ALK-negative primary cutaneous T-cell anaplastic large cell lymphoma, myxoid variant; masquerading as sarcoma: unveiling the diagnostic dilemma

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SUMMARY

We present a case of 50-year-old man with history of ulcerative right axillary mass for 6 months. Axillary lymphadenopathy and organomegaly were absent. Microscopic examination showed sheets of pleomorphic cells which were mitotically active. Distinctive myxoid change was seen throughout the tumor. These cells were strongly positive for CD30 and vimentin but were negative for CD3, CD5, CD20, CD15, anaplastic lymphoma kinase protein (ALK), CD56, cytokeratin, melan A, desmin, myogenin, CD68, S100, epithelial membrane antigen and CD34. The final diagnosis of primary cutaneous ALK-negative T-cell anaplastic large cell lymphoma (PCALCL), myxoid variant was made. Work-up revealed no systemic involvement. The patient received eight cycles of cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide chemotherapy with complete resolution of disease. This case report highlights that a high index of suspicion is necessary in patients of PCALCL due to varied clinical presentation, and to discuss in brief the histopathologic and immunophenotypic features of this entity along with its differential diagnosis.

BACKGROUND

Anaplastic lymphoma kinase protein (ALK)-negative anaplastic large cell lymphoma (ALCL) is defined by the WHO as a CD30-positive T-cell neoplasm that are not reproducibly distinguishable from ALK-positive ALCL except on the basis of absence of ALK protein.[1] The most common presentations of primary cutaneous ALCL are as an ulcerating mass or a nodule and less commonly as multiple nodules limited to a single area on the skin with the usual size smaller than 2.5 cm.[2 3] The peak incidence of ALK-negative ALCL is in fifth and sixth decades with the median age of 58 years, unlike ALK-positive forms which usually occurs in children and young adults. These ALK-negative ALCLs have male preponderance and worse prognosis. They can involve lymph nodes as well as extranodal sites including bone, soft tissue and skin.[4] The systemic form of ALCL commonly presents with lymphadenopathy as well as extranodal involvement. ALK-negative forms are less likely to involve extranodal sites as opposed to ALK-positive forms.[5] Most patients present with advanced stage disease with peripheral and/or abdominal lymphadenopathy and/or bone marrow involvement and 'B' symptoms including high-grade fever and weight loss.[6 7] It has also been noticed that there is an associated cutaneous involvement in nearly 20% of ALK-positive cases of systemic ALCL.[8] The myxoid variant of ALK-negative ALCL has been described seldom, either in the primary cutaneous form or systemic form.[9–11] With the best of our knowledge Chan *et al* in 1990 reported the very first case of a primary cutaneous ALCL in a 45-year-old man with prominent sarcomatoid and myxoid features occurring as a solitary tumour nodule on leg.[9]

CASE PRESENTATION

A 50-year-old man presented to the physician with an ulcerative right axillary mass which was present for the past 6 months. The mass was progressively increasing in size and was associated with pain and tenderness. There were no complaints of cough, dyspnoea or evening rise of temperature. The patient had no history of diabetes. There was no relevant family history present. On physical examination, an ulcerated, irregular and firm mass of approximately 5 cm was noted in the right axilla (figure 1). Axillary lymphadenopathy and organomegaly were absent. An excisional biopsy of the mass was performed and sent to us for histopathological examination.

INVESTIGATIONS

Non-contrast computerised tomography and contrast-enhanced CT of the thorax, neck and abdomen showed normal scans. For histopathological examination, we received a single greyish brown soft tissue piece measuring 3×2.5×1.5 cm without the overlying skin. On light microscopy, sections showed sheets of pleomorphic population of large polygonal to round cells having hyperchromatic nuclei and abundant eosinophilic cytoplasm. These neoplastic cells were mitotically active and at places were arranged in perivascular pattern. Distinctive myxoid change was seen throughout the tumour. Eosinophils, neutrophils, small lymphocytes and histiocytes were intimately admixed with the cells throughout the lesion (figures 2 and 3).

