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CASE REPORT

ALK-positive anaplastic large cell lymphoma with soft tissue involvement in a young woman

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Introduction: Anaplastic large cell lymphoma (ALCL) is a type of non-Hodgkin lymphoma that has strong expression of CD30. ALCL can sometimes involve the bone marrow and in advanced stages, it can produce destructive extranodal lesions. But anaplastic large cell lymphoma kinase (ALK)+ ALCL with soft tissue involvement is very rare.

Case report: A 35-year-old woman presented with waist pain for over 1 month. The biopsy of soft tissue lesions showed that these cells were positive for ALK-1, CD30, TIA-1, GranzymeB, CD4, CD8, and Ki67 (90%+) and negative for CD3, CD5, CD20, CD10, cytokeratin (CK), TdT, HMB-45, epithelial membrane antigen (EMA), and pan-CK, which identified ALCL. After six cycles of Hyper-CVAD/MA regimen, she achieved partial remission. Three months later, she died due to disease progression.

Conclusion: This case illustrates the unusual presentation of ALCL in soft tissue with a bad response to chemotherapy. Because of the tendency for rapid progression, ALCL in young adults with extranodal lesions are often treated with high-grade chemotherapy, such as Hyper-CVAD/MA.

Keywords: anaplastic large cell lymphoma, ALK+, soft tissue involvement, Hyper-CVAD/MA

Introduction

In 1988, anaplastic large cell lymphoma (ALCL) was included in the revised Kiel classification, and is nowadays classified as a non-Hodgkin lymphoma of T-cell origin by the World Health Organization with strong expression of CD30.[1,2] ALCL is common in Asian countries, which can be divided into three separate groups with different prognosis: anaplastic large cell lymphoma kinase (ALK)-positive ALCL, ALK-negative ALCL, and primary cutaneous ALCL. Systemic ALCL has an aggressive clinical course, and patients frequently present with systemic symptoms, advanced-stage disease, and extranodal localizations.[3,4] Response to treatment and overall survival of systemic ALCL in children are good. In adults, however, it is not clear. ALCL sometimes can involve the bone marrow, and in advanced stages, it can produce destructive extranodal lesions. But ALK+ ALCL with soft tissue involvement is very rare. Here, we report a case of ALK-positive ALCL with soft tissue involvement in a young woman.

Case

A 35-year-old woman who presented with waist pain for over 1 month was examined in our hospital. The patient had no fever or weight loss. Physical examination revealed hepatosplenomegaly and a lump in the waist but no lymphadenopathy. Serum lactate dehydrogenase was elevated to 1,500 IU/L (normal 200–460 IU/L), and other laboratory data showed anemia. ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scanning showed that accumulation of FDG was observed in the

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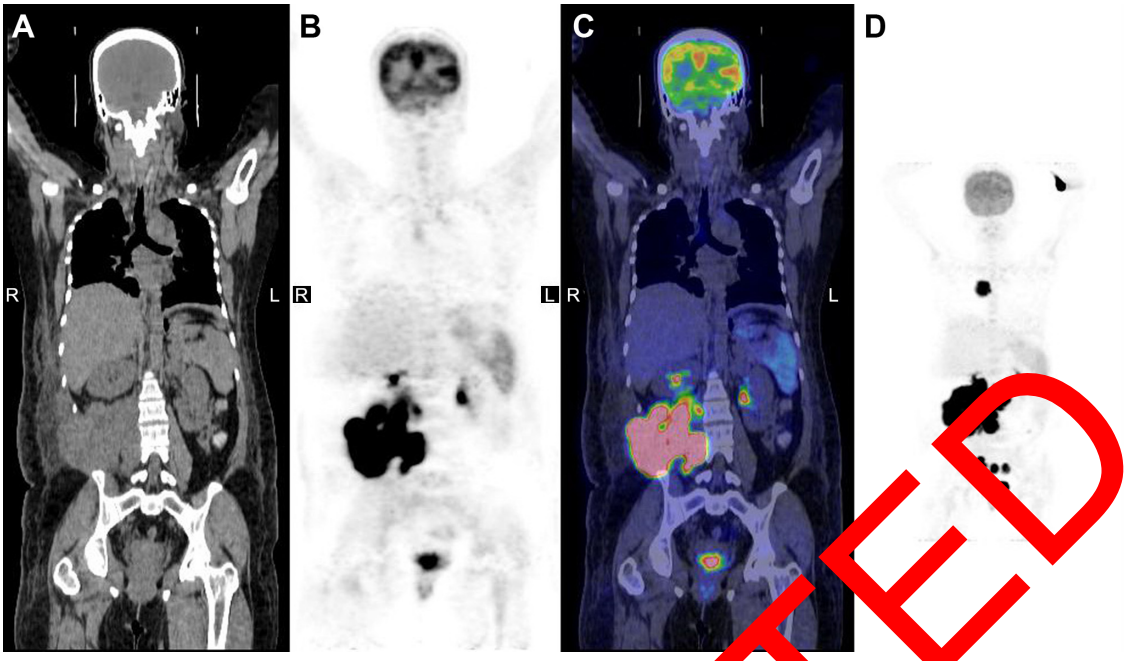

