

Case Report

Hodgkin lymphoma and bone marrow tuberculosis: A coincidence

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ABSTRACT

Hodgkin lymphoma is a type of lymphoma that occurs due to mutations in B cells of the lymphatic system. Cases of lymphoma often have identical clinical manifestations with tuberculosis (TB), making the diagnosis difficult. Case of lymphoma coincidence with TB is rare, but can probably cause complexity in the diagnosis and treatment of patients. We report the case of a 20-year-old male patient who presented with symptoms of prolonged fever, enlarged lymph nodes, loss of weight, and weakness. The patient was treated with antituberculosis medication, but the symptoms did not improve. Several investigations were carried out on the patient. Lymph node biopsy showed scattered tumor cells consisting of mononuclear Hodgkin cells with several Reed–Sternberg cells. On the other hand, the bone marrow aspiration examination was positive for *Mycobacterium tuberculosis*. Reconsideration of confirmed diagnosis and repeated diagnostic process are required when there is a discrepancy in clinical features, radiological findings, or treatment responses.

Keywords: Hodgkin, Tuberculosis, Bone marrow

INTRODUCTION

Lymphoma is a type of cancer that arises from the lymphatic system and is characterized by abnormal cell division of B and T lymphocytes which plays a role in the body's immune system. It is the sixth most common type of cancer in Indonesia.^[1] Hodgkin lymphoma is a type of lymphoma that occurs due to mutations in B cells of the lymphatic system.^[2] Hodgkin lymphoma accounts for 10–15% of all lymphoma cases and 1% of all cancer cases worldwide.^[2,3] In Asia, the incidence of Hodgkin lymphoma was reported to be 0.4 per 1,00,000 people per year.^[3]

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. The prevalence of TB in Indonesia was reported to be 759 per 1,00,000 people aged 15 years and above.^[4] The clinical manifestations of TB vary widely, from pulmonary TB to extrapulmonary TB, which includes bone marrow TB. Cases of lymphoma, especially in the early stages, and TB often have identical clinical manifestations, making the diagnosis difficult.^[5] Several case reports have noted that the difficulty in diagnosing lymphoma

or TB can cause delay in treatment and worsen the patient's prognosis.^[1,6,7] Moreover, cases of lymphoma and TB can also occur simultaneously, resulting in additional complexity in the diagnosis and treatment of patients.

Here, we present the case of a patient with Hodgkin lymphoma who has coexisting bone marrow TB. We also conducted a review of the relevant literature.

CASE REPORT

A 20-year-old male patient presented with a main symptom of fever for three months, especially at night. The patient also complained of enlarged lymph nodes in the neck, armpits, and groin. In addition, the patient experienced night sweats as well as weight loss of up to 9 kg in the last three months. Initially, the patient was treated with antituberculosis medication, however even after one month of treatment his symptoms did not improve. The patient then complained of additional symptoms, namely, weakness, and we found that his levels of red blood cells were continuing to fall even though he had repeatedly received blood transfusions.

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Several investigations were carried out on the patient. According to a laboratory examination of blood, he had anemia and thrombocytopenia. Examination of the peripheral blood morphology showed anisopoikilocytosis with the presence of target cells and fragmentocytes. The Coombs test revealed a warm type of autoimmune hemolytic anemia. The patient then underwent a positron emission tomography-computed tomography scan (PET-CT scan), and multiple lymphadenopathy were found in the neck, axillary, retropectoral, paratracheal, gastrosplenic, paracolic, pericaval, aortocaval, paraortic, parailiac, and inguinal regions, with the highest variable standardized uptake value (SUV) at 20.56 [Figure 1a]. In addition, splenomegaly with multiple nodules was observed, as well as multiple hypermetabolic lesions in the bone marrow [Figure 1b].

