Int J Clin Exp Pathol 2014;7(12):9086-9089
www.ijcep.com /ISSN:1936-2625/IJCEP0002795

Case Report

ALK-positive anaplastic large cell lymphoma with an unusual alveolar growth pattern

Guohua Yu[2], Zifen Gao[1], Xin Huang[1]

[1]*Department of Pathology, School of Medical Science, Peking University Health Science Center, Beijing, China;*
[2]*Department of Pathology, Affiliated Yuhuangding Hospital, Medical College of Qingdao University, Yantai, China*

Received September 26, 2014; Accepted November 26, 2014; Epub December 1, 2014; Published December 15, 2014

Abstract: Anaplastic large cell lymphoma (ALCL) possesses a broad morphological spectrum. Currently, we present a case of ALK-positive ALCL presenting with an alveolar growth pattern in a 22-year-old Chinese female. This patient complained of a progressively enlarged mass in the right axillary region for 6 months. Excisional biopsy revealed a well-developed alveolar structure with nests of dyscohesive tumor cells separated by delicate fibrovascular septae. The large pleomorphic cells have irregular nuclei with prominent nucleoli and fine chromatin and abundant pale cytoplasm. The neoplasm stained positively for CD2, CD3ε, CD30, ALK1, EMA and cytotoxic molecules (TIA1 and Granzyme B). Cytogenetic study via interphase Fluorescence in-Situ Hybridization disclosed the rearrangement involving ALK gene. The patient received 6 cycles of CHOP chemotherapy and achieved complete remission. She is alive in good condition up to the present. Our case is biologically similar to the conventional ALK-positive ALCLs and may just represent an unusual morphological appearance.

Keywords: ALK, immunohistochemistry, alveolar, differential diagnosis

Introduction

Anaplastic large cell lymphoma (ALCL), ALK-positive is a T-cell non-Hodgkin lymphoma that has been recognized as a distinct disease entity in WHO classification of hematopoietic neoplasms [1]. In contrast to the ALK-negative ALCLs, ALK-positive ALCLs frequently occurs in the children and young adults and have a more favorable prognosis [2]. A hallmark cytogenetic abnormality in ALK-positive ALCL is the chromosomal translocation involving ALK gene, of which the t (2; 5) (p23; q35) is the most common [3]. ALCLs are recognized to be highly heterogeneous in the clinical presentations and the histological characteristics [2, 4]. ALCLs usually present with enlargement of lymph node, however, primary extranodal ALCLs were also not rare [5]. Morphologically, ALCLs are characterized by a proliferation of cohesive clusters of pleomorphic large tumor cells that preferentially invade lymphoid sinuses [2, 4]. Due to its various histological appearances, sometimes they can mimic sarcomas or poorly differentiated carcinomas, thereby render great confusion to pathologists [2, 4, 6, 7]. Herein, we reported a case of ALK-positive ALCL with an alveolar growth pattern in a 22-year-old Chinese female presenting with a soft tissue mass. This article emphasizes the potential diagnostic pitfalls and the use of a combination of histological and immunohistochemical findings in establishing the differential diagnosis.

Case report

A 22-year-old Chinese female presented to the clinic with a complaint of a fast-growing lump in the right armpit for 6 months, accompanied with high fever for 1 month. The patient first noted the lump 6 months ago on self-examination. According to the patient, the lump was initially about 2 cm in diameter and was growing since. She did not have any symptom until the last month that she started suffering the high fever. On palpation, the lump was hard and immobile with an ill-defined border. And the overlying skin was reddened and ulcerated (**Figure 1A**). Examination of the superficial lymph nodes was unremarkable. Computed tomography (CT) scan confirmed the presence of an ill-defined

