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CASE REPORT

Multiple Nonleukemic Myeloid Sarcoma Associated Hemophagocytic Lymphohistiocytosis in an Adult

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SUMMARY

Background: **Nonleukemic myeloid sarcoma (MS) occurs rarely. Hemophagocytic lymphohistiocytosis (HLH) is a rare and potentially fatal condition. We report a rare case of nonleukemic MS associated with HLH.**
Methods: **Hematologic investigation, 18F-FDG PET/CT, bone marrow aspirate and biopsy, and lymph node biopsy were performed in a 25-year-old male patient.**
Results: **The patient was given a short-term treatment of etoposide and dexamethasone to control HLH. Then he received chemotherapy and responded well.**
Conclusions: **It is important to find the underlying cause of HLH in high-risk patients. HLH can occur secondary to nonleukemic MS. Early diagnosis and treatment can improve survival.**
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KEY WORDS

myeloid sarcoma, sarcoma, hemophagocytic lymphohistiocytosis, acute myeloid leukemia

CASE PRESENTATION

A 25-year-old critically ill male patient presented with high fever, pancytopenia, epistaxis and melena lasting a week before visiting our hospital on February 19, 2017. His medical history was unremarkable. Physical examination revealed anemia, petechia and ecchymosis, superficial lymphadenopathy, and mild splenomegaly. Laboratory data showed leukocyte count 310/mm^3, hemoglobin 6.5 g/dL, platelet count 2,000/mm^3, alanine aminotransferase 116 U/L, aspartate transaminase 42 U/L, triglyceride concentration 3.56 mmol/L, serum ferritin 3,195 μg/L, prothrombin time 18.8 seconds, partial thromboplastin time 67.4 seconds, fibrinogen 1.19 g/L, soluble CD25 4,728 U/mL. Bone marrow aspiration revealed a hypocellular marrow. Based upon the patient's fever, splenomegaly, pancytopenia, hypertriglyceridemia and hypofibrinogenemia, ferritinemia, elevated soluble CD25. A diagnosis of HLH was made based on meeting six of the eight HLH 2004 Diagnostic Criteria

[1].

To explore possible deep etiology, a whole-body 18F-FDG PET/CT was performed (Figure 1). Increased FDG accumulation was detected in several areas: left nasopharyngeal wall thickening (SUVmax 7.3), anterior superior mediastinum tubercle (size 16 mm x 29 mm, SUVmax 4.6), bilateral cervical, retropharyngeal and intraparotid lymph nodes (SUVmax 9.6), anterior mediastinal lymph nodes, paratracheal and subcarinal lymph nodes (SUVmax 5.7), harnpan, spinal column, and limb bones (SUVmax 10.1).

Nasopharyngeal biopsy with pathological analysis showed leukemia and lymphoma aspects. Immunohistochemistry exhibited diffuse positive for CD34, CD117 and scattered positive for myeloperoxidase (MPO) (Figure 2). A bone marrow biopsy showed no evidence of medullary involvement. Eventual pathologic diagnosis was nonleukemic myeloid sarcoma (MS).

The patient was first given a short-term treatment of etoposide (100 mg, daily for three days and then 200 mg once weekly for three weeks) and dexamethasone (10 mg, daily for three days) to control HLH. His body temperature dropped to normal. And the patient showed a significant improvement of peripheral blood pictures and coagulative function. Then he received chemotherapy similar to that used to treat acute myeloblastic leukemia. The initial course consisted of cytosine rabinoside 100 mg/m^2/day for 7 days and idarubicin 12 mg/m^2/day for 1 day. The second course consisted of cytosine rabinoside 100 mg/m^2/day for 7 days and doxorubicin 40 mg/m^2/day for 1 day. Then 18F-FDG PET/CT reexamination revealed abnormal FDG accumulation was significantly decreased or disappeared (Figure 1). Then the patient continued to receive further treatment.

DISCUSSION

Hemophagocytic lymphohistiocytosis (HLH), a potentially fatal condition that is often under recognized contributing to its high mortality and morbidity. The term primary HLH refers to an underlying genetic abnormality causing the disorder, whereas secondary HLH indicates that the disorder is secondary to underlying conditions such as infection, autoimmune/rheumatologic, malignant, or metabolic conditions [2]. HLH is defined by meeting at least five of eight HLH 2004 diagnostic criteria [1]. These criteria include: fever, splenomegaly, cytopenias affecting at least two of three lineages in the peripheral blood, hypertriglyceridemia (≥ 3 mmol/L) and/or hypofibrinogenemia (≤ 1.5 g/L), hemophagocytosis in the bone marrow, spleen, lymph nodes or cerebrospinal fluid, soluble CD25 > 2,400 U/mL, low or absent natural killer cell (NK-cell) activity, ferritin ≥ 500 μg/L [1]. Early recognition and identifying the underlying cause is crucial for any reasonable attempt at curative therapy to be made.

Based on HLH-2004 diagnostic criteria, it is not mandatory to demonstrate histological evidence to make the diagnosis of HLH. The presence of hemophagocytosis, a hallmark of activated macrophages, is only considered supportive for HLH [3]. The current diagnostic criteria have been questioned because of the lack of specificity of the various criteria [4]. However, their utility reflects the severity of the condition and the importance of early recognition of HLH. In this case, although typical hemophagocytosis was not observed on bone marrow aspirates, HLH could be quickly diagnosed by meeting 6 of 8 diagnostic criteria, enabling a timely start of chemoimmunotherapy for the patient.