The patient then underwent neck lymph node biopsy as well as aspiration and bone marrow biopsy. Bone marrow aspiration examination did not reveal any abnormalities, but mycobacterium TB was found during polymerase chain reaction (PCR) examination. Bone marrow biopsy revealed hypocellular bone marrow and no lymphocyte infiltration. The results of the lymph node biopsy revealed scattered tumor cells consisting of mononuclear Hodgkin cells and several Reed–Sternberg cells [Figure 2a–b]. The tumor background was predominantly mature lymphocytes. Immunohistochemistry examination showed a Cluster determinant (CD) CD30-positive status in tumor cells and a CD15-positive status in some [Figures 2c and 2d]. Paired box 5 (PAX5) and CD20 were weakly positive [Figure 2e–2g], while MUM1 was highly positive in tumor cells [Figure 2f]. CD3 was positive only in reactive mature lymphocytes [Figure 2h].

In this case, the diagnosis confirmed lymphocyte-rich classical Hodgkin lymphoma, and chemotherapy was planned for the patient. However, his condition during treatment worsened,

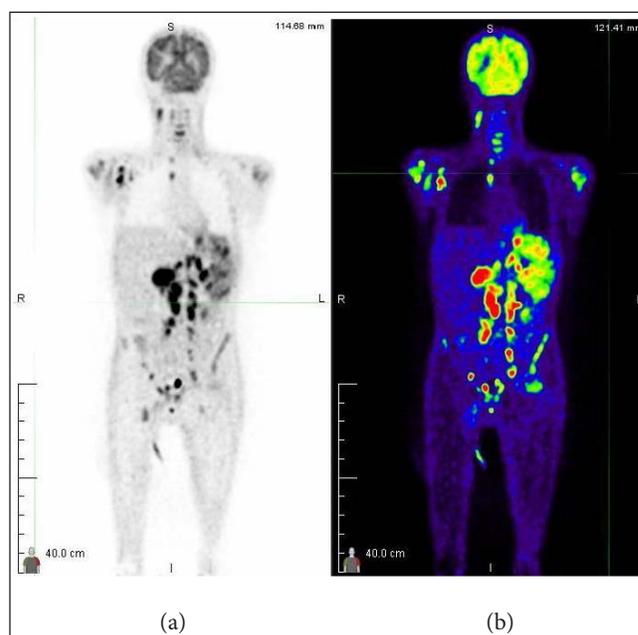


Figure 1: (a) PET-CT scan showed multiple lymphadenopathies in multiple regions. (b) PET-CT scan showed multiple hypermetabolic lesions in the bone marrow. PET-CT: Positron Emission Tomography and Computed Tomography.

and eventually the patient died from sepsis due nosocomial pneumonia.

DISCUSSION

Hodgkin lymphoma accompanying TB is a rare finding. There are only a few case reports of TB and Hodgkin lymphoma coinfection.^[8] Rokitansky noted the antagonistic relationship between cancer and TB. Subsequently, this was contradicted by a study involving 13 cases of lung TB with co-occurring cancer.^[9] In a study of 201 cases,

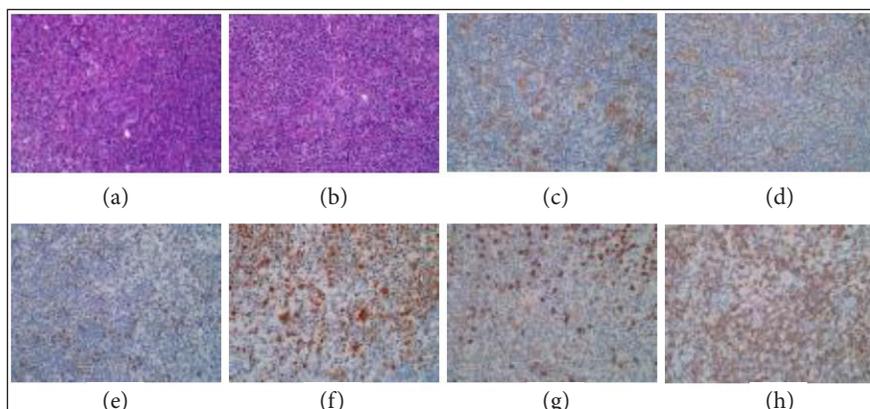


Figure 2: (a) HE; 400X (b) HE; 400X (c) IHC; CD30-positive; 400X (d) IHC; CD15 some positive 400X, positive; 400X (e) IHC; PAX5 weakly positive; 400X (f) IHC; MUM1 positive; 400X (g) IHC; CD20 weakly positive; 400X (h) IHC; CD3-negative; 400X. HE: Histopathology Examination; IHC: Immunohistochemistry; PAX5: Paired box; MUM1: Multiple myeloma oncogene 1; CD: Cluster of Determinant.

