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Case report

Recurrent episodes of hemophagocytic lymphohistiocytosis preceding the diagnosis of subcutaneous panniculitis-like T-cell lymphoma

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening disease caused by cytokine storm-induced severe inflammation, and malignant lymphoma is the leading cause of HLH in adults. We herein have reported the case of a 28-year-old man afflicted with subcutaneous panniculitis-like T cell lymphoma who presented to our facility complaining of fever, cough and myalgia for one week. Following an examination, the patient was diagnosed with hemophagocytic lymphohistiocytosis according to the diagnostic criteria of HLH 1994 protocol published in 1997. Treatment with the HLH 1994 protocol (chemotherapy with etoposide combined with steroid based regimen) was initiated and the patient recovered well. However, subcutaneous panniculitis-like T cell lymphoma was diagnosed by neck soft tissue biopsy nine months later. Thereafter, this patient then received chemotherapy using the ESHAP regimen for one cycle (etoposide 40 mg/m^2 BSA, cisplatin 25 mg/m^2 BSA and methylprednisolone 500 mg at day 1 to day 4, and cytarabine 2000 mg/m^2 at day 5). Currently, this patient continues his regular follow-up at our hematologic outpatient department.

1. Introduction

Hemophagocytic lymphohistiocytosis (HLH), also known as hemophagocytic syndrome (HPS), is a life-threatening disease caused by extreme inflammation. It is believed that uncontrolled activated lymphocytes and macrophages proliferation result in a cytokine storm, which is responsible for this critical clinical scenario. Etiologies of HLH are different in pediatric and adult patients. Primary HLH (as observed in familial HLH), X-linked lymphoproliferative syndrome, and Chediak–Higashi syndrome or viral infections, are common causes of HLH in pediatric patients.[1] On the other hand, malignancies are the leading causes of HLH in adults, particularly malignant lymphoma.[2] The most commonplace presenting signs and symptoms of HLH are fever, hepatosplenomegaly, and cytopenias. This immune dysregulatory disorder is prominently associated with cytopenias and clinical signs and symptoms of extreme inflammation. Prompt initiation of immunochemotherapy is essential for survival, but timely diagnosis may be challenging.[3] Among all the possible etiologies, malignant lymphoma is the predominant cause of HLH in adults. In 1991, Gonzalez et al[4] described a new type of T-cell lymphoma with clinicopathological features simulating panniculitis. This new type of T-cell lymphoma had an aggressive clinical course and was often presenting with HLH. Herein, we reported a patient with subcutaneous panniculitis-like T cell lymphoma-associated HLH, although his underlying lymphoma was not diagnosed until nine months later.

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2. Case report

A 28-year-old man visited our emergency department because of intermittent fever, dry cough, and myalgia for one week. According to the patient, he had a generally unremarkable prior health history, and denied history of hepatitis or any other systemic diseases; he also denied alcohol drinking. In addition to the complained of fever and cough, the patient also described night sweating and body weight loss. However, local clinical information revealed the patient suffered from leukopenia and impaired liver function. Furthermore, our hospital laboratory data revealed leukopenia (leukocyte: 1600/μL; normal range: 3900–10,600), anemia (hemoglobin: 12.4 g/dL; normal range: 13.5–17.5), and thrombocytopenia (platelet: 108 × 10^3/uL; normal range: 150–400). Liver function tests showed elevated GOT (aspartate aminotransferase): 364 U/L; normal range: 8–38, and GPT (alanine aminotransferase): 235 U/L; normal range: 10–50. Abnormal LDH (lactate dehydrogenase) (2212 U/L; normal range: 120–240) was also found. The patient's abdominal computed tomography scan indicated only splenomegaly, with normal liver and gallbladder appearance (Fig. 1). In addition, hyperferritinemia: 59,384 ng/ml, low fibrinogen: 139.3 mg/dl and increased cell free IL-2R (interleukin-2 receptor): 1155.4 pg/ml were noted. A Gallium-67 scan revealed no evidence of gallium-avid tumor. The possible causes of fever were evaluation, including EBV infection, HSV, CMV or HIV and rheumatologic disease, but all of the above generated negative results. With a preliminary diagnosis of HLH, the patient then received a bone marrow examination which showed hypercellular marrow with increased infiltration of histiocytes and profound hemophagocytosis (Fig. 2). After treatment by HLH 1994 protocol (chemotherapy with etoposide combined with steroid based regimen),[5] the patient's fever subsided and liver function improved. After that, the patient further underwent three cycles of chemotherapy with weekly etoposide.