DIFFERENTIAL DIAGNOSIS

The differentials that were considered based on light microscopy findings were myxoinflammatory fibroblastic sarcoma, inflammatory myofibroblastic tumour, myxoid liposarcoma, myxofibrosarcoma and malignant melanoma.

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Figure 1 Clinical photograph of an ulcerated lesion over right axilla.

On immunohistochemistry (IHC), the neoplastic cells were negative for cytokeratin, melan A, desmin, myogenin, CD68, S100, epithelial membrane antigen (EMA) and CD34 with positivity for vimentin only (figure 4). Retrospective examination of the tumour showed cells having horseshoe-shaped (hallmark cells) and wreath-like nuclei along with few binucleated cells (figures 3 and 5). The second panel of IHC showed that the neoplastic cells were strongly positive for CD30. The cells were negative for CD3, CD5, CD20, CD15, CD56 and ALK-1 (figure 4). The final diagnosis of primary cutaneous ALK-negative T-cell ALCL, myxoid variant was made.

The involvement of lymph node was never confirmed because the specimen was diffusely involved by the myxoid process. Moreover, the apparent absence of axillary lymphadenopathy suggested that the process was primarily cutaneous rather than systemic.

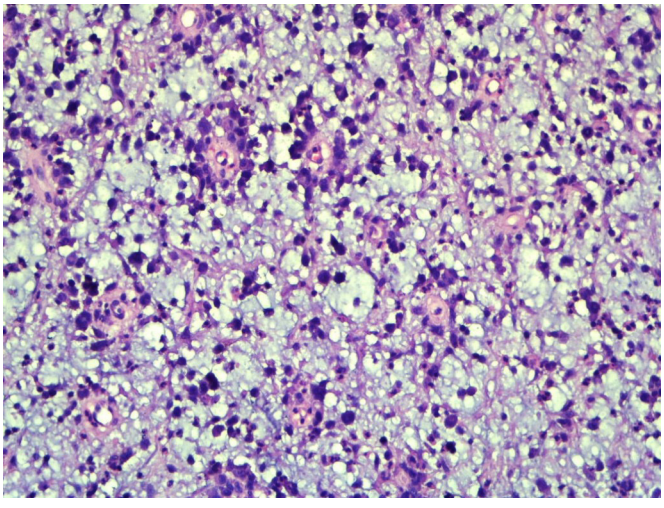

Figure 2 ×100 magnification image showing large atypical cells with perivascular arrangement and diffuse myxoid areas in the background.

TREATMENT

The patient received eight cycles of cyclophosphamide, doxorubicin, vincristine,prednisone and etoposide (CHOP-E) chemotherapy.

OUTCOME AND FOLLOW-UP

During 6-month follow-up period, there was complete resolution of symptoms with no residual cutaneous disease. Bone marrow examination showed no evidence of infiltration by tumour cells.

DISCUSSION

Primary cutaneous T-cell lymphomas (CTCLs) include clinically and biologically heterogenous group of non-Hodgkin lymphomas defined by clonal proliferation of skin-homing malignant T lymphocytes.[12] Primary cutaneous CD30+

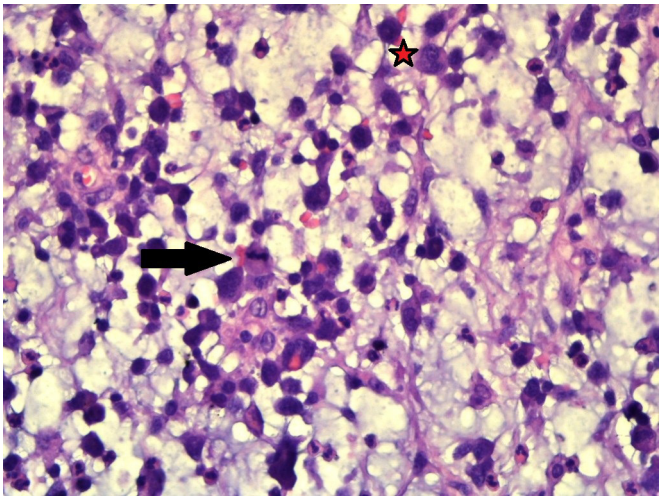

Figure 3 ×400 magnification shows abundant mucin, which is easily seen intermingled with the inflammatory cells comprising of eosinophils, neutrophils and small lymphocytes along with binucleated cells (star) with mitotic figures (arrow head).

