

## Original Article

# Sarcomatoid variant of anaplastic large cell lymphoma: a diagnostic challenge

Hong Yu<sup>1\*</sup>, Wenchao Wang<sup>2\*</sup>, Haihui Sheng<sup>3</sup>, Hengjun Gao<sup>3</sup>, Junxing Huang<sup>4</sup>, Chaofu Wang<sup>5</sup>

<sup>1</sup>Department of Pathology, Taizhou People's Hospital, Taizhou, Jiangsu Province, China; <sup>2</sup>Department of Pathology, Yangzhou University School of Medicine, Yangzhou, Jiangsu Province, China. <sup>3</sup>Shanghai Engineering Center for Molecular Medicine, National Engineering Center for Biochip at Shanghai, Shanghai, China; <sup>4</sup>Department of Oncology, Taizhou People's Hospital, Taizhou, Jiangsu Province, China; <sup>5</sup>Department of Pathology, Ruijin Hospital, Shanghai Jiaotong University School of medicine, Shanghai, China. \*Equal contributors.

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**Abstract:** Sarcomatoid variant of anaplastic large cell lymphoma (ALCL) is an extremely rare variant of ALCL with an abnormal morphology and immunophenotype, which is easily misdiagnosed as a high-grade sarcoma, poorly differentiated cancer or melanoma. Here, we reported the case of a 7-year-old boy with a sarcomatoid variant of ALCL involving the right neck lymph node, and compared it with those of the reported cases.

**Keywords:** Anaplastic large cell lymphoma, sarcomatoid variant, diagnosis, differential diagnosis

## Introduction

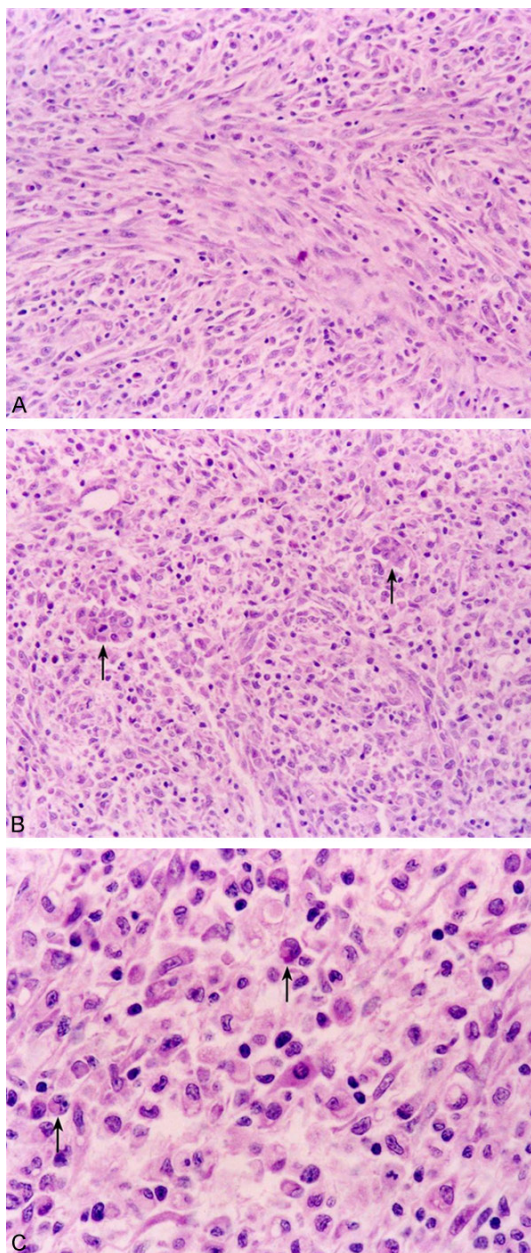
Anaplastic large cell lymphoma (ALCL) is a T-cell or null-cell lineage lymphoma that consistently expresses the activation marker CD30, is usually composed of large neoplastic cells exhibiting abundant cytoplasm, marked nuclear atypia, and horse-shoe shaped nuclei. The sarcomatoid variant of ALCL is one of the rarest and most easily misdiagnosed ALCL subtype first described by Chan [1] in 1990. To date, only 12 cases have been reported. Herein, we described a case of sarcomatoid variant of ALCL arising in the right neck lymph node to increase awareness of this rare disease.

## Case report

A 7-year-old boy presented with one-month history of progressive enlarged right neck lymph node followed by low-grade fever. Physical examination detected a tender mass measuring 2.0 cm × 1.5 cm × 1.5 cm in the right neck. No other superficial mass was found by physical examination. No additional mass or lymphadenopathy was detected by magnetic resonance imaging (MRI) of the thorax and abdomen. Bone marrow biopsy and laboratory tests demonstrated no abnormalities. The mass was ex-

cised and the initial pathological diagnosis was a poorly differentiated carcinoma or a spindle cell sarcoma.

