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Case Report

Primary bone natural killer/T cell lymphoma, nasal type without EBV infection: a case report

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Abstract: Primary bone NK/T cell lymphoma is very rare. We report a case of 52-year-old man of primary bone NK/T cell lymphoma and then progressed to NK leukemia. The patient had low-grade fever for 4-month, and Ultrasonic B revealed a diffuse hepatosplenomegaly without lymphadenopathy. PET scanning showed increased FDG uptake in many bones of the whole body. The diagnosis was established by bone specimen. These neoplastic cells demonstrated a typical immunophenotype of CD56, CD3, CD2 and MPO positive, and CD5, CD20, CD30, PAX-5, CD4 and CD8 negative. Primary bone ENKTL is very rare; it should be made with the combination of clinical feature, PET-CT image, and pathological characteristics, and should be distinguished from other lymphomas or leukemia involved in bone.

Keywords: Primary bone, NK/T cell lymphoma, SMILE regimen

Introduction

Extranodal NK/T cell lymphoma (ENKL), nasal type, is an uncommon tumor that occurs with a higher prevalence among Asians, and the native American population of Mexico, Central America and South America [1]. It is well known as an aggressive tumor associated with Epstein-Barr Virus (EBV). The most common site of involvement is upper aerodigestive tract (nasal cavity, nasopharynx, paranasal sinuses and palate). Preferential sites of extranasal involvement include the skin, soft tissue, gastrointestinal tract, and testis [1-3]. Rare sites of involvement such as prostate [4], pancreas [5] and adrenal glands [6] have been reported. Primary bone NK/T cell lymphoma is very rare. Herein, we report a case of primary bone extranodal NK/T cell lymphoma, nasal type, and then progressed to NK leukemia.

Case report

A 52-year-old man presented with a 4-month history of low grade fever. On examination, he had hepatosplenomegaly but no lymphadenopathy. A full blood count showed anaemia and thrombocytopenia while results of other laboratory examinations, including liver function tests and serum lactate dehydrogenase were normal. Ultrasonic B of the neck, chest and abdomen showed no lymphadenopathy except hepatosplenomegaly. ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scanning showed increased FDG uptake in many bones of the whole body (**Figure 1**). PET-CT also showed a FDG-avid adrenal gland, suggesting high metabolism. A CT-guided biopsy of the ilium lesion was performed and showed extranodal natural killer/T cell lymphoma, nasal type. Lymphoma cells were positive for CD56, CD3, CD2 and MPO, and were negative for CD5, CD20, CD30, PAX-5, CD4 and CD8. Flow cytometry analysis of bone marrow, bone marrow aspiration and trephine biopsy showed no evidence of lymphoma. Karyotype analysis of lymphoma cells showed-Y, del (1) (q), +2, +8, +15, +17, +20. But the patient had no Epstein-Barr virus (EBV) infection. A diagnosis of primary bone extranodal NK/T cell lymphoma, nasal type was made. Then the patient was treated with SMILE regimen (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide). After 2 cycles of SMILE regimen, the

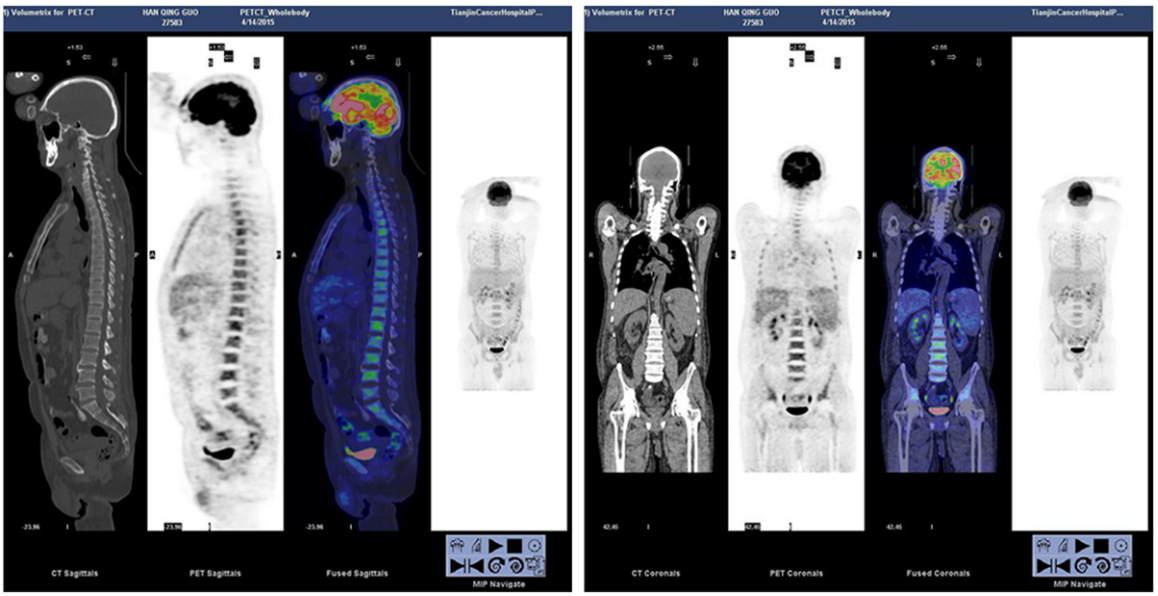

Figure 1. PET-CT of the patient.

