoma Non-Hodgkin lymphomas Lymph node draining neoplasm (sarcoid-like reaction) Lymph node draining Crohn's disease Berylliosis

Lymphadenitis is the most common form of extrapulmonary tuberculosis (TB) (5-10%) and in the developing countries its overall incidence is estimated at approximately 40%. Distinctively, in about 90% of cases superficial lymph nodes in the head and neck region are involved; rarely generalized lymphadenopathy and hepatosplenomegaly are described. Major histological features are: chronic granulomas, predominantly with caseation necrosis, concentric layers of epithelioid cells, Langhans giant cells. Extended fibrosis and hyalinization may be present in later phases. Acid-fast bacilli can be visualized by Ziehl-Neelsen staining. [4]

TBLN or lymph node TB is considered a local manifestation of the systemic disease. TBLN most frequently involves the cervical lymph nodes followed in frequency by mediastinal, axillary, mesenteric, hepatic, portal, perihepatic and inguinal lymph nodes. The systemic symptoms are not common in TBLN. It presents as unilateral painless swelling of the lymph nodes, most commonly at posterior cervical and supraclavicular sites, it represents 63-77% of the cases and bilateral disease is uncommon (26% of the cases). In initial stage, TBLN usually shows marked hyperemia, swelling, necrosis, and caseation of the center of the nodes. Then develops into a matted non-tender mass over time and may result in ulceration, fistulous tract draining caseous material or abscess formation. [5]

The diagnosis can be established by (1) Fine-needle Aspiration Biopsy (FNA) (with a yield up to 80%). Caseating granuloma with acid-fast bacilli (AFB) positivity is fairly sensitive and specific for the diagnosis of TB (85%). FNA and Mantoux test were able to diagnose 90% of the cases; (2) Surgical Excision Biopsy, is preferred over incisional biopsy, the latter may be associated with sinus

tract formation. Surgical biopsy-excision of the lymph node is the best examination for diagnostic confirmation with sensitivity of 100% for histological analysis and 60-90% for the bacilli culture. (3) Bacteriologic confirmation is achieved in the vast majority of cases, granulomatous lesion or without visible AFBs are typically seen, and cultures are positive in 70-80% of cases. However, the negative culture does not necessarily exclude the diagnosis because not all enlarged lymph nodes necessarily contain live bacilli. ;(4) Molecular Diagnosis or Nucleic Acid Amplification (NAA) is used to detect mycobacterial DNA instead of detection of Mycobacteria and drug resistance earlier compared to conventional methods. ;(5) Ultrasound (USG) and CT scan are known to be effective for detecting enlarged lymph nodes and widely used to obtain information about the size of lymph nodes, localization and accessing their relation with major structure in the neck. They are also useful in guidance for biopsy aspiration. [5]

Mediastinal TB is also characterized by enlarged hilar and mediastinal nodes although more often it is mentioned that TB lymphnodes are unilateral and Hodgkin's is bilateral asymmetrical. It is not uncommon to find mediastinal TB with bilateral involvement of mediastinal nodes. It is often said that fine needle aspiration cytology (FNAC) is not a good method to diagnose Hodgkin's disease as the core and smears are not sufficient to make a confident diagnosis. The yield is higher with mediastinoscopy and anterior mediastinotomy. Ann Arbor classification is used for staging this disease.[2]

Malignant pleural effusion (MPE) is presentation of many malignancies. In 10% of patients with undiagnosed pleural effusion, a lymphoma is finally detected. MPE is observed in 10-30% of patients with Hodgkin's lymphoma at presentation (3-5) up to 20% (7,8) of Non Hodgkin's lymphoma. In pleural effusion caused by lymphoma, to make a definitive diagnosis of lymphoma is not easy, as either lymphomatous cells in pleural fluid are sparse or cells in pleural fluid looks similar to lymphocytes in other tissues involved, such as lymph nodes. MT has been a routine method for patients with exudative pleural effusion that remain undiagnosed by clinical, radiologic, laboratory or cytological investigation. It was found in one study that extensive infiltration of pleura indicates that the major mechanism for the development of PE is the direct involvement of the pleura by lymphoma, rather than obstruction to lymphatic flow as seen in present case.[9][13][14]

There are no definite investigative modalities other than histopathological examination to establish the diagnosis. Because of the underlying immune suppression, diagnostic utility of tuberculin skin test is very low in the background of a malignancy. Also modern imaging modalities such as FDG PET, FDG PET/CT fusion, whole body MRI (WB MRI) and multidetector CT (MDCT) shown promise in staging of lymphoma but not in arriving at the diagnosis. Thus the treatment of this condition is invariably targeted at treating TB simultaneously with Hodgkin's disease. [2]