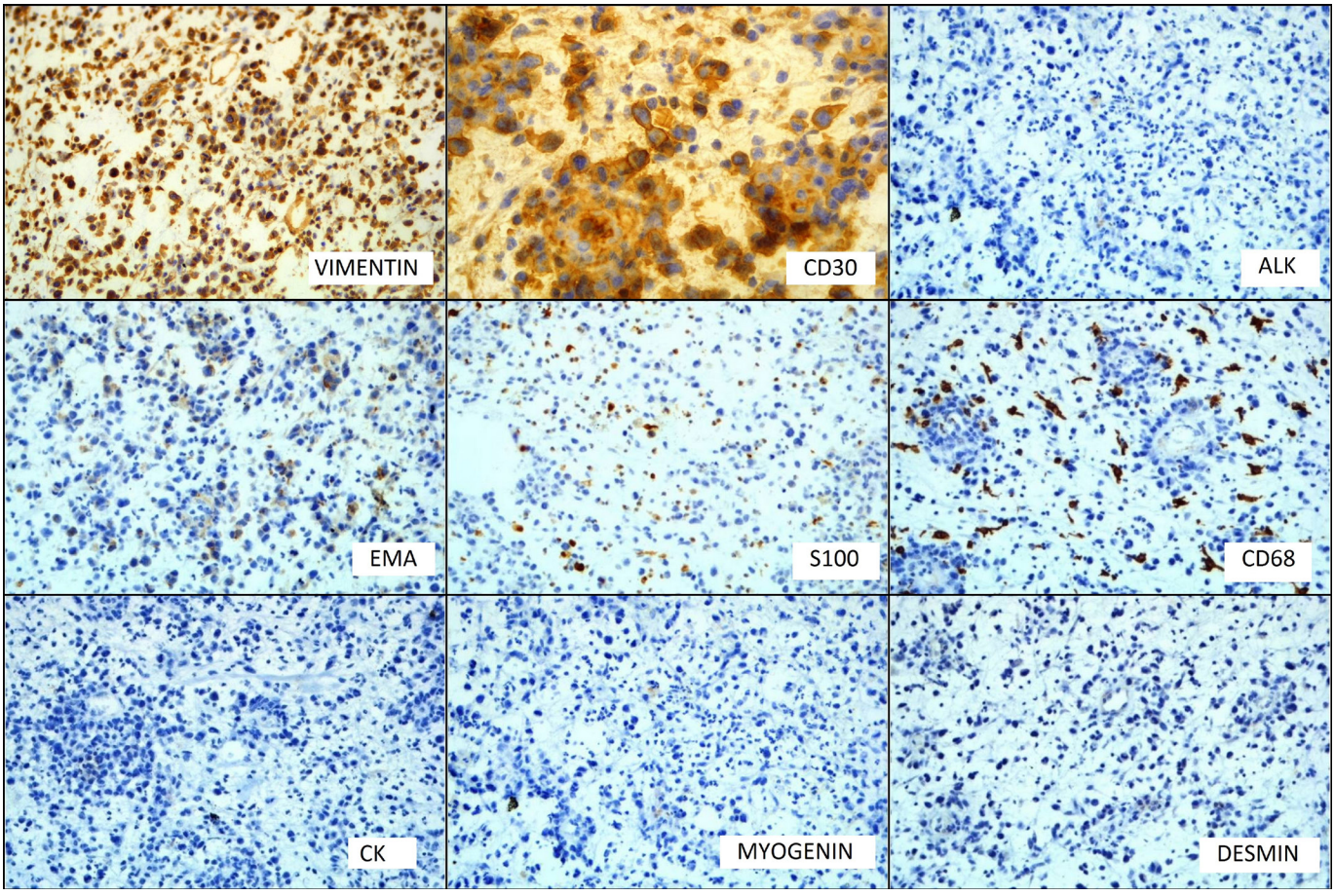

Figure 4 Immunohistochemistry Images: vimentin and CD30 show positive immunostaining, while anaplastic lymphoma kinase (ALK), epithelial membrane antigen (EMA), S100, CD68, cytokeratin, myogenin and desmin do not show immunoreactivity.

