Case Report

An Incidental Finding of Anaplastic Large Cell Lymphoma (ALCL) in A 16-Year-Old Boy with Multiple Painful Soft Tissue Swellings

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ABSTRACT

Anaplastic large cell lymphoma (ALCL) is rare. Approximately 2% of adult non-Hodgkin lymphoma diagnoses are ALCL. Most people are diagnosed when the cancer is more advanced. In advanced stages, the cancer may have spread to organs, like lungs, liver and bone. Patients experience symptoms based on which body parts are affected, e.g., pressure in the chest and a frequent cough may signify the presence of the ALCL affected the lungs. Here, we present an incidental finding of anaplastic large cell lymphoma (ALCL) in a 16-year-old boy with multiple painful soft tissue swellings. The case is presented out of an academic interest and to recognize its rarity in clinical practice. Most children and adolescents with ALCL have presenting symptoms of advanced stage disease (70% present with stage III–IV disease). Peripheral or abdominal lymphadenopathy, extranodal infiltrates, bone marrow involvement, systemic symptoms (especially high fever, weight loss). One-third of the affected children usually relapse and one-half of them ultimately die. Essential features include: T-cell lymphoma, characteristic hallmark cells, CD30 diffusely and strongly positive, ALK positive, and ALK gene rearrangement. Among the treatment modalities, the first line of treatment includes chemotherapy with APO regimen in accordance with ALCL 99, or NHL-BFM 90 protocol. In relapsed or refractory cases, combination or single agent chemotherapy are effective. High dose chemotherapy followed by stem cell transplant are also in practice. Another available treatment is targeted therapy with brentuximab vedotin (anti-CD30), or ALK inhibitors (e.g., crizotinib). In immunotherapy, checkpoint inhibitors (e.g., nivolumab) are under trial. Last but not the least, radiotherapy can be applied on the affected sites.

Keywords: *Anaplastic large cell lymphoma, non-Hodgkin lymphoma, painful soft tissue swelling, childhood cancer*

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INTRODUCTION

Anaplastic large cell lymphoma (ALCL) is relatively rare type of non-Hodgkin lymphoma and Approximately 2% of adult non-Hodgkin lymphoma diagnoses are ALCL. Patients usually have lymphadenopathy or an extranodal mass and may have fever, night sweats, and weight loss.[1-3] Because of several factors, the patient may present an atypical and more severe form of the disease, leading to a particular difficulty for the doctor regarding the diagnosis. It is essential that, at this moment, the doctor can consider the most diverse differential diagnoses and perform the correct management of the patient to provide the best possible care.[4,5] Most children and adolescents with ALCL have presenting symptoms of advanced stage disease (70% present with stage III–IV disease).[5] Peripheral or abdominal lymphadenopathy, extranodal infiltrates, bone marrow involvement, systemic symptoms (especially high fever, weight loss). One-third of the affected children usually relapse and one-half of them ultimately die.[5-7] Essential features include: T-cell lymphoma, characteristic hallmark cells, CD30 diffusely and strongly positive, ALK positive, and ALK gene rearrangement.[6] Here, we present an incidental finding of anaplastic large cell

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lymphoma (ALCL) in a 16-year-old boy with multiple painful soft tissue swellings. The case is presented out of an academic interest and recognize its rarity in clinical practice.

CASE SUMMARY

A 16-year-old boy, hailing from Tongibari upazila under Munsiganj district, Bangladesh, got admitted into our hospital with the complaints of pain and swelling of the left upper limb for 2.5 months, along with few nodular swellings of the left arm, left leg and right thigh for 2 months. Our patient was reasonably well 2.5 months back. Gradually he developed pain and swellings at left upper limb. He also complained about nodular swellings of the left arm, left leg and right thigh for 2 months. On query, he gives history of fever associated with pain. Highest recorded temperature was 103ºF. He gives history of weight loss around 10 kg within the course of illness. His bowel and bladder habits were normal. With these complaints, he consulted local physician and MRI was advised. MRI of the left arm showed an intramuscular soft tissue mass (suggestive of mesenchymal tumour) in posterolateral aspect of the left proximal arm without any underlying bony involvement (Fig. 1). Then, CT guided FNAC of right thigh lesion was done, which revealed small round cell neoplasm. Subsequently, CT guided core biopsy of the left arm lesion was done, which showed round cell neoplasm. IHC could not be done due to scanty amount of tissue.

On systemic examination, left arm was found swollen, tender, erythematous, local temperature was raised. There was a nodular swelling in the left axilla involving the posterolateral area of left arm, which was firm to hard in consistency, tender, erythematous initially, later it became ulcerated with friable vessels, which were associated with massive bleeding with little movement (Fig. 2). There was a swollen, tender area in the anterolateral aspect of the left leg. All other systemic examinations including genitalia revealed normal status. Repeat core biopsy of the left arm lesion

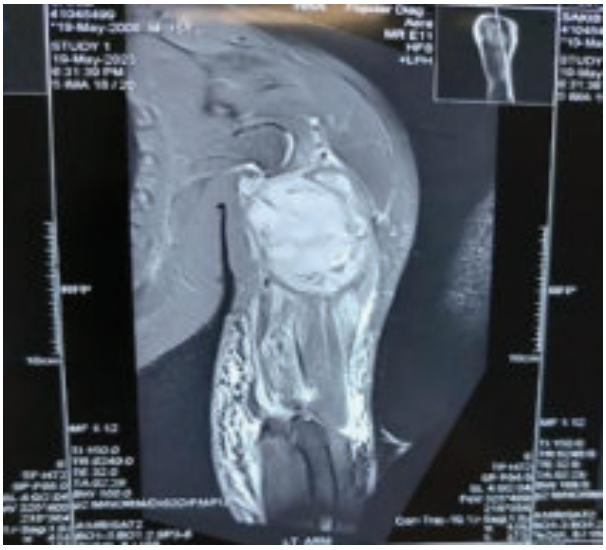

Fig. 1: *Pre-admission MRI showing an intramuscular soft tissue mass (suggestive of mesenchymal tumour) in posterolateral aspect of the left proximal arm without any underlying bony involvement.*

and immunohistochemistry (IHC) test were done. Examination revealed the following: HPR: Small round cell tumor, IHC: CD3 positive, CD30 positive, anaplastic large cell lymphoma, ALK-negative (Fig. 3). The patient was given chemotherapy, followed by radiotherapy to the affected areas.

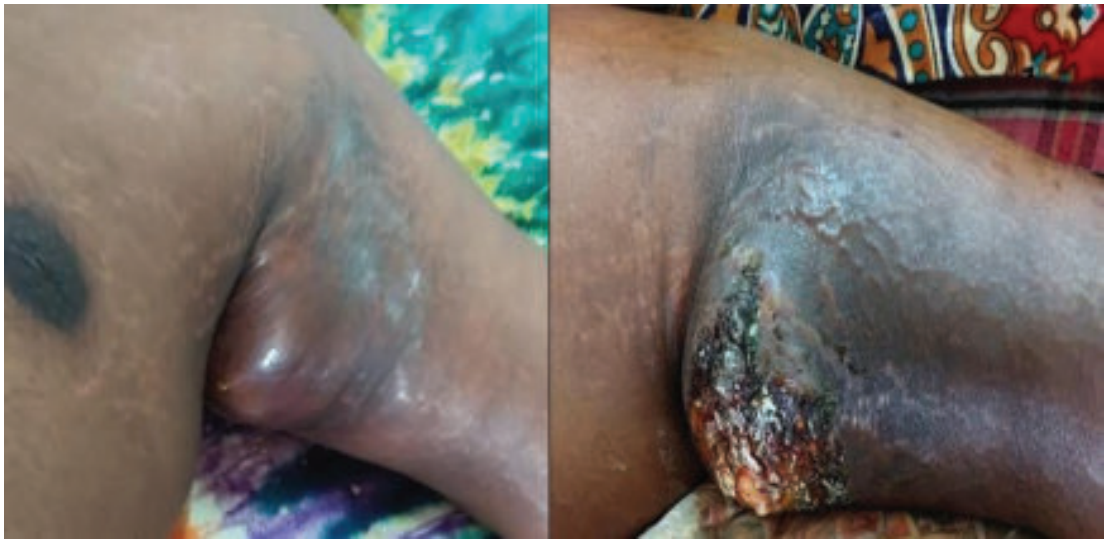

Fig. 2: *Soft tissue swelling and lesions (during admission and hospital stay)*

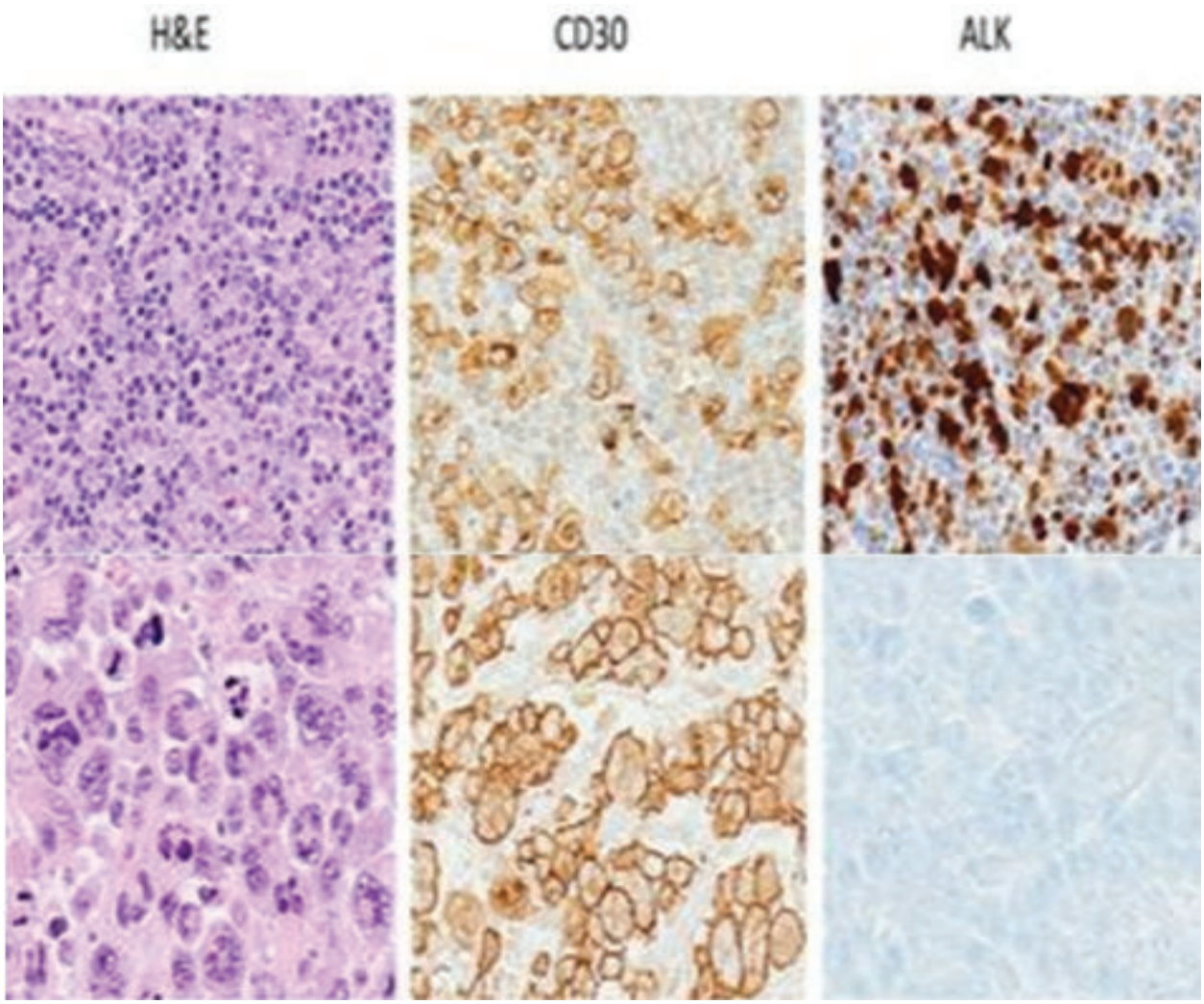

Fig. 3: *Histopathology showing stained with haematoxylin and eosin (H&E); immunohistochemistry examination with CD30 revealed anaplastic large cell lymphoma; and anaplastic lymphoma kinase (ALK) negative.*

DISCUSSION

The various types of ALCL are classified based on the cancer's location in the body and the cancer cells' characteristics. Systemic ALCL may affect lymph nodes and organs. Other types of ALCL primarily affect only a particular body part, like skin or breasts. Systemic forms of ALCL are classified based on whether there's a mutation (change) in the 'anaplastic lymphoma kinase' (*ALK*) gene. Systemic ALCL that has a mutation on the *ALK* gene is called "*ALK*-positive" ALCL. Systemic ALCL that does not have the mutation is called "*ALK*-negative." **Primary systemic ALCL, *ALK*-positive**, is a fast-growing, i.e., aggressive cancer, most common in children and young adults.[6-8] This type of cancer usually responds well to chemotherapy treatments. **Primary systemic ALCL, *ALK*-negative**, is also an aggressive cancer that primarily affects older adults. The cancer usually goes away for a short period following chemotherapy and then returns.[8-12] *ALK*-negative ALCL is harder to treat and has a worse prognosis than *ALK*-positive ALCL.[8] Other types of ALCL grow more slowly than the systemic types. Among them, p**rimary cutaneous ALCL** causes skin changes, like bumps or a rash. In most cases (90% of the time), it does not spread beyond skin. However, b**reast implant-associated ALCL (BIA-ALCL)** forms around breast implants. BIA-ALCL is usually diagnosed about 10 years following a breast augmentation or breast reconstruction procedure.[8]

A vast majority of pediatric cases (>95%) demonstrate overexpression of ALK. The classic chromosomal translocation, t(2:5) (p23;q35) which fuses the

anaplastic lymphoma kinase (ALK) gene on chromosome 2 with the nucleophosmin (NPM) gene on chromosome 5, resulting in a NPM-ALK fusion protein, ALK over-expression and constitutive tyrosine kinase. Frequent sites of involvement are: lymph nodes or extranodal sites like skin, bone, soft tissues, lung and liver, bone marrow and the central nervous system (CNS).[1,3,8]

Histopathological examination reveals Anaplastic large cells with abundant cytoplasm, wreath-like or multiple nuclei, open chromatin, multiple nucleoli, perinuclear eosinophilic region (prominent Golgi zone); Cells with horseshoe-kidney/embryo shaped nuclei are referred to as hallmark cells. Immunohistochemistry shows positive stains for ALK, CD30, EMA (in the majority of the cases).[1,5,8]

Among the treatment modalities, the first line of treatment includes chemotherapy with APO regimen in accordance with ALCL 99, or NHL-BFM 90. In relapsed or refractory cases, combination or single agent chemotherapy are effective. High dose chemotherