Case Report

Extranodal anaplastic large cell lymphoma mimicking sarcoma: A report of an interesting case

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Abstract

Lymphomas are malignancies of the lymphoid tissues involving cells of the immune system. Primary systemic anaplastic large cell lymphoma (ALCL) represents an aggressive lymphoma characterized by neoplastic proliferation of lymphoid cells with an anaplastic appearance. Large pleomorphic cells are "hallmark" cells with horseshoe-shaped or kidney-shaped nuclei and a constant expression of the CD30 molecule on all neoplastic cells. There is a vast morphological spectrum posing a challenge to pathologists in the diagnosis of ALCL.

Key words: Anaplastic large cell lymphoma, extranodal, lymphoma, pleomorphic, sarcoma

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Introduction

Lymphomas are malignancies of the lymphoid tissue. They involve cells of the immune system, which at times may result in a devastating type of cancer.

Primary systemic anaplastic large cell lymphoma (ALCL) represents 2-8% of adult non-Hodgkin's lymphoma (NHL) cases and as much as 30% of childhood NHL cases.[1] It is an aggressive lymphoma that was first described in 1985 as Ki-1 lymphoma, characterized by neoplastic proliferation of lymphoid cells which are anaplastic in appearance.[2] ALCL is a lymphoma category defined as a tumor composed of large pleomorphic cells, some with prominent nucleoli and multinucleation, and shows a variable number of "hallmark" cells with horseshoe-shaped or kidney-shaped nuclei[3] and a constant expression of the CD30 molecule on all neoplastic cells.[4] Involvement of lymph nodes as well as extranodal sites such as skin, soft tissue, and the gastrointestinal tract is seen.[5] Morphological similarity between ALCL and other lymphomas has been reported, and their growth in a cohesive pattern often mimics nonhematologic malignancies such as sarcomas, carcinomas, germ cell tumors, and melanoma.[6] Hence, the presence of a vast morphological spectrum may pose a challenge to pathologists in the diagnosis of ALCL.

We describe here a case of ALCL mimicking a high-grade sarcoma in a 16-yearold girl.

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Case Report

A 16-year-old female patient was referred to the surgery outpatient department with complaints of right infra-auricular mass for the past 5 months. A previous fine-needle aspiration cytology of the mass done at another hospital reported it as undifferentiated carcinoma. Histopathologic examination of the biopsy specimen that was taken at the same hospital was reported as a high-grade malignant soft-tissue tumor. On examination, ulcero-proliferative growth in the right infra-auricular area was seen with non-healing ulcer of the overlying skin for the past 1 month. No significant lymph node involvement was seen.

Routine laboratory investigations were within normal range as follows: Hemoglobin (Hb) 11.2 g/dl; total leukocyte count (TLC) 14,200/mm^3, *P* 71%, L 21%, E 06%, and M 02%; platelets 3.34 lacs/mm^3; bleeding time 2 min 30 s; and clotting time 6 min 45 s. Biochemical investigations comprising liver

function tests, renal function tests, and serum electrolytes were within normal limits.

Radiological investigations comprised chest X-ray which showed no abnormality, along with contrast-enhanced computerized tomography (CECT) and magnetic resonance imaging (MRI). Both the imaging modalities revealed a 6 × 6 cm mass lesion involving the right parotid region, extending into the infra-auricular area with irregular margins. No significant lymph node involvement was seen. The patient was taken up for surgery under general anesthesia and a wide right neck composite resection with excision of the mass was done along with lymph node dissection from level I to level V and the sample was sent for histopathology.