Histologically, normal architecture of the resected cervical lymph node was completely effaced by neoplastic cells. The neoplastic cells were composed of atypical spindle and epithelioid cells with scattered small lymphocytes and histiocytes. The spindle-shaped neoplastic cells focally displayed a storiform growth pattern. The spindle cells exhibited eosinophilic cytoplasm with indistinct borders and contained oval or elongated nuclei with one to several small nucleoli. The epithelioid cells grew in a cohesive manner, with clusters of adhesion cells. They possessed round or irregularly folded nuclei, coarse chromatin, and large nucleoli. Occasional multiple nuclei occurred in a wreath-like pattern. The cytoplasm appeared clear, basophilic or eosinophilic. Hallmark cells with eccentric, horse-shoe or kidney-shaped nuclei with an eosinophilic region near the nucleus often appeared. The mitotic count averaged two to three per high-power field (**Figure 1**). For Immunohistochemical assay (IHC), the tumor cells were positive for ALK-1, epithelial membrane antigen (EMA), CD30, CD45RO, CD45, granzyme B and TIA-1, alpha smooth muscle



**Figure 1.** The tumor was composed of spindle cells and epithelioid cells with scattered small lymphocytes and histiocytes. A. The spindle cells focally displayed a storiform growth pattern (100 ×). B. Clusters of adhesion cells (arrow) (100 ×). C. Highly pleomorphic cells and scattered hallmark cells (arrow) (400 ×).

actin (SMA) (only spindle cells), and partially positive for CD68, whereas negative for CD3, CD20, CD79 a, cytokeratin, S-100, and Melan-A (Figure 2). Furthermore, the clonal rearrangement of T cell receptor  $\beta$ 1 chain gene (TCR $\beta$ 1) was found (Figure 3). The final pathological diagnosis was confirmed as sarcomatoid vari-

ant of ALCL. The boy was treated with three cycles of CHOP chemotherapy, and remains disease free after 42-month follow-up.

