

## Anaplastic large cell lymphoma in a child presenting with cutaneous nodules and blisters

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**SUMMARY:** Çağlar K, Akyüz C, Üner A, Kutluk T, Yalçın B, Varan A, Büyükpamukçu M. Anaplastic large cell lymphoma in a child presenting with cutaneous nodules and blisters. Turk J Pediatr 2005; 47: 188-190.

A 13-year-old girl was admitted to our hospital with a one-month history of bullous skin lesions. Physical examination revealed ulcerated and nonulcerated cutaneous plaques, bullae, enlarged cervical and supraclavicular lymph nodes and hepatomegaly. In another hospital, histopathological diagnosis of a skin biopsy was reported to be consistent with tuberculosis and she was treated with antimycobacterial drugs. Since no response was obtained, she was referred to our center after a new lymph node biopsy was obtained. At our center, histopathological diagnosis was anaplastic lymphoma kinase (ALK)-negative anaplastic large cell lymphoma (ALCL). We started LMT chemotherapy regimen and initial response was complete. Eight months after initial admission, she experienced cutaneous recurrence of disease while on maintenance protocol. Chemotherapy was changed to LSA4 regimen. She is still on chemotherapy and has been in complete remission for nine months. Clinicians should be aware of this uncommon presentation of ALCL, which can be confused with other diseases clinically or histologically.

**Key words:** children, lymphoma, skin lesions, tuberculosis.

Anaplastic large cell lymphoma (ALCL) is recognized as a subtype of large cell lymphoma and is mostly of T-cell origin<sup>1,2</sup>. Three forms of ALCL have been identified: systemic, anaplastic lymphoma kinase (ALK) positive; systemic, ALK negative; and primary cutaneous ALCL<sup>1</sup>. Lymphomas constitute 11% of all childhood malignancies<sup>3</sup>. In the pediatric age group, non-Hodgkin's lymphomas (NHL) may present in extranodal locations<sup>4,5</sup>. Large cell histologic subtype of NHL may present primarily in skin or involve the skin secondarily<sup>3-5</sup>. Two-thirds of pediatric ALCL cases present with systemic disseminated disease at diagnosis, including extranodal tissues such as skin<sup>6,7</sup>.

We report a case of CD 30 positive ALCL with a T-cell phenotype who presented with ulcerated plaques and bullous skin lesions, which is very rare in childhood.

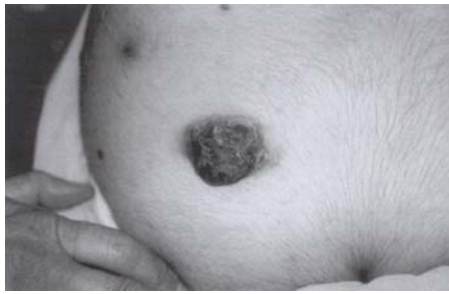
### Case Report

A previously healthy 13-year-old girl with a one-month history of bullous skin lesions was admitted to our hospital. On admission she had

multiple nonulcerated cutaneous plaques, five bullous skin lesions surrounded by erythematous induration and multiple ulcerated skin lesions (Fig. 1a-b).

On physical examination, anterior and posterior cervical and left supraclavicular lymphadenopathies (the largest being 2x2 cm) were noted. The lungs had asymmetric ventilation. Liver was enlarged 4 cm below the right costal margin.

She had been evaluated with a skin biopsy at another hospital before she was admitted. Although the actual biopsy material could not be obtained, the biopsy report stated that the lesion showed microscopic changes consistent with tuberculosis. In light of this report, cutaneous manifestations and organ involvement were thought to be consistent with disseminated tuberculosis. Since there was no response to antimycobacterial therapy, biopsy of a cervical lymph node and fine needle aspiration of skin lesions were performed which showed proliferation of atypical large lymphoid cells. With these findings she was referred to our center.



(a)



(b)

Fig. 1a-b: Bullous skin lesions surrounded by erythematous induration and multiple ulcerated skin lesions.

