Case Report

Hemophagocytosis lymphohistiocytosis associated with HIV-negative Primary Bone Marrow Hodgkin Lymphoma (PBMHL)

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Abstract:

Hemophagocytosis lymphohistiocytosis associated with Primary Bone Marrow Hodgkin Lymphoma (PBMHL) is a rare condition that uncommonly seen in clinical practice, especially in HIV-negative patients. Herein, we reported an elderly man manifested with prolonged fever without initial evidence of infection or malignancy. After cytopenia was progressed, he was proceeded to bone marrow examination. Increasing of histiocytes with hemophagocytic activity was reported. Pathology of bone marrow showed atypical Reed Sternberg cells. Immunohistochemical staining was done for diagnosis. Positivity of CD 15, CD 30 and Epstein-Barr virus encoded small RNA (EBER) in situ hybridization in the atypical Reed Sternberg cell suggested Primary Bone Marrow Hodgkin Lymphoma (PBMHL). Chemotherapy ABVD regimen was given as definite treatment.

Keywords : ● *Hodgkin lymphoma* ● *Bone marrow* ● *Hemophagocytic syndrome*

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รายงานผู้ป่วย

Hemophagocytosis lymphohistiocytosis associated with HIV-negative Primary Bone Marrow Hodgkin Lymphoma (PBMHL)

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บทคัดย่อ

Hemophagocytosis lymphohistiocytosis associated with Primary Bone Marrow Hodgkin Lymphoma เป็นภาวะที่พบได้น้อยในเวชปฏิบัติ โดยเฉพาะอย่างยิ่งในกลุ่มคนไข้ที่ไม่มีการติดเชื้อ HIV ด้วยเหตุนี้ ทางคณะผู้วิจัยจึงได้ทำการรายงานผู้ป่วย ซึ่งมีอาการนำมาด้วยไข้ ไม่ทราบสาเหตุ หลังจากทำการส่งตรวจเพิ่มเติม ไม่พบหลักฐานของการติดเชื้อ หรือ มะเร็ง รวมทั้งไม่มีต่อมน้ำเหลืองที่โตขึ้น อย่างมีนัยสำคัญ อย่างไรก็ตามหลังจาก ติดตามผู้ป่วยไประยะหนึ่งพบว่ามี เม็ดเลือดแดง เม็ดเลือดขาว และเกล็ดเลือด ลดลงผิดปกติ จึงได้ทำการเจาะตรวจไขกระดูก พบ Histiocyte รวมถึง Hemophagocytic activity ที่เพิ่มมากขึ้น และพบ เซลล์ผิดปกติ คล้าย Reed Sternberg เซลล์ หลังจากการย้อมพิเศษเพิ่มเติม พบว่าผล CD 15, CD 30 และ Epstein-Barr virus encoded small RNA (EBER) in situ hybridization เป็นบวก จึงได้ทำการวินิจฉัย Primary Bone Marrow Hodgkin Lymphoma และได้ทำการเริ่มยาเคมีบำบัด สูตร ABVD

คำสำคัญ : ● *Hodgkin lymphoma* ● *Bone marrow* ● *Hemophagocytic syndrome*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต 2562;29:55-9.

Introduction

The most common cause of pancytopenia is bone marrow defect ranging from benign to malignant process. Hemophagocytosis lymphohistiocytosis (HLH) associated with Primary Bone Marrow Hodgkin Lymphoma (PBMHL) is a rare condition, hardly seen in clinical practice.

Case report

A 64-year old man presented with prolonged fever for 2 months, accompanied with drenching night sweat and significant weight loss. His physical examination revealed mild pallor without palpable lymph node, liver or spleen.

Complete blood count showed hemoglobin (Hb) of 10.4 g/dL, white blood cell (WBC) count of 2.9 x 10^9/L (neutrophil 46.9% lymphocyte 36.2% monocyte 15.2%) and platelet count of 66 x 10^9/L. Septic work-up, as well as the serologic tests for viral hepatitis and Human Immunodeficiency Virus (HIV), were negative. There was neither abnormal cell nor leukoerythroblastic blood picture observed from the peripheral blood smear.