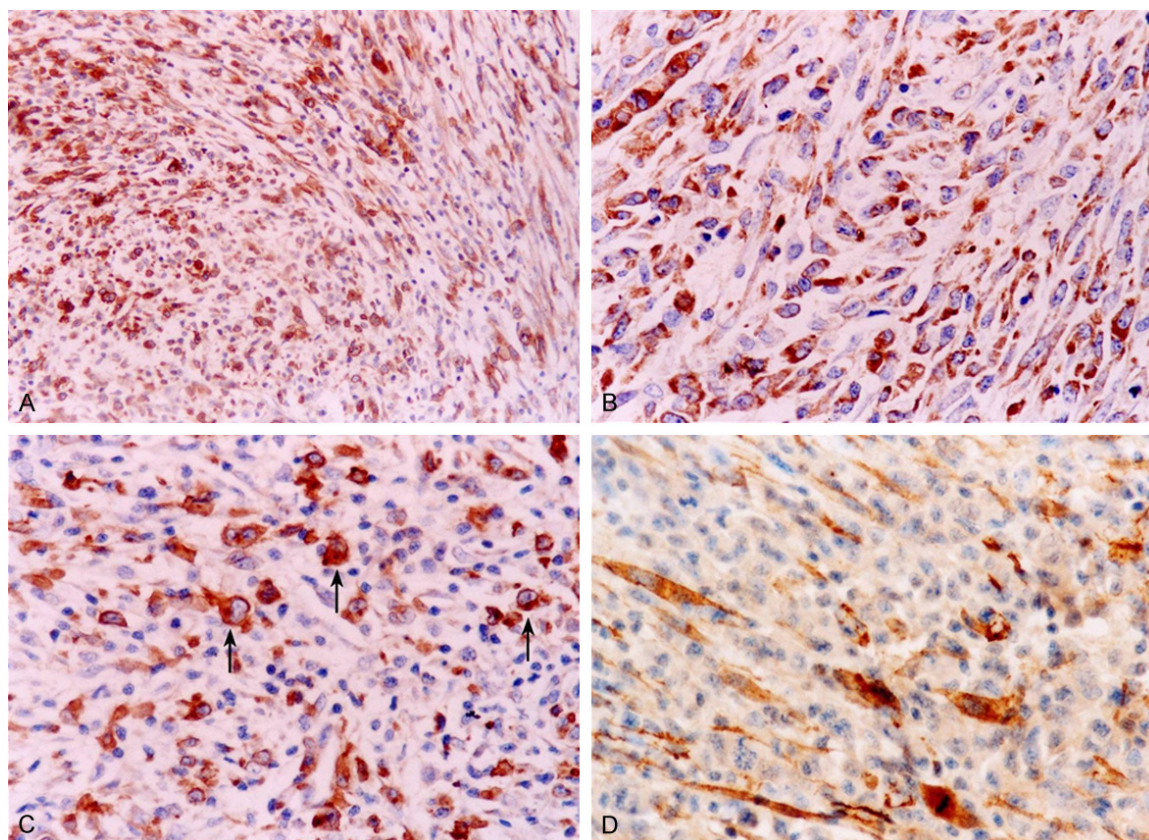
## Discussion

ALCL shows a wide variety of morphological variants including classical, small cell, Hodgkin-like, lymphohistiocytic, sarcomatoid and mixed subtypes. Sarcomatoid variant of ALCL is one of the rarest histologic variant of ALCL, which was first reported by Chan in 1990, so far only 12 cases have been reported in the English literature [1-12]. **Table 1** shows the clinicopathological features of the 13 cases including the present case, with the mean age of 52.2 years old (range 6~92 years). Among 13 cases, the lesions were extensively involved in multiple system and organs in 7 cases, and the lesions were limited in 6 cases including our case. According to the above clinical characteristics, men and women were equally affected, and sarcomatoid variant of ALCL was more common in adults but relatively rare in children. Sarcomatoid variant of ALCL is frequently misdiagnosed as other malignant tumors. Among 12 previous reported cases, initial diagnosis was breast cancer in 1 case [7], and sarcoma in 10 cases [1-5, 8-12]. Furthermore, 1 case was correctly diagnosed after autopsy [2]. The initial diagnosis was large cell lymphoma only in 1 case [6]. Among previous reported cases, only 6 cases were followed 3 to 14 months. The tumor only involved the cervical lymph nodes in the present case. The patient received three cycles of CHOP chemotherapy, and remained disease free after 42-month follow-up.

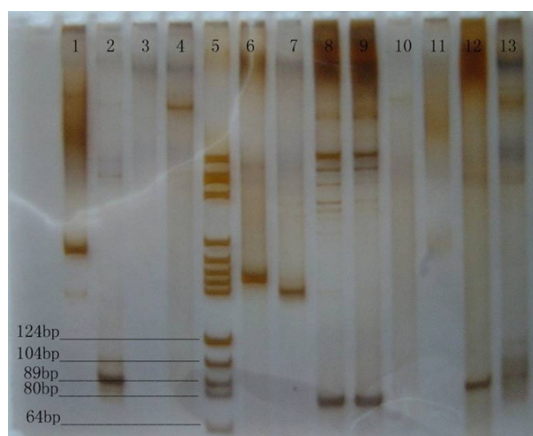
Sarcomatoid variant of ALCL is different from common type ALCL in morphologic features. It is composed of atypical spindle-shaped tumor cells which are often arranged in a storiform pattern even with myxoid stroma. The appearance of storiform pattern and myxoid stroma is the main cause of misdiagnosis. In our case, the nodal lesion showed sarcomatoid histologic features composed of spindle-shaped tumor cells and storiform pattern, but no sure myxoid stroma was found. Despite morphologic atypical, the cytological features of any type of ALCL including sarcomatoid variant of ALCL include the presence of hallmark cells. The hallmark cells show an eccentrically placed nuclei with horse-shoe, wreath, reniform or embryoid appearing morphology. The nuclei show multiple



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**Figure 2.** IHC assay. A. Neoplasm cells were strongly positive for ALK-1 (100 ×). B. Neoplasm cells were strongly positive for EMA (400 ×). C. Neoplasm cells were strongly positive for CD30. The stain of CD30 was localized to the cell membrane, Golgi zone, or both in the tumor cells (arrow) (400 ×). D. Spindle-shaped neoplasm cells were positive for a-SMA (200 ×).



**Figure 3.** Gene rearrangement of TCRβ1. 1. FR2 positive control. 2. FR3A positive control. 3. FR2 in tumor tissues. 4. FR3A in tumor tissues. 5. Marker. 6. TCRγ1 positive control. 7. TCRγ2 positive control. 8. TCRβ1 positive control. 9. TCRβ2 positive control. 10. TCRγ1 in tumor tissues. 11. TCRγ2 in tumor tissues. 12. TCRβ1 in tumor tissues. There was a clear clone band at 90 bp. 13. TCRβ2 in tumor tissues.

small to prominent nucleoli with an eosinophilic region near the nucleus. There were many hall-mark cells in the epithelioid component of this case, so we first consider the ALCL from differential diagnosis. We believe that one of the key to avoid pathological misdiagnosis and missed diagnosis is the careful observation of morphology and to search for characteristic from untypical features.