At the time of admission, laboratory tests revealed hemoglobin 8.5 g/dl, leukocytes  $18,200/\text{mm}^3$  and platelet count  $414 \times 10^3/\text{mm}^3$ . HIV, Epstein-Barr virus and hepatitis markers were negative. Plain chest X-ray showed multiple nodular lesions involving both lungs. A PPD test was non-reactive at 72 hours. Abdominal and thoracic computerized tomography (CT) showed bilateral nodular lesions involving kidneys, left-sided pleural effusion and multiple nodular lesions in lung parenchyma. Bone marrow aspiration was normocellular with no evidence of involvement by a neoplastic process. Fine needle aspiration biopsy of the skin lesions and biopsy of the lymph nodes were evaluated at our center. The fine needle aspiration of one of the skin lesions showed numerous mononuclear cells including some with multiple nuclei and bizarre shapes (Fig. 2). These cells were large with vacuolated markedly basophilic cytoplasm and nuclei exhibiting multiple nucleoli. There was extensive necrosis in the lymph node, with viable areas showing proliferation of pleomorphic atypical cells in a background of lymphocytes, histiocytes and eosinophils. Immunohistochemical examination performed on the lymph node biopsy showed that these cells were positive for CD30 and a T-cell marker, UCHL-1 and negative for ALK-1. Rare cells were EMA-positive.

She was diagnosed as ALK-negative systemic ALCL involving skin and cerebrospinal fluid, and treated with LMT chemotherapy regimen containing cyclophosphamide ( $500 \text{ mg}/\text{m}^2$ ), vincristine ( $2 \text{ mg}/\text{m}^2$ ), prednisone ( $60 \text{ mg}/\text{m}^2$ ), adriamycin ( $60 \text{ mg}/\text{m}^2$ ) and methotrexate ( $3 \text{ g}/\text{m}^2$ )<sup>8</sup>.

One month after the beginning of chemotherapy, the skin lesions regressed and no ulcerative lesions were detected in the physical examination (Fig. 3a-b). She remained well and free of disease for eight months, at which time she had a relapse

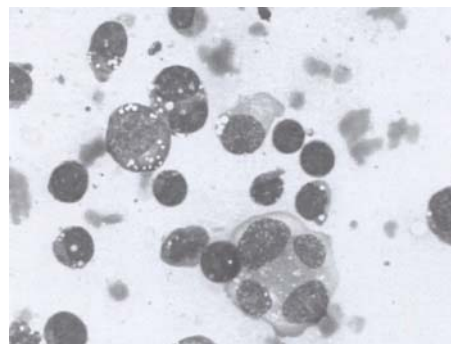


Fig. 2. Appearance of the cells seen in fine needle aspiration of the skin lesion.



(a)



(b)

Fig. 3a-b: Regressed skin lesions.

in skin with erythematous lesions. We started LSA4 chemotherapy regimen which includes dexamethasone (25 mg/m<sup>2</sup>), cyclophosphamide (2100 mg/m<sup>2</sup>) and etoposide (250 mg/m<sup>2</sup>)<sup>3</sup>. Skin lesions regressed after the second month of the new chemotherapy regimen. Nine months into the new chemotherapy protocol she is well without evidence of disease.

## Discussion

Anaplastic large cell lymphoma was first recognized in 1985<sup>7</sup>. Primary cutaneous CD30+ALCL is characterized with good prognosis. Unlike in the systemic forms, a four-year survival rate of 92% is reported. CD30+ALCL can be misdiagnosed as Hodgkin's lymphoma<sup>9,10</sup>. Immunohistochemical studies are important in discriminating ALCL from Hodgkin's lymphoma<sup>11,12</sup>.

Pediatric large cell lymphomas usually present with abdominal and mediastinal involvement. Lymph nodes, soft tissues, bone marrow and internal organs can be involved in disseminated ALCL<sup>12</sup>. Cutaneous manifestations of ALCL in the skin are characterized by papules, nodules or plaques, often with ulceration<sup>12</sup>. This uncommon manifestation in children is characterized by infiltration of the dermis by large neoplastic cells which mostly show T-cell markers. Mora et al.<sup>3</sup> studied 52 pediatric patients with large cell lymphoma, only nine of whom showed skin involvement.

Skin involvement in tuberculosis is characterized by erythematous macules, papules and vesicles<sup>13</sup>. Cutaneous manifestations are seen in less than 0.5% of patients with disseminated tuberculosis<sup>13</sup>. Mycobacterial infections may be considered in the morphologic differential diagnosis of lymphomas involving lymph nodes or skin if there is prominent accompanying granulomatous reaction<sup>13</sup>.

Cutaneous involvement by lymphomas is infrequent in children. This unusual clinical presentation of lymphomas can be confused with tuberculosis clinically and histologically. The biopsy of a cervical lymph node or skin lesions can help to distinguish these two entities. In our patient, chemotherapy was very effective. Both initial and relapsed skin lesions regressed rapidly with chemotherapy.

In conclusion, it is important to realize that this uncommon presentation of ALCL can be confused with other diseases clinically and histologically.

Clinicians and pathologists should be aware of the differential diagnosis in order to correctly diagnose this uncommon presentation.

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