CT scan of the chest and abdomen showed only subcentimeter mediastinal lymph nodes and mild hepatosplenomegaly without focal lesion.

After receiving board spectrum antibiotic for a week, he continued having a low-grade fever and worsening pancytopenia with Hb of 6.3 g/dL, WBC of 1.4 x 10^9/L (neutrophil 55.9% lymphocyte 24.7% monocyte 6.5%) and platelet count of 20 x 10^9/L. Serum ferritin was remarkably elevated of 10,043 ug/L.

Bone marrow examination showed trilineage hematopoiesis with a left shift of myeloid maturation. Intracellular organism or abnormal cells were not detected. There were increasing numbers of histiocytes with hemophagocytic activity. Bone marrow histopathology demonstrated atypical Reed Sternberg (R-S) like cells. (Figure. 1)

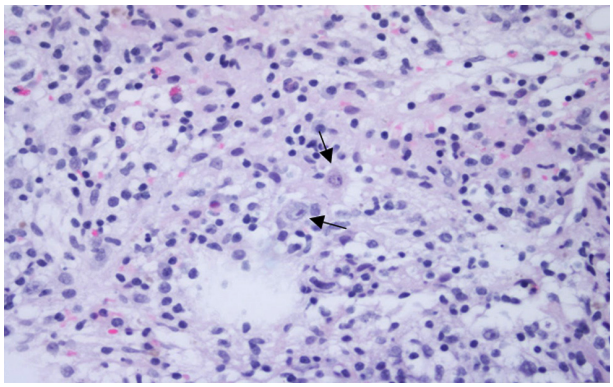

Figure 1 Bone marrow biopsy H&E show some large atypical Reed- Sternberg cells in the background of small lymphocytes

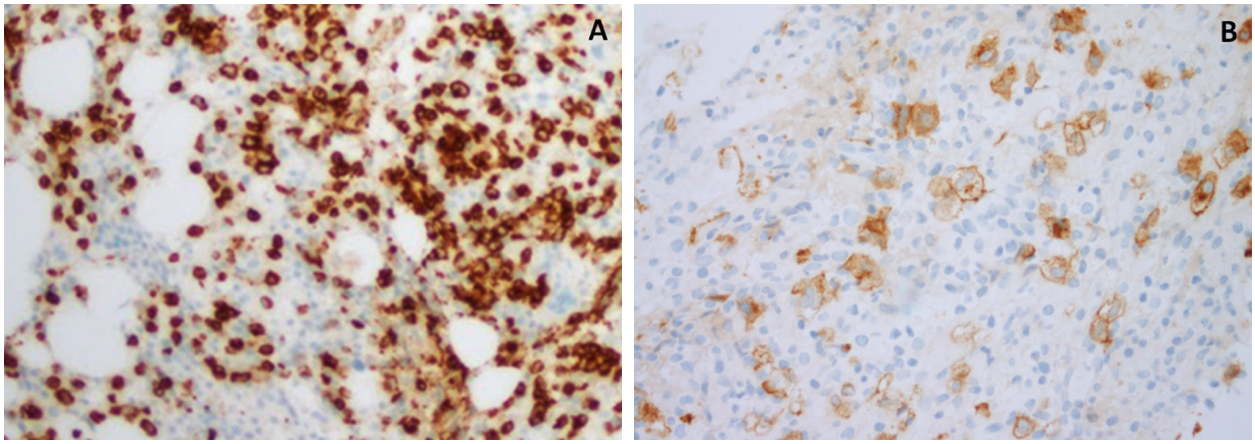

Figure 2 Immunohistochemical stains show CD 15 positive including tumor cells and background (A). CD 30 positive in atypical Reed- Sternberg cell with cytoplasmic and nuclear staining pattern (B).

