

Anaplastic large cell lymphoma with primary involvement of the skeletal muscle: A case report

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Abstract. The present study reported the case of a patient with primary anaplastic large cell lymphoma (ALCL) occurring in the left major psoas. A 24-year-old male patient presented with one-month history of left lower back pain, which had been exacerbated for 10 days prior to admission. Magnetic resonance imaging (MRI) scans revealed an enlarged major psoas muscle that protruded into the inguinal region. The presence of an intense soft tissue mass on MRI scans, as well as the results of fine-needle aspiration biopsy and immunohistochemical analysis of the mass, may help establish an early diagnosis, allowing for the appropriate treatment strategy to be initiated.

Introduction

Lymphoma was one of the first hemopathies to be identified, and at present, lymphoma exhibits incidence rates of 1.39 and 0.84 cases per 100,000 individuals in males and females in China, respectively (1). In 1985, Stein *et al* first identified anaplastic large cell lymphoma (ALCL), which is characterized by the strong expression of antigen Ki-1 (2). ALCL is classified as a non-Hodgkin lymphoma (NHL) derived from peripheral T-cells and is estimated to account for 2-3% of all lymphoid neoplasms, according to the World Health Organization (WHO) classification (3,4). ALCL represents a group of diseases which are heterogeneous with regard to histology, phenotype, cytogenetics and clinical course and thus, diagnosis remains difficult (5,6) and the treatment for ALCL varies considerably in different patients, involving the

CCG-5941, AIEOP LNH-97 and BFM-95 protocols (7-9). The expression of the anaplastic lymphoma kinase (ALK) protein is the main characteristic used to classify ALCLs into two different systemic forms, which included the ALK-positive (ALK+) and ALK-negative (ALK-) tumors (8-11). ALK-ALCL is more clinically aggressive and predominantly occurs as advanced-stage disease in older patients (9-11). It has been reported that ALK+ ALCLs exhibit a predominance for the involvement of bone, bone marrow and subcutaneous tissue whereas ALK- ALCLs are more likely to invade the liver and the gastrointestinal tract (10). Although ALCL tends to invade extranodal sites (10), primary involvement of the skeletal muscle is extremely rare. The present study described the case of a 24-year-old male patient diagnosed with an ALK- ALCL originating in the left psoas muscle, suggesting that multiple examinations may help the early recognition and correct diagnosis of ALCL. Written informed consent was obtained from the patient.

Case report

A 24-year-old male patient was admitted to the Third Hospital of Hebei Medical University (Shijiazhuang, China) in March 2013 with one-month history of progressively increasing pain in the lower back, which had been exacerbated for 10 days. The patient had been initially treated for suspected strained back muscle with no alleviation of the symptoms. The pain radiated down the front of the left distal thigh three days before admission. No fever, night sweats or weight loss were reported, with the exception of the irregular sphincter disturbances. In addition, the patient had no previous medical history of trauma or cancer. Upon physical examination, a 15x7 cm elastic hard mass underlying the rib cage and protruding to the left inguinal region was detected. Furthermore, cervical, axillary and inguinal lymph node enlargement was detected. The muscle strength of the left lower limb was assessed by manual muscle testing according to Medical Research Council scale (12) and was determined to be grade 4. Other vital signs were within the normal limits. Laboratory examinations performed upon admission revealed a white blood cell count of $3.98 \times 10^9/l$ [normal, $(4 \sim 10) \times 10^9/l$], C-reactive protein level of 18.52 mg/l (normal, <8 mg/l), platelet count of $121.7 \times 10^9/l$