Grossly, the specimen was a gray-white, globular, soft-tissue mass, partially covered with skin, and measured 7 × 6 × 4 cm with ulceration on the surface. On cutting, a variegated, firm yellow-white tumor mass infiltrating the skeletal muscle was seen. Microscopic examination showed large atypical cells arranged in sheets, clusters, and alveolar pattern. The cells were bizarre, and anaplastic with numerous multinucleated giant cells along with lobulated (embryo-like) nuclei and a prominent nucleolus [Figures 1 and 2]. Mitosis was brisk with several atypical forms. The lymph nodes showed reactive change. A histopathologic diagnosis of malignant soft-tissue sarcoma was made with the possibilities of pleomorphic sarcoma, rhabdomyosarcoma, and ALCL. Immunohistochemistry (IHC) was advised for further characterization. A panel of antibodies comprising cytokeratin (CK), epithelial membrane antigen (EMA), desmin, leukocyte common antigen (LCA), CD30, and anaplastic lymphoma kinase (ALK) was put up. Anaplastic cells were positive for LCA, CD30 [Figure 3], and ALK [Figure 3], and weakly positive for EMA.

Discussion

Morphology of tumors is known to vary on hematoxylin and eosin (H and E) stained sections due to many reasons such as artifacts, pattern of infiltration, and the tissue being infiltrated.[7] NHL has been reported to mimic many non-lymphoid tumors; large cell lymphomas at different sites mimic carcinoma, gastrointestinal stromal sarcoma, thymoma, and melanomas (CD30+).[7] In the present case also, the histomorphological features resembled an aggressive sarcoma which on biopsy had initially been diagnosed as pleomorphic sarcoma.

A review of literature highlights ALCL in pediatric age groups, which mimics non-lymphomatous tumors. In the report by Gustafson *et al.*, a 6-year-old girl had ALK-positive ALCL that arose in soft tissue of the neck, which was initially interpreted as a neuroblastoma. The panel of antibodies did not assess CD30 and ALK as there was no suspicion of ALCL; however,

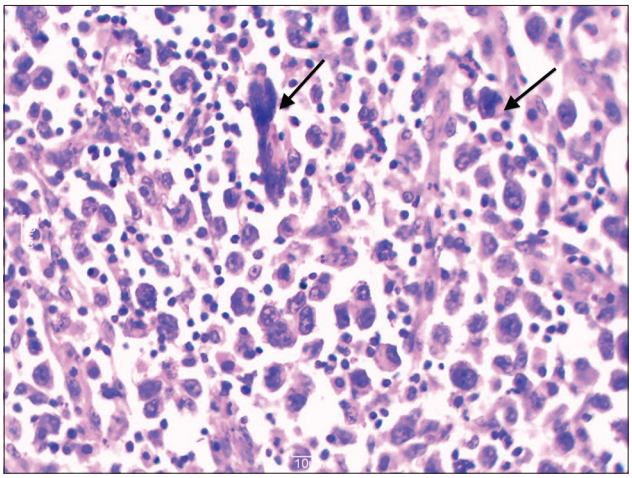

Figure 1: Microphotograph showing large atypical cells arranged in sheets with bizarre, anaplastic forms, along with numerous multinucleated giant cells (H and E, ×20)

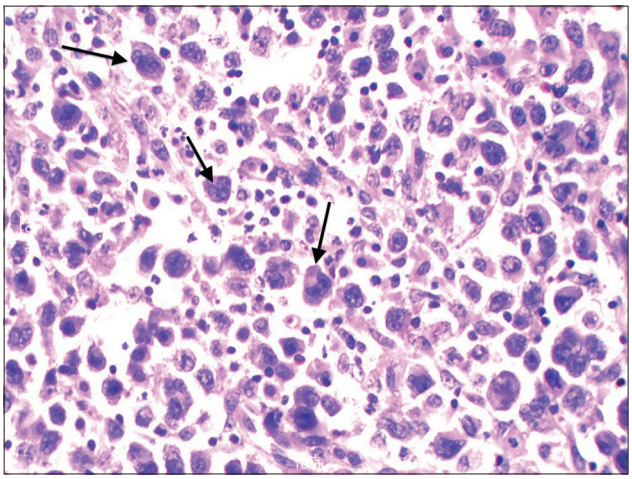

Figure 2: Morphological appearance of anaplastic large cell lymphoma. The arrow indicates typical hallmark tumor cells with lobulated (embryo-like) nuclei and a prominent nucleolus (H and E, ×20)