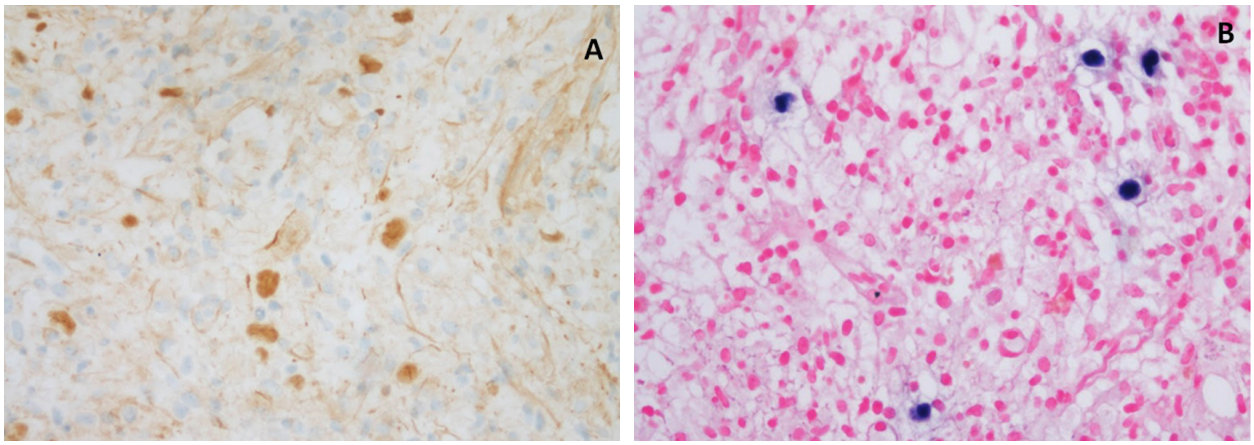

Figure 3 Immunohistochemical stains of show PAX-5 positive (A). EBV positive in atypical Reed- Sternberg cell with cytoplasmic and nuclear staining pattern (B).

By immunohistochemistry, the atypical R-S like cells were positive for CD15 and CD30. Epstein-Barr virus-encoded small RNA (EBER) in situ hybridization was positive in the atypical R-S cell. Finally, the patient was diagnosed with hemophagocytosis lymphohistiocytosis (HLH), secondary to primary bone marrow Hodgkin lymphoma. He then was treated with ABVD chemotherapy regimen.

Discussion

Hemophagocytosis lymphohistiocytosis (HLH) is an aggressive condition that characterized by increasing activity of histiocyte with hemophagocytic activity. Pancytopenia is a prominent consequence, leading to high rates of morbidity and mortality. The previous report showed the inferior long-term survival of HLH patients of 4% with a median survival without treatment for less than 2 months[1]. Generally, HLH is categorized into familial and secondary HLH. Familial HLH is a genetic disease caused by dysfunction of several genes[1]. However, secondary HLH, induced by other conditions including infection, autoimmune disease, and malignancy, is found more frequent. The etiologies inducing secondary HLH have to be investigated and treated in order to eradicate the cytokine, which stimulates macrophage, leading to termination of hemophagocytic activity.

PBMHL is a rare condition, mostly described in HIV-positive patients. Due to the high prevalence of Epstein-Barr virus infection, HIV-positive patients had a ten-fold increased risk of developing Hodgkin lymphoma, commonly in advanced stage with extranodal involvement.

For HIV-negative patients, only 4 cases have been reported. Morita et al. reported the series of patients with HIV-negative PBMHL which revealed that patients tended to be older and had the worse outcome than HIV-positive cases.[2] Most patients with PBMHL were treated with standard ABVD regimen. Nonetheless, only one reported case achieved the long-term survival with standard treatment.[2-5] The others died early during therapy due to either disease progression or treatment toxicity.

In conclusion, patients with unexplained fever with HLH, even without a sign of organomegaly, the primary bone marrow lymphoma should be in the differential diagnosis including PBMHL. Unfortunately, primary marrow lymphoma is often associated with the dismal outcome as the standard treatment might not adequately be able to control the disease aggressiveness of PBMHL. Therefore, high-intensity chemotherapy with best supportive care and upfront autologous stem cell transplantation should be considered for improving the patients'outcome.[6-10]

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