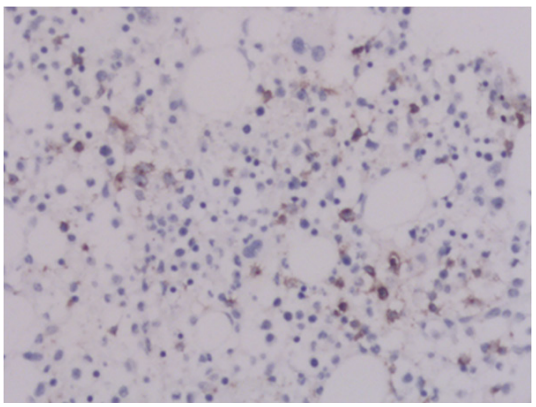

Figure 2. Infiltration of lymphoma cells to bone marrow showing CD56 positive.

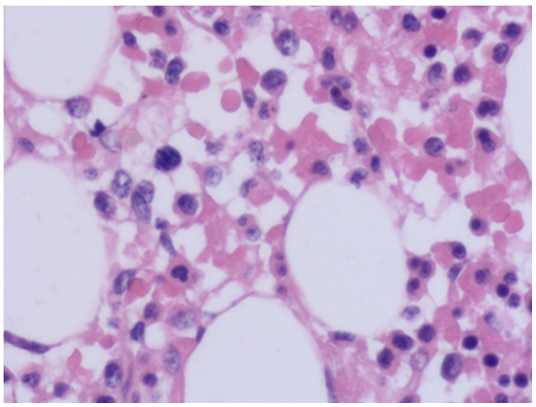

Figure 3. HE staining of bone marrow.

patient remained in stable state. But at the end of the third cycle of SMILE, the patient starts to fever. A full blood count showed anaemia, high white blood cells and thrombocytopenia. Bone marrow aspiration and trephine biopsy showed lymphoma cells infiltration, considering NK cell leukemia (**Figures 2** and **3**). The patient gave up treatment and died one month later.

Discussion

Extranodal natural killer/T cell lymphoma shows a mark geographical preference for East Asia, including China. It usually invades the upper aerodigestive tract, such as nasal cavity. Primary bone NK/T cell lymphoma, as shown in this patient, is very rare. The diagnosis of primary lymphoma of the bone should be limited to involvement of only the bone. As bone can be involved by other types of lymphomas, the final diagnosis should be made with the combination of clinical feature, PET-CT image, pathological morphology, immunophnotype, and genetic features.

To our knowledge, this is the first reported case of primary bone extranodal NK/T cell lymphoma, nasal type. The symptoms of the patient were fever and hepatosplenomegaly, without lymphadenopathy. The most important differential diagnosis is aggressive NK cell leukemia (ANKL). There are two disease entities in the

WHO classification of NK cell malignancies: ENKL and ANKL. Both are characterized by aggressive clinical course and refractoriness to chemotherapy. Yet the relationship and boundary between ENKL with advanced stage and ANKL remains unclear. The immunophenotype of ANKL is identical to that of ENKL neoplastic cells, and ANKL has been suggested to represent the leukemic manifestation of ENKL [7]. But ANKL has a younger median age by more than a decade, and high frequency of hepatosplenic and BM involvement [8]. ANKL often has multi-organ failure, coagulopathy and haemophagocytic syndrome, and the median survival is less than 2 months. In this case, the patient had only hepotosplenomegaly. And the age of the patient was 52 which beyond the median age of ANKL.

While CHOP chemotherapy has been a mainstay for the treatment of aggressive lymphoma, the CHOP or other anthracycline-containing regimens were ineffective for NK cell malignancies [9-11]. Recently, SMILE regimen, consisting of MDR-unrelated agents (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide), was found to be effective to advanced ENKL [12]. The role of stem cell transplantation in the treatment of NK cell leukemia has been studied by the NK-cell Tumor Study Group who performed a survey of 40 patients with NK-cell lymphoproliferative diseases treated with either allogeneic (n = 15) or autologous (n = 25) stem cell transplantation. The results indicate a beneficial effect of stem cell transplantation, but the criteria for transplantation were not uniform [13].

Disclosure of conflict of interest

None.

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