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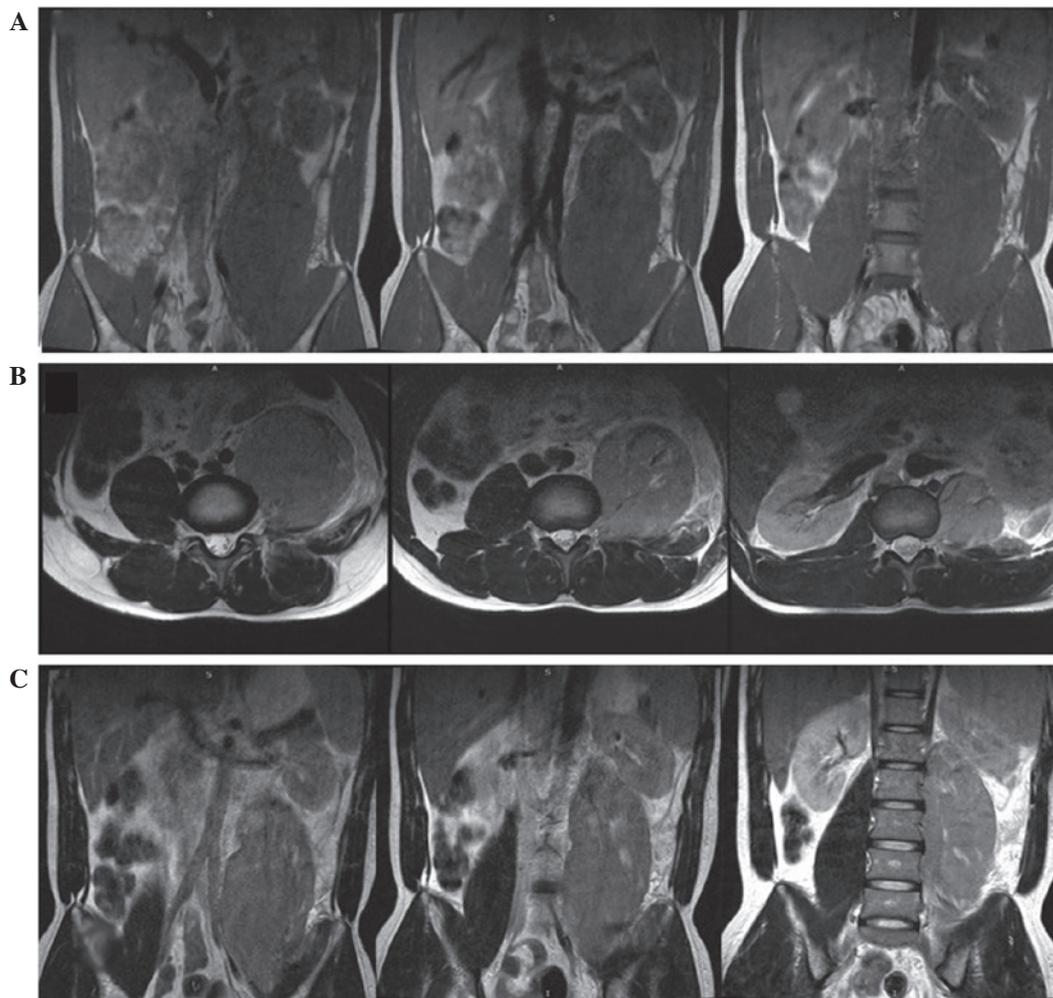


Figure 1. Magnetic resonance imaging scans of enlarged psoas. (A) Coronal T_1 -weighted images identified a hypointense mass in the left psoas. (B) Axial T_2 -weighted images revealed a relatively homogeneous mass of intermediate signal intensity. (C) Coronal fat-suppressed contrast-enhanced T_1 -weighted images are shown.

[normal, $(100\sim 300)\times 10^9/l$], and lactate dehydrogenase level of 1,958 U/l (normal, $104\sim 245$ U/l) (13). Using magnetic resonance imaging (MRI), swelling of the psoas muscle was identified (Fig. 1). Radiologically, the mass was initially considered to be a soft tissue tumor, such as rhabdomyosarcoma. Surgical resection of the left psoas muscle was performed, and subsequent histopathological examination revealed diffuse infiltration of large neoplastic cells with irregular mitosis (Fig. 2). Immunohistochemical analysis of the resected tumor was performed and the neoplastic cells were found to be positive for CD30 and leukocyte common antigen, whereas they were negative for ALK, CD15, paired box-5, Epstein-Barr virus (EBV), Melan-A and HMB-45. Therefore, the patient was diagnosed with ALK- ALCL at stage IV of the disease according to the Ann Arbor classification (14). Subsequently, three 21-day cycles of bortezomib (1.3 mg/m^2 , days 1 and 8) and EPOCH [etoposide (50 mg/m^2 , days 1-4), adriamycin (50 mg/m^2 , days 1-4), vincristine (0.4 mg/m^2 , days 1-4), prednisone (60 mg/m^2 , days 1-5) and cyclophosphamide (750 mg/m^2 , day 5)], and one 42-day cycle of bortezomib (1.3 mg/m^2 , days 1 and 8) and hyper-CVAD [cyclophosphamide (300 mg/m^2 , days 2-4), epirubicin (16.6 mg/m^2 , days 5-7), intravenous vindesine (2 mg , days 5

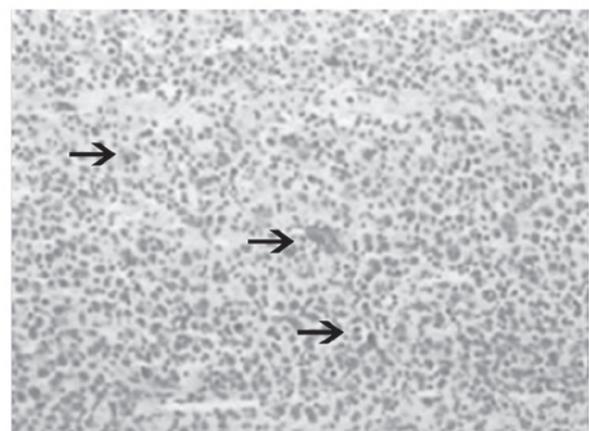


Figure 2. Histopathological analysis of the mass demonstrated invasion of tumor cells into the muscle fibers and pathological mitosis (arrows). 10% formalin; hematoxylin and eosin staining; magnification, $\times 40$.

and 12), dexamethasone (400 mg , days 2-5 and 12-16), methotrexate ($1,000\text{ mg/m}^2$, day 23) and cytarabine (3 g/m^2 , days 24 and 25)] were administered. The chemotherapy was complicated by myelosuppression, however, the patient

Table I. Previously reported cases (n=8) of anaplastic large cell lymphoma with primary skeletal muscle involvement.