The CT imaging showed numberless miliary opacity and was similar to miliary tuberculosis, but histopathological

analysis revealed that lesions was found in both perilobular and bronchovascular distribution. Lymphoma cells flowing in the peripheral blood and lymphatic system might have spread throughout the whole body from the capillaries, settling in the lymphohematopoietic system, such as lymph nodes, bone marrow, liver. Eventually, they might allow colonizing in the mucosa-associated lymphoid tissue of the bronchi and bronchioles, forming nodules.[10]

5. Conclusion

The coexistence of HL and granulomas can be tricky and may lead to inappropriate diagnosis. Cases of HL and tuberculosis are very rare and require additional tests to confirm the presence of microorganisms. Treatment of M. tuberculosis infection usually improves the outcome and effect of chemotherapy. Each elderly patient with HL suspicion is recommended for revised, histopathological examination. The morphology of HRS/lacunar cell as well as immunohistochemical profile are most helpful in differential diagnosis. In cases where granulomas coexist with negative acid-fast staining, pathologists should always recommend further and broader diagnostic procedures to be performed.

6. Disclosure

The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study.

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None declared

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References

- [1] Kandukuri Mahesh Kumar, KaziWajid Husain, ChinthakindiSravan, R. Swarupa, KonduruOmkareshwar. Early-stage Hodgkin's lymphoma in a child: a case report". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 10, March 10; Page: 2649-2654
- [2] Ramanjula C. Reddy, Meghena Mathew, Ashok Parameswaran1, R. Narasimhan. A case of concomitant Hodgkin's lymphoma with tuberculosis. Lung India • Vol 31 • Issue 1 • Jan - Mar 2014
- [3] Promil Jain, Deepak Jain, KajareeGiri. Co-Existent Hodgkin's Lymphoma and Tuberculosis A Rare Case Report. The Journal of International Medical Sciences Academy 2018 ; (July – Sept.); Vol 31; No. 3
- [4] Anna Szumera-Ciećkiewicz z1, Monika Proc horec-Sobieszek1, Ewa Lech-Marańda2. Hodgkin's lymphoma mimicking tuberculosis in cervical lymph node. Polish Journal of Pathology.2014; 65 (1): 83-88
- [5] NenciSiagian, Bramantono, Usman Hadi. Tuberculous Lymphadenitis coexists with Non-Hodgkin Lymphoma. Current Internal Medicine Research and Practice Journal of Surabaya. Agustus 2020Vol 1 no 2.
- [6] Abdul Khaleque, Golam Hafiz. Tuberculosis Lymphadenitis in a Child with Hodgkin Lymphoma. Oncopedia. July 2010. No 395
- [7] Christine Mauz-Körholz, Monika L. Metzger, Kara M. Kelly, Cindy L. Schwartz, Mauricio E. Castellanos, Karin Dieckmann, Regine Kluge, Dieter Körhol. Pediatric Hodgkin Lymphoma. Journal of Clinical Oncology. September 2015. Vol 33. Number 27
- [8] Mehmet Erkan Kaplama, Ahmet Kursad Gunes, Burk Erden. Evaluation of the predictive role of neutrophil/lymphocyte ratio in the diagnosis of lymphoma in patients with asymptomatic and isolated cervical lymphadenopathy. Brazilian Journal of Otorhinolaryngology. April 2020. Page 7.
- [9] Asmita A. Mehta, Tajik M. Shafi, Ajit Nambiar, Keechilat Pavithran. Diagnostic utility of medical thoracoscopy in T cell lymphoblastic lymphoma presenting with pleural effusion. Respiratory Medicine Case Reports 32 (2021) 101322.
- [10] K. Yagy, et al. Malignant lymphoma mimics miliary tuberculosis by diffuse micronodular radiographic findings. Respiratory Medicine Case Reports 31. 2020. 101239.
- [11] SinanDeeba, TareqAlib, HaithemRehanc. Rare incidence of concomitant Hodgkin's lymphoma with tuberculous lymphadenitis: A case report. Otolaryngology Case Reports 14. 2020. 100142
- [12] Rama Kumari Badyal, et al. Hodgkin Lymphoma Masquerading as Tuberculosis in a Young Chronic Smoker. Indian Society of Haematology & Transfusion Medicine. 2014. S428–S432.
- [13] Rui Lin Chen, Yong Qing Zhang, Jun Wang, Hua Wu. Diagnostic value of medical thoracoscopy for undiagnosed pleural effusions. Experimental and Therapeutic Medicine. 2018. 16: 4590-4594.
- [14] Zhen Wang, Yan Bing Wu, Li Li Xu. Diagnostic value of medical thoracoscopy in malignant pleural effusion induced by non Hodgkin's lymphoma. Oncology Letters. 2017. 14: 8092-8099
- [15] James R. Stier, Robert J. Vasquez. Lymphocyte-Predominant Hodgkin's Disease in Children: A Case Study and Review of the Literature. Case Report in Oncological Medicine. Vol 2015. Page 5.