Figure 1 PET–CT of the patient.
Notes: (**A**) CT of the patient. (**B**) PET of the patient. (**C**) PET-CT of the patient. (**D**) Multum in pa
Abbreviations: PET, positron emission tomography; CT, computed tomography; L, left; R, rig

soft tissue lump near the lumbar vertebra 1–5, considering malignant tumor (Figure 1). PET–computed tomography (CT) also showed many FDG-avid mass in mediastinu and mesenterium, suggesting lymphatic metastasis. A CT-guided biopsy of soft tissue lesions revealed A CL. These cells were positive for ALK-1, CD30, TIA , GranzymeB, CD4, CD8, and Ki67 (90%+) and negative r CD , CD CD20, CD10, cytokeratin (CK), Td , HMB-4 epithelial membrane antigen (EMA), and m K (Figure 2 Bone marrow aspiration and trephine biopsy sho d no infiltration. She was diagnosed as AL positive ALCL th soft tissue involvement. After two ycles of yper-CVAD/MA chemotherapy, her condition s w no signi cant improvement. After four cyc s Hyp CVA MA chemotherapy, she achieve partiall remissi (PR). After six cycles of Hyp -CVAD/M regimen, she still remained in PR. Three month ter, sh died of disease progression.

Discussion

Malignant lymphoma with prominent soft tissue involvement is n infrequent, and often diagnostically challenging neoplasm, which represents ~3% of all primary malignant bone tumors and 1% of all malignant lymphomas. Among those studies that reported the T- or B-cell phenotype of primary soft tissue lymphoma, B-cell accounted for over 90%. B symptoms such as fever, night sweats, and weight loss, were frequent in ALCL patients. A majority of patients with ALCL had a disseminated disease (Ann Arbor Stage III or IV) and a limited number of extranodal sites.[5] Bone marrow involvement has been initially considered a rare event in ALCL.[6]

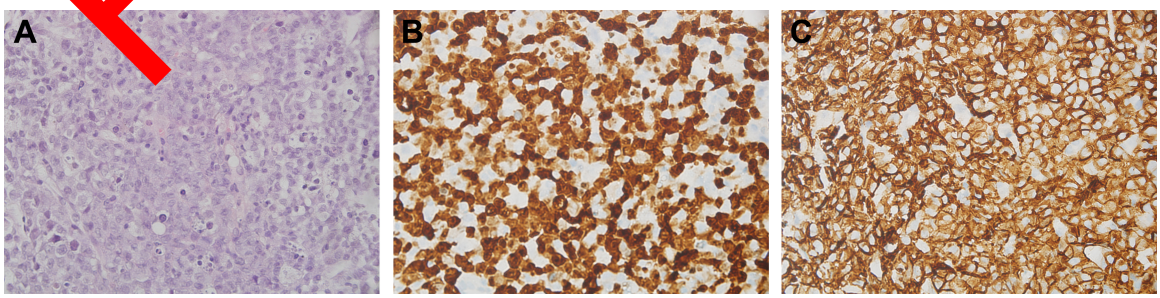

Figure 2 Biopsy of soft tissue lesions: (**A**) HE staining, (**B**) ALK staining, and (**C**) CD30 staining.
Note: Magnification for all images: 400×.
Abbreviations: HE, hematoxylin and eosin; ALK, anaplastic large cell lymphoma kinase.