Author (ref.)	Year	ALK status ^a	Age, years	Gender	Site
Chim <i>et al</i> (19)	1999	N/A	34	M	Forearm
Ishii <i>et al</i> (20)	2000	ALK+	11	F	Right upper arm, chest wall, left arm, left leg
Menon <i>et al</i> (21)	2001	N/A	10	F	Upper arm, thigh, chest wall
Liao <i>et al</i> (22)	2005	ALK-	21	M	Femoral muscle
Recavarren and Yang (23)	2009	ALK-	83	F	Psoas muscle
Driss <i>et al</i> (24)	2009	ALK+	8	M	Buttock
Wu <i>et al</i> (25)	2009	ALK+	14	M	Sarcospinal, lumbar and femoral muscles
Kounami <i>et al</i> (26)	2012	ALK+	14	F	Psoas muscle

^aALK-positive or -negative. ALK, anaplastic lymphoma kinase; N/A, not available; M, male; F, female.

experienced sustained remission for around 6 months subsequent to discharge. The patient was lost to follow-up.

Discussion

ALK- ALCL, characterized by the strong expression of CD30 and its aggressive growth, is classified as a provisional entity of systemic type according to the 2008 WHO classification (3,4). However, ALK- ALCL should be distinguished from other ALCL types, due to the different clinical features, treatment outcomes, and immunophenotypic and genetic markers used for the diagnosis of the disease (10).

Systemic ALCLs, among which ALK- ALCLs represent 15-50% of cases, account for 2-3% of NHLs (3,4). ALCL may involve the extranodal organs, gastrointestinal tract, skin and central nervous system (15-17). This type of lymphoma rarely arises in the skeletal muscle, particularly with primary involvement. A 10-year study by Travis *et al* (18) described a 0.1% rate of primary lymphomas in the soft tissue and only eight cases with primary muscle involvement were identified in a review of 7,000 lymphoma patients. However, a search of PubMed (1950 to August 2013) using the search terms ‘primary*’ AND ‘anaplastic large cell lymphoma’ AND ‘muscle’, identified only a small number of studies in English reporting primary skeletal muscle CD30+ ALCL (Table I) (19-26). To the best of our knowledge, the present study is the ninth reported case in the English literature.

The present study reported the case of a CD30+ and ALK- ALCL originating in the left psoas of a young adult. No particular risk factors have been previously identified for ALCL. At present, no convincing evidence exists suggesting that any viruses, including EBV and the human T-cell leukaemia/lymphoma virus family, may result in the development of NHL in humans. However, a previous study has demonstrated that T-cell ALCL risk was increased for patients with psoriasis and celiac disease suggesting that autoimmune disorders may lead to the development of this lymphoma (27).

At presentation, the possible diagnoses may include a broad spectrum of tumors, such as neuroectodermal tumor or sarcoma. Therefore, recognizing the MRI features of ALCL may promote the identification between primary skeletal muscle lymphoma and other soft-tissue neoplasms. The initial

manifestations are typically abnormal muscle signal intensity and muscle enlargement. Generally, the neoplasms have slightly increased signal intensities compared with normal muscles on T1-weighted images and intermediate signal intensities compared with fat tissues on T2-weighted images (28). In addition, fine-needle aspiration (FNA) biopsy is normally conducted. However, considering the variable degree of cellular pleomorphism and number of anaplastic cells on the smears, the characteristic hallmark cells of ALCL are not always identified in a FNA biopsy sample, and an accurate diagnosis of ALCL is difficult. Therefore, performing ancillary tests, including immunohistochemical and flow cytometric analyses, may assist the diagnosis of ALCL (29). All the aforementioned examinations may help to confirm the diagnosis in order to initiate an appropriate chemotherapy regimen.

In conclusion, the present study represents a rare case of ALCL, primarily involving the skeletal muscle. This disease should be considered when establishing the diagnosis of a hematogenous disease in cases where the patient presents diffuse muscle swelling. The presence of a soft tissue mass on MRI scans, as well as the results of a FNA biopsy and immunohistochemical analysis of the mass, may help the early recognition and correct diagnosis of ALCL, allowing for the appropriate treatment strategy to be initiated.

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