HLH is a hyperinflammatory, uncontrolled immune response triggered by different stimuli. Although control of hyperinflammation is important, the search for a medically treatable stimulus is also necessary [5]. 18F-FDG PET/CT has been widely applied in the process of malignant and benign diseases, such as fever of unknown origin [6]. Several studies have shown 18F-FDG PET/CT may effectively be applied in differential diagnosis of sHLH, with high SUV pointing toward underlying malignancy [7,8]. PET/CT with 18F-FDG, an analogue of glucose, provides valuable functional information based on the increased glucose uptake and glycolysis of cancer cells and depicts metabolic abnormalities before morphological alterations occur [9]. However, infectious and/or inflammatory diseases are known causes of a false-positive 18F-FDG PET/CT scan [10, 11]. The final diagnosis depends on the histopathologic and immunohistochemical examination. In the present case, PET/CT suggested the existence of a multiple malignant disease and appeared helpful for the determination of a biopsy site. In addition, subsequent follow-up PET/CTs helped in assessing the therapeutic effect. Therefore, it might be necessary to perform 18F-FDG PET/CT early in patients with a high-risk of sHLH.

MS is a rare, extramedullary tumor that consists of immature myeloid cells. Histological sections typically demonstrate infiltrating myeloid cells that exhibit either granulocytic or monocytic lineage [12]. Multiple nonleukemic MS is a rare form of MS that is developed in multiple anatomic sites other than bone marrow at diagnosis, without a preceding myeloid neoplasm. Treatment of MS, if given in time with intensive chemotherapy used in AML, can help to achieve clinical remission and reduces the subsequent risk of development of overt leukemia [11]. In this case, the diagnosis of MS was established by immature myeloid phenotype CD34, CD117, and myeloperoxidase positivity in the neoplastic cells. After two courses of chemotherapy, the patient was obviously improved.

CONCLUSION

It is important to find the underlying cause of HLH in high-risk patients. Despite occurring very rarely, HLH can occur secondary to nonleukemic MS. Both of these two diseases can be fatal. Early diagnosis and treatment

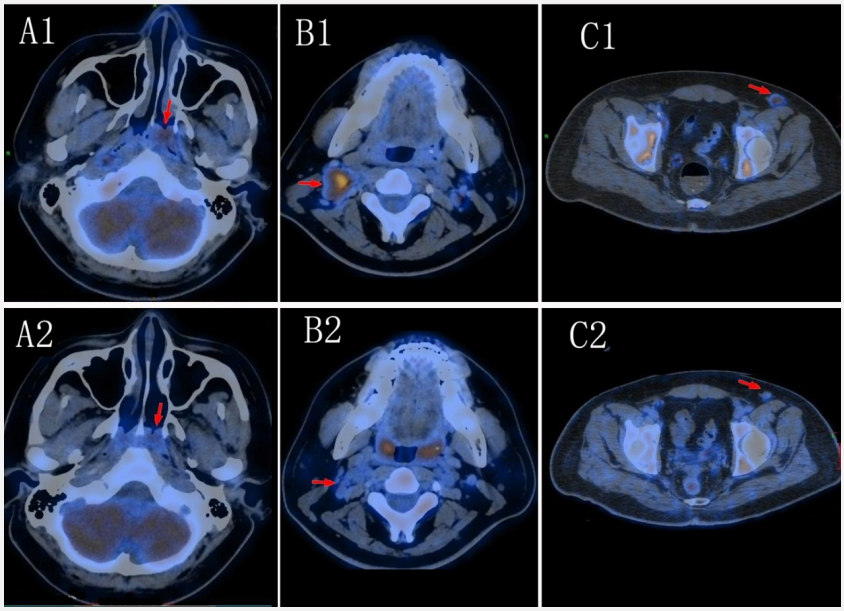

Figure 1. 18F-FDG PET/CT imaging changes before and after chemotherapy (arrows).

A. Left nasopharyngeal lesion before chemotherapy (A1) and after chemotherapy (A2); B. Carotid sheath adenopathy before chemotherapy (B1) and after chemotherapy (B2); C. Left inguinal adenopathy before chemotherapy (C1) and after chemotherapy (C2).

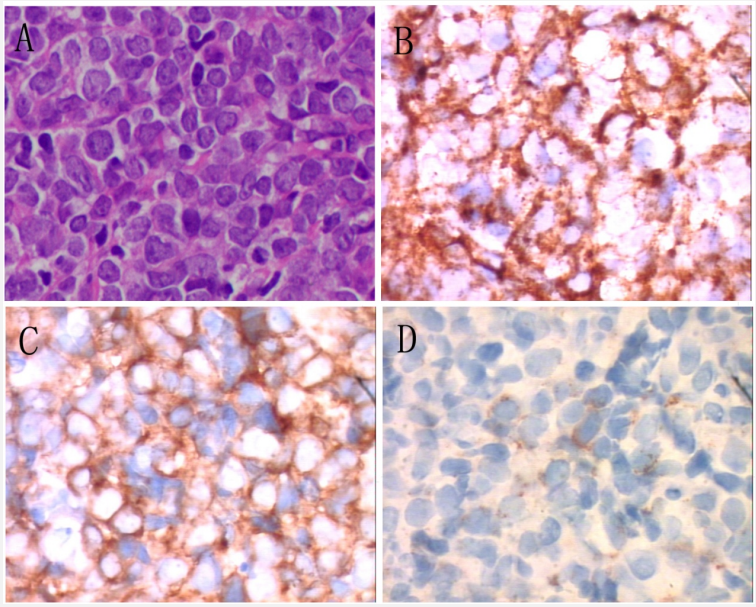

Figure 2. Hematoxylin-eosin staining (HE staining) and immunohistochemical staining of the left nasopharyngeal specimen.

A. HE staining; B. diffuse positivity for CD34 staining; C. diffuse strong positivity for CD117 staining; D. scattered positive for MPO staining; x 1,000.

improves survival.

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Declaration of Interest:
The authors declare no conflict of interest associated with this manuscript.

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