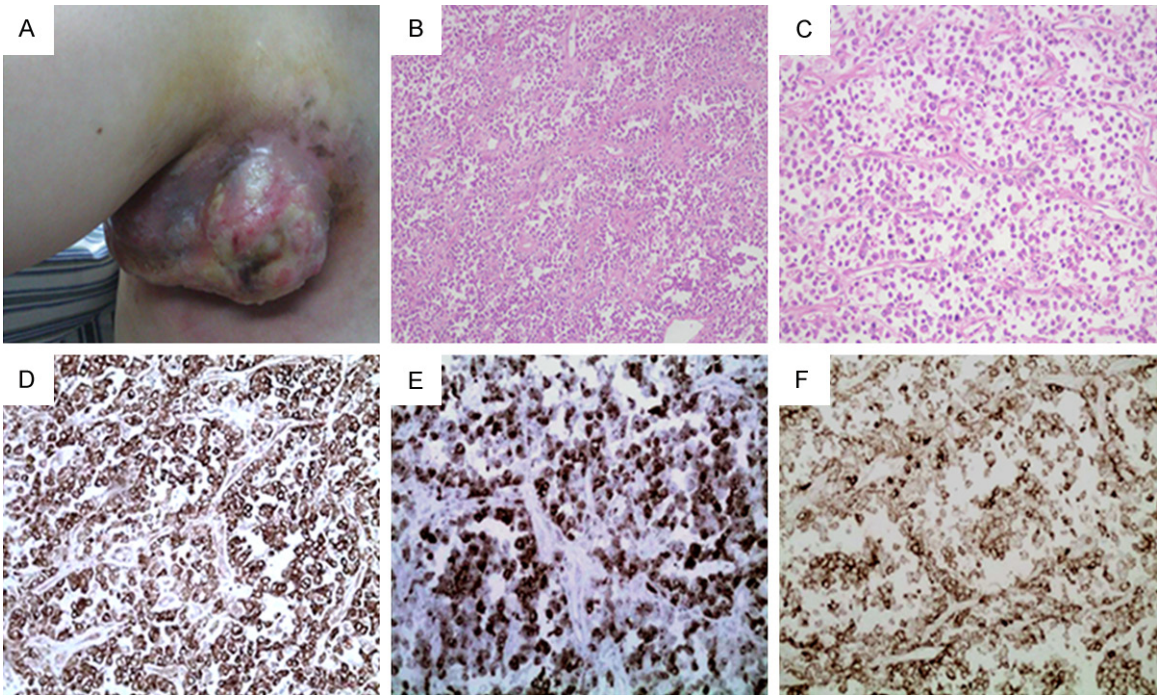

Figure 1. A. A soft mass was noted in the right armpit region. B. Low-power photomicrograph demonstrates well-defined nests of cells separated by delicate fibrovascular septae. C. Within the nests, the tumor cells were lack of cellular cohesion and they were large plemorphic with irregular nuclei, prominent nucleoli and abundant pale or eosinophilic cytoplasm. D-F. The tumor stains diffusely and strongly for CD30, ALK1 and CD3ε.

13 cm × 7 cm soft tissue mass in her right axillary region. Biopsy was taken from the mass, and a diagnosis of ALK-positive ALCL was made. Chest and abdominal CT scan did not show abnormalities. Routine laboratory examination including complete blood counts, blood biochemistry, and erythrocyte sedimentation rate were all unremarkable. A staging bone marrow biopsy was negative for lymphoma. The patient subsequently received CHOP (cylcophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy. After the first course of chemotherapy, CT scan was performed and a 30% reduction in the tumor size was observed. And after 6 cycles of CHOP, she achieved complete remission (CR). Up to the present, she is alive after 20 months and still in follow-up.

Materials and methods

Morphologic and Immunophenotypic studies

Formalin-fixed paraffin-embedded tissue block of tumor mass specimen from this patient was obtained. Histological evaluation was done with haematoxylin and eosin stained section. Immunohistochemical analysis was performed using a standard Avidin Biotin Complex (ABC) immunoperoxidase method. Diaminobenzidine was used as the chromogen and hematoxylin was used for counterstaining. A broad panel of primary antibodies including CKpan, TFE3, myogenin, desmin, CD2, CD3ε, CD20, PAX5, CD30, ALK1, EMA, LCA, TIA1, Granzyme B, and Ki-67, was used. All these antibodies except for TFE3 (Santa Cruz Biotech) were from Dako, Glostrup, Denmark.

FISH analysis

Fluorescence in situ hybridization (FISH) was performed on paraffin section according to the manufacturer's instructions (Vysis/Abbott Molecular) with minor modifications. Commercially available ALK dual color break-apart probe (Vysis/Abbott Molecular) was used to look for ALK gene rearrangement. About 200 interphase nuclei were screened for the probe.

Results

Histopathological findings

Microscopically, the tumor was composed of well-defined nests of cells separated by deli-

cate fibrovascular septae (**Figure 1B**). Within the nests, the tumor cells were lack of cellular cohesion and they were large plemorphic with irregular nuclei, prominent nucleoli and abundant pale or eosinophilic cytoplasm (**Figure 1C**). Mitoses can be easily found.

Immunohistochemical findings

The pleomorphic large neoplastic cells stained strongly for CD30 on the cell membrane and in the Golgi region (**Figure 1D**) and for ALK1 in the nuclei and the cytoplasm (**Figure 1E**). They also showed a diffuse cytoplasmic positivity for CD-3ε (**Figure 1F**) and CD2. Additionally, the tumor cells were positive for LCA, EMA, TIA-1 and Granzyme B. Approximately 90% tumor cells were Ki-67 positive, indicating a high cell proliferation index. Negative markers included CD20, PAX5, CKpan, TFE3, myogenin, and desmin.

FISH analysis

ALK gene rearrangement was identified in this case in almost all nuclei.