However, 10 days after he completed the last chemotherapy round with etoposide, the patient again visited our emergency department manifesting a fever. Lab data reported leukopenia, anemia, and elevated LDH (leukocyte:3600/μL, hemoglobin:10.9 g/dL, platelet:168 × 10^3/μL, and LDH:498 U/L). Thereafter,

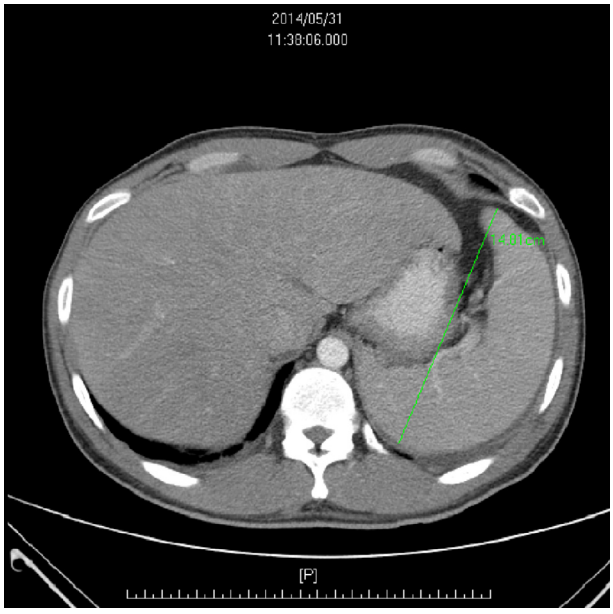

Fig. 1. CT, Abdomen (at initial diagnosis). 1. Mild splenomegaly. 2. No abnormal lymphadenopathy in retroperitoneum or pelvis.

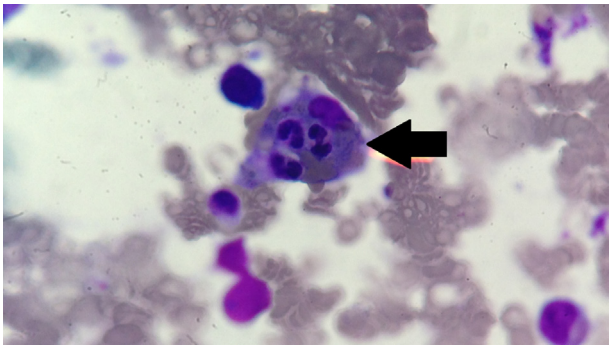

Fig. 2. Bone marrow aspiration (at initial diagnosis). Bone marrow smear showed that neutrophils are found within the cytoplasm of histiocyte (arrow), indicating hemophagocytosis.

pneumocystis jirovecii pneumonia was strongly suspected due to the patient's chest X-ray and clinical presentation. After the antibiotic Sevatrim was administered (Trimethoprim 80 mg/Sulfamethoxazole 400 mg), the patient's fever subsided. At the same time, steroid medication was discontinued to avoid occult infection.

Six weeks later, the patient's fever recurred, and subsequent examination again noted progressive leukopenia, thrombocytopenia, and elevated LDH. Repeated bone marrow examination further revealed hypocellular marrow with hemophagocytosis. Therefore, the patient received two cycles of weekly etoposide. Follow-up lab data showed improved leukopenia and decreased LDH, after which he then received another five cycles of weekly etoposide. Unfortunately, induration over the bilateral cheek with skin erythematous change and progressive facial swelling was found. Lab data indicated recurred leukopenia (1700/μL) and elevated LDH (729 U/L). A CT scan of the nasopharynx reported an increased infiltration and swelling over the bilateral face, submandibular region and submental region. Furthermore, several neck lymph nodes were noted, and PET (positron emission

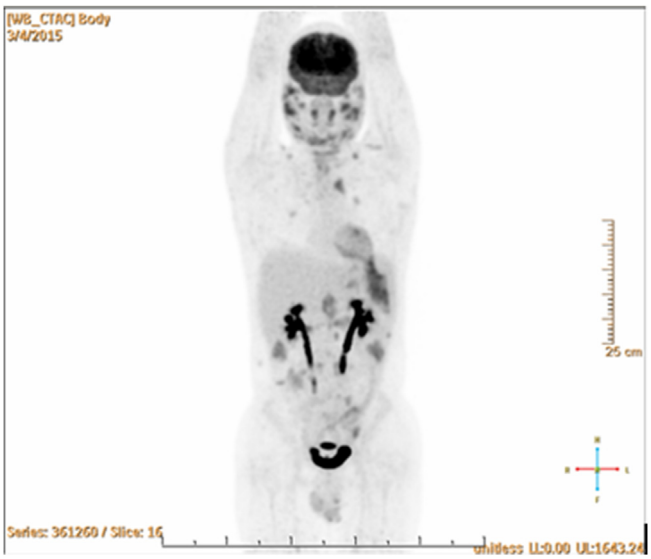

Fig. 3. Pet whole body scan (9 months after diagnosis of HLH). 1. Tumor involvement at the bilateral upper neck (level II), posterior portion of the bilateral lower neck (level V), left upper mediastinum, abdomen (mesentery), left para-aortic region, left iliac region and left deep inguinal region (Grade 3). 2. The increased FDG uptake at the superficial soft tissue of the face, anterior neck, posterior neck, bilateral upper chest wall, left upper back, right lateral abdominal wall and bilateral flank, the posterior portion of the bilateral abdominal wall (Grade 2).