Morphology of sarcomatoid variant of ALCL is similar to sarcomatoid carcinoma, high-grade sarcoma, and malignant fibrous histiocytoma (MFH). Therefore, the detection of immune phenotype is very important for the diagnosis and differential diagnosis of sarcomatoid variant of ALCL. **Table 1** showed that all 13 case were positive for CD30, 12 cases were positive for EMA. Eight cases were tested for ALK, and only 4 cases were positive for ALK. Two cases were null cell type, and all T-cell markers are negative. Abnormal immune phenotype might app-

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**Table 1.** Clinicopathological features of 13 cases of sarcomatoid variant of ALCL

Reference	Age (y)/Sex	Site	Size (cm)	IHC	Treatment	Follow-up
1	45/M	Soft tissue of right leg	Not reported	LCA, CD30, UCHL1, EMA (focal)	Wide local excision, chemo-radiotherapy	6-month died of infection
2	42/F	Inguinal, paratracheal, mediastinal, thoracic, para-aortic, right groin, breast, etc.	Not reported	CD30, UCHL1, EMA, Vimentin	Not reported	Died of rapidly progressive disease
3	79/M	Soft tissues of left elbow	2	LCA, CD30, UCHL1, CD43	Local excision	Not reported
4	44/M	Left inguinal	4	CD30, UCHL1, EMA	Chemotherapy	Not reported
5	6/F	Axillary and supraclavicular	Not reported	ALK-1, CD30, CD4, EMA, granzyme B, TIA-1	Chemotherapy	10-month free of disease
6	60/M	Right pre-auricular skin mass	20	CD30, CD2, CD43, CD45, Actin, ALK1-negative	Chemotherapy	Not reported
7	92/F	Left breast	2.7	CD30, EMA, UCHL1, LCA, Vimentin, ALK1-negative	Local resection, chemotherapy	3-month died of infection
8	51/M	Superficial mass in left groin	23	CD30, EMA, UCHL1, Vimentin, ALK1-negative	Local resection, chemotherapy	14-month free of disease
9	78/F	Bladder	Not reported	ALK-1, CD2, CD3, CD5, CD30, EMA, granzyme B, TIA-1	Not reported	Not reported
10	14/M	Right sternoclavicular joint	5	ALK-1, LCA, CD3, CD30	Not reported	Not reported
11	68/F	Right and left lower back skin mass	1.5	CD3, CD4, CD30, ALK1-negative	Without treatment	6-month free of disease
12	47/F	Bilateral lung	5.4	CD30, CD45, EMA, granzyme B, TIA-1, ALK1-negative	Chemotherapy	10-month free of disease
Our case	7/M	Right neck	2	ALK-1, EMA, CD30, CD45RO, CD45, granzyme B, TIA-1, SMA	Chemotherapy	42-month well

ear in sarcomatoid variant of ALCL. Three cases were positive for vimentin, 1 case was positive for actin, and our case was partially positive for a-SMA and CD68. If the diagnostic idea is limited and the number of antibodies is not enough, sarcomatoid variant of ALCL is more likely to be misdiagnosed. Therefore, it is necessary to select the sufficient markers based on the morphological characteristics.

There was no report on the genetic testing of the sarcomatoid variant of ALCL in the reported cases. The present case showed the clone rearrangement of TCR $\beta$ 1. This indicates that the cytogenetic changes of the sarcomatoid variant of ALCL may be similar to that of the classical type ALCL.

The differential diagnosis of sarcomatoid variant of ALCL includes MFH, sarcomatoid carcinoma, malignant melanoma, inflammatory myofibroblastic tumor (MT), and lymphocyte depleted Hodgkin lymphoma (LDHL). Although MFH and sarcomatoid variant of ALCL show positive for SMA, vimentin, and CD68, and have spindle-shaped tumor cells and myxoid stroma, MFH does not express CD30, EMA, LCA, ALK-1, TIA-1, GB, and T cell markers which are usually positive in sarcomatoid variant of ALCL. Furthermore, despite EMA could show positivity both in sarcomatoid variant of ALCL and sarcomatoid carcinoma, the former does not express cytokeratins and the latter usually does not express CD30, LCA, ALK-1, TIA-1, GB and T cell markers. Malignant melanoma usually shows strong positivity of melan-A, HMB-45, and S100 protein, while sarcomatoid variant of ALCL does not express melanocytic markers, but always shows CD30, LCA, TIA-1, GB, and T cell markers. In addition to the morphologic differences, MT is negative for EMA, CD30 and T cell markers and thus could be distinguished from sarcomatoid variant of ALCL. LDHL may be positive for CD15 and CD20 but negative for ALK-1, TIA-1, GB, and T cell markers, which could be helpful to distinguish LDHL from sarcomatoid variant of ALCL. Of course, it is necessary to detect gene rearrangement when the disease is difficult to diagnose.

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### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Chaofu Wang, Department of Pathology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China. E-mail: wangchaofu@126.com; Dr. Junxing Huang, Department of Oncology, Taizhou People's Hospital, Taizhou, Jiangsu Province, China. E-mail: hjxtz@sina.cn

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