As ALCL is a highly curable disease, it is important for it to be differentiated from other causes of lytic bone lesions, such as carcinomas and other primary bone tumors. Although this may include cortical or soft tissue invasion, the diagnosis generally excludes lymph node or distant visceral involvement to be considered a primary lymphoma of bone non-Hodgkin's lymphoma (NHL) of bone is a rare entity that is limited to the long bones and axial skeleton, with the femur being the most common site of involvement. Besides, ALCL has to be distinguished from classical Hodgkin lymphoma, CD30$^+$ non-Hodgkin B-cell lymphomas, and very rare ALK-1-positive (and eventually CD30-negative) large B-cell lymphomas.

ALCL is characterized by the expression of CD30 on malignant cells, and its prognosis is related with the expression of the ALK protein.[7] ALCL is divided into three separate entities based on ALK expression: ALK-positive ALCL, ALK-negative ALCL, and primary cutaneous ALCL. ALCL commonly involves in children and young adults that presents progressive disease with a high incidence of extranodal involvement.[8] The case we report is ALCL with soft tissue involvement diagnosed with PET–CT, and pathology which is rare. It is known that ALK is an indicator of better responses to treatment in ALCLs. However, this case did not show complete remission (CR) after six cycles of treatment partially because of the soft tissue involvement that affected its response to the treatment. Besides, CD30 expression was reported to link with bad outcomes that may affect the response of this patient.

Although magnetic resonance imaging and CT are the standard imaging modalities for the detection of ALCL with prominent soft tissue involvement, the imaging features are usually nonspecific and the lesion cannot be fully detected because magnetic resonance imaging and CT often were performed in a part of the body. PET–CT plays an important role in the diagnosis, staging, and surveillance of lymphoma.

Although no comparative studies have been published, most investigators reported that the response of ALCL to chemotherapy was good, ranging from 60% to 90%. The overall survival of localized disease is known to be good, especially in children. More advanced stages have a high relapse rate, and their prognosis in comparison to that of other large cell lymphomas is controversial. Because ALCL belongs to NHL, so it is believed that CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) regimen is generally applicable to ALCL. Besides, modified B-NHL-BFM-90 protocol is shown to be efficacious for Chinese children with ALCL.[9] It is reported that both autologous and allogeneic hematopoietic stem cell transplantation (HSCT) can offer the prospect of durable disease-free survival for ALCL in childhood and adolescence. Patients with CR at the time of autologous HSCT had significantly greater event-free survival than patients with non-CR at the time of autologous HSCT.[10] Recently, brentuximab vedotin, which is a CD30-targeted antibody, have emerged.[9] Novel therapies may soon radically change the treatment paradigm for this disease and hopefully lead to less toxicity and improved outcomes.[11] In this case, the patient was treated with high-grade chemotherapy, such as hyper-CVAD/MA. But there was still no significant improvement and after six cycles of chemotherapy, she only achieved PR. Then she gave up the treatment and died 3 months later.

Conclusion

ALCL is a rare but biologically well-characterized disorder with a wide spectrum of presentation. It may present with soft tissue involvement. Recognition of a combination of symptoms including anemia, renal failure, and bone pain in the presence of normal bone marrow biopsy and serum electrophoresis should trigger aggressive clinical workup to rule out the possibility of lymphoma. A meticulous examination of early biopsies based on PET–CT of deeply situated soft tissue or lymph nodes are recommended to yield an early diagnosis of ALCL.

Acknowledgment

The subject and her parents/guardians gave their informed written consent, and the study protocol was approved by the Ethics Committee of Yidu Central Hospital.

Disclosure

The authors report no conflicts of interest in this work.

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