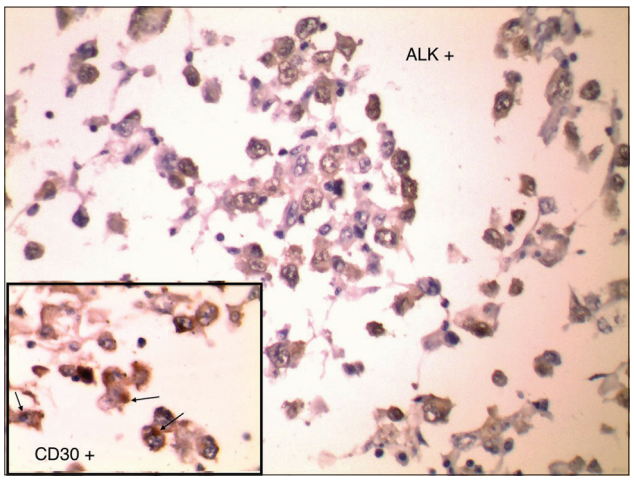

Figure 3: Microphotograph showing nuclear and cytoplasmic ALK positivity in tumor cells along with CD30 positivity (inset) (IHC, ×20)

on review, the possibility of ALCL was considered and was supported by CD30 and ALK positivity.[8] In another report, two patients aged 9 and 16 years, respectively, who presented with soft tissue and axillary nodes and showed pleomorphic cells in loosely cohesive cells around the blood vessels and embryoid nuclei were differentially diagnosed as rhabdomyosarcoma and a lymphoma. IHC was conclusive in diagnosing ALCL.[9] An 8-year-old child also presented with ALCL of the gluteal muscles.[10] In all these cases, the morphological suspicion as well IHC played an important role in arriving at the correct diagnosis.

An accurate recognition of a lymphoma at an extranodal site is essential to avoid unnecessary excisions.[9] ALCL should be considered in the differential diagnosis of pediatric soft-tissue tumors, especially in cases with multifocal involvement.[9] Other lesions which may also be considered in the differential diagnosis of ALCL are small round blue cell tumors,[8] rhabdomyosarcoma,[9] sarcomas including Ewing's/primitive neuroectodermal tumor,[11] osteosarcoma,[11] and even tuberculosis.[11] Pant *et al*., in their study of 12 cases, concluded that the pleomorphic cytomorphology of ALCL leads to confusion with the bone and soft-tissue sarcomas affecting the musculoskeletal system.[11] In our case also, the adolescent girl was initially diagnosed with an aggressive pleomorphic sarcoma on biopsy; however, histopathologic evaluation of the resected specimen revealed classical ALCL morphology of hallmark cells, prompting an appropriate panel of antibodies. Thus, as suggested by some authors, a high index of suspicion is necessary to initiate the correct panel of immunohistochemical markers to first confirm the lymphomatous nature of this tumor and to subsequently characterize it.[11]

ALCL is the most common mature T-cell neoplasm in children and adolescents, comprising approximately 30% of all NHLs in this age group. Unlike adults, in children, it is nearly universally ALK positive, as was seen in the present case also.[12] The common type is characterized by sheets of large lymphoid cells with chromatin-poor horseshoe-shaped nuclei containing multiple nucleoli. Such cells with these cytologic features have been called hallmark cells, which are seen in all ALCL variants.[4,13]

To conclude, ALCL is a distinctive type of NHL that can masquerade as a variety of neoplastic and non-neoplastic conditions. ALCL in children is universally ALK positive and should be considered in the differential diagnosis of pediatric soft-tissue tumors. Since the morphological spectrum of ALCL is wide it may pose a challenge to pathologists; identification of classical hallmark cells and a high index of suspicion are necessary to initiate the correct panel of immunohistochemical markers in establishing the diagnosis. Histopathologic examination with IHC is the gold standard in establishing the diagnosis.

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