Kaplan *et al.*^[10] found that the prevalence of Hodgkin lymphoma was 96 out of 10,000 in at-risk TB patients. A recent retrospective study in Guatemala and Argentina from 2010 to 2019 reported ten patients with Hodgkin lymphoma coexisting with TB.^[11] Costa *et al.*^[12] reported three cases of Hodgkin lymphoma with simultaneous pulmonary or nodal TB. Several studies have reported the concomitant occurrence of Hodgkin lymphoma and lymphadenitis TB, as lymph node involvement in TB is its most frequent manifestation.^[13,14] Bone marrow involvement is an uncommon manifestation of extrapulmonary TB.^[15] Although a few cases have been reported, the diagnosis of bone marrow TB is still challenging due to the variety of manifestations.^[16,17] Numerous prior case reports stated that the incidence of TB and Hodgkin lymphoma was based on biopsies of the lymph nodes or lungs. In this case report, TB infection was discovered on bone marrow examination.

The coincidence of Hodgkin lymphoma and TB is difficult to diagnosis, and thus diagnosis is often delayed.^[5,13] The two diseases manifest similar symptoms, including fever, weight loss, night sweats, decreased appetite, and lymphadenopathy.^[8] In this case, cervical gland biopsy and bone marrow aspiration were performed simultaneously. This was done based on clinical and radiological evaluations. The patient had received TB drugs when referred to our center, but his clinical condition worsened. A high fever, weight loss, and night sweats persisted despite three months of TB treatment. Additionally, the patient had anemia and thrombocytopenia. These findings were the basis for performing a bone marrow aspiration and biopsy in this case.

After being referred to the hematology polyclinic, a PET-CT scan was performed, which revealed multiple lymph node enlargements. Many case reports have stated that PET-CT scan images with multiple lymphadenopathies with contrast uptake, which were initially presumed to be lymphoma, turned out to be a TB infection.^[1] Accordingly, we must be careful when assessing the relationship between clinical and radiological features, and histopathological results play an important role. In our patient, the site of lymph node biopsy was selected based on the high contrast uptake value and accessibility, so it was more likely that the results would be representative.

Malignancies and chemotherapy are well-known risk factors for TB.^[18,19] The meta-analysis by Dobler *et al.*^[20] found that malignancies, especially hematologic malignancy, significantly increased the risk of TB in adults (IRR 3.53; 95% CI 1.63–7.64) and children (IRR 16.82, 95% CI 8.81–32.12). Principal immunity against TB infection is a cell-mediated immune response primarily led by CD4 T-lymphocytes.^[14,21] Patients with Hodgkin lymphoma experience cell-mediated

immunity impairment, predisposing them to TB infection or reactivation.^[14] Additionally, there is a decrease in glutathione (GSH) in Hodgkin lymphoma. This results in the weakening of the defense system against the pathogen.^[22] Based on this, it is assumed that the mortality rate following concomitant TB infection and Hodgkin lymphoma is high.

The survival rates of patients with Hodgkin lymphoma improve with the advancement of therapy.^[23] However, infections are a major cause of mortality in Hodgkin lymphoma patients.^[24] Stimulation by infectious antigens disrupts the microenvironment and sustains the growth of neoplastic cells, contributing to the failure of oncology therapy.^[25] Furthermore, concomitant Hodgkin lymphoma and infection may hinder diagnosis, resulting in increased mortality due to inadequate treatment.^[26]

CONCLUSION

This case report involved the co-occurrence of bone marrow TB and Hodgkin lymphoma. Clinicians should reconsider confirmed diagnoses and repeat the diagnostic process when there is a discrepancy in clinical features, radiological findings, or treatment responses.

Ethical Approval

Not applicable.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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