lymphoproliferative disorders account for 30% of the CTCL.[13] Under the group of primary cutaneous CD30+ lymphoproliferative disorders, the following diseases are included: primary cutaneous anaplastic large cell lymphoma (PCALCL), lymphomatoid papulosis (LyP) and borderline cases. The criteria for the diagnosis of PCALCL include: (a)>75% infiltration of CD30+ large anaplastic cells in skin biopsy, (b) no clinical history of LyP, mycosis fungoides or other cutaneous lymphomas and (c) no extracutaneous localisation after extensive investigations at presentation.[14]

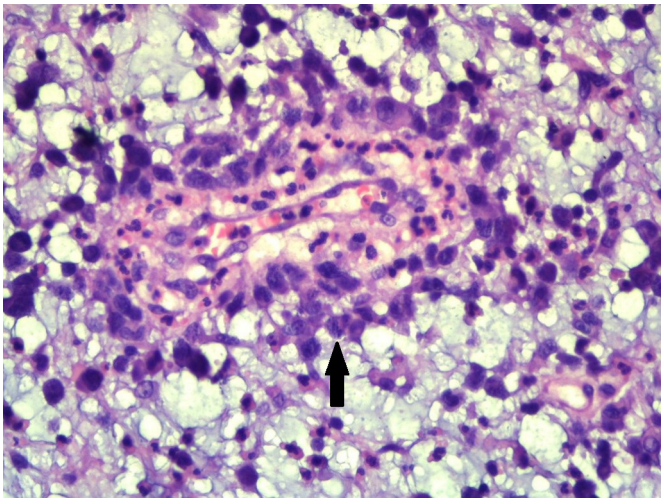

Figure 5 ×400 magnification shows large atypical cells with hallmark cells (arrow head).

This case represents a unique example of a myxoid variant of ALK-negative primary cutaneous T-cell ALCL. Until today myxoid variant has been described rarely.[9–11] This tumour can be easily misdiagnosed as high-grade sarcoma. In our case also, ALCL was not the leading diagnostic consideration initially because of the prominent myxoid change, the mixed cellular infiltrate and pleomorphic population of large polygonal to round cells. A myxoid sarcoma was initially considered because of the deep dermal and subcutaneous involvement, the nodular growth pattern and the observation that myxoid change is commonly seen in many soft tissue sarcomas. The differentials that were initially considered were myxoinflammatory fibroblastic sarcoma, inflammatory myofibroblastic tumour, myxoid liposarcoma, myxofibrosarcoma and malignant melanoma. It was only after the negative findings of the first IHC panel (cytokeratin, melan A, desmin, myogenin, CD68, S100, EMA, and CD34) that the morphology was reviewed and hallmark cells were identified, after which the possibility of myxoid ALCL was considered

PCALCL is a chemosensitive and radiosensitive lymphoma. Treatment strategies include excision, local radiotherapy, CHOP chemotherapy or combination of these modalities.[15 16] The overall complete response of PCALCL to CHOP therapy is 83%.[16]

Learning points

- Primary cutaneous myxoid anaplastic large cell lymphoma (ALCL) is a diagnostic challenge for both clinicians and histopathologists. Establishing a proper diagnosis is possible based on thorough medical history, clinical and imaging examinations, and histopathological evaluation of the biopsy sample from the lesion site.
- We suggest including myxoid ALCL in the histopathologic differential diagnosis of cutaneous lesions with a prominent myxoid background.
- Careful examination for the presence of a hallmark cells and the use of immunohistochemistry, particularly CD30, can help avoid a misdiagnosis which can lead to inappropriate therapy and result in disease progression or unnecessary harm to the patient.

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