Discussion

ALCLs possess a wide morphological spectrum and a few histological subtypes such as the common, small cell, lymphohistiocytic, giant cell-rich, sarcomatoid, monomorphic, and neutrophil-rich variant have been reported [2, 4]. For the current case, a diagnosis of alveolar soft part sarcoma (ASPS) was considered at the preliminary histological evaluation because of its predominant alveolar structure. Likewise, ASPSs typically occurred in young patients. But they stained strongly for muscle-related proteins such as desmin and myogenin. In addition, ASPSs have been recently identified to carry a characteristic chromosomal translocation, namely der(17)t(X;17) (p11;q25), that creates an ASPL-TFE3 fusion protein. Our lesion stained negatively for TFE3, myogenin, and, desmin, ruling out the possibility of ASPS. This lesion was positive for LCA, supporting a hematological origin. Additionally, immunopositivity for T-cell markers, CD2 and CD3ε, together with the coexpression of CD30 and ALK1 established the diagnosis of ALK-positive ALCL. The ALK expression in the current case exhibited a classic pattern with nuclear and cytoplasmic staining. In addition, consistently with the previous studies, the present ALK-positive ALCL also showed a cytotoxic phenotype as defined by the immunoreactivity for TIA-1 and Granzyme B [4, 8]. ALK-positive ALCL affects children and young adults more frequently and usually has a more favorable prognosis [4]. Treatment with anthrocycline-based chemotherapy regimens, most commonly CHOP, is generally recommended for the ALK-positive ALCLs, with approximately 90% response rate [9]. The current patient is a young female and received 6 cycles of CHOP chemotherapy and showed good response to it. ALK gene rearrangements not only contribute to the tumorigenesis of a variety of human malignancies such as ALCL, it also has become a potential therapeutic target. Nowadays, ALK tyrosine kinase inhibitor e.g. crizotinib has demonstrated dramatic response in treating tumors carrying ALK gene rearrangement including ALCL. Our patient would also possibly benefit from it in the near future.

In conclusion, we describe a case of ALK-positive ALCL that displayed an unusual alveolar growth pattern. Its clinicopathologic features was in consistency with the conventional ALK-positive ALCLs. We report this case to expand the histological spectrum of this entity and to emphasize the importance of careful microscopic and immunohistochemical examination for such challenging cases to avoid diagnostic errors.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xin Huang, Department of Pathology, School of Medical Science, Peking University Health Science Center 38 Xueyuan Road, Haidian District, Beijing 100191, China. Tel: +86-10-82805060; Fax: +86-10-82802623; E-mail: huangxin@bjmu.edu.cn

References

[1] Swerdlow SH. International Agency for Research on Cancer. World Health Organization. WHO classification of tumors of haematopoietic and lymphoid tissues. 4th edition. Lyon, France: International Agency for Research on Cancer; 2008. pp. 317-334.

[2] Benharroch D, Meguerian-Bedoyan Z, Lamant L, Amin C, Brugières L, Terrier-Lacombe MJ, Haralambieva E, Pulford K, Pileri S, Morris SW, Mason DY, Delsol G. ALK-positive lymphoma: a single disease with a broad spectrum of morphology. Blood 1998; 91: 2076-2084.

[3] Ladanyi M. The NPM/ALK gene fusion in the pathogenesis of anaplastic large cell lymphoma. Cancer Surv 1997; 30: 59-75.
[4] Jaffe ES. Anaplastic large cell lymphoma: the shifting sands of diagnostic hematopathology. Mod Pathol 2001; 14: 219-228.
[5] Falini B, Pulford K, Pucciarini A, Carbone A, De Wolf-Peeters C, Cordell J, Fizzotti M, Santucci A, Pelicci PG, Pileri S, Campo E, Ott G, Delsol G, Mason DY. Lymphomas expressing ALK fusion protein(s) other than NPM-ALK. Blood 1999; 94: 3509-3515.
[6] Suzuki R, Seto M, Nakamura S, Nakagawa A, Hara K, Takeuchi K. Sarcomatoid variant of anaplastic large cell lymphoma with cytoplasmic ALK and alpha-smooth muscle actin expression: a mimic of inflammatory myofibroblastic tumor. Am J Pathol 2001; 159: 383-384.
[7] Bueso-Ramos CE, Pugh WC, Butler JJ. Anaplastic large cell lymphoma presenting as a soft-tissue mass mimicking sarcoma. Mod Pathol 1994; 7: 497-500.
[8] Foss HD, Anagnostopoulos I, Araujo I, Assaf C, Demel G, Kummer JA, Hummel M, Stein H. Anaplastic large-cell lymphomas of T-cell and null-cell phenotype express cytotoxic molecules. Blood 1996; 88: 4005-4011.
[9] Ferreri AJ, Govi S, Pileri SA, Savage KJ. Anaplastic large cell lymphoma, ALK-positive. Crit Rev Oncol Hematol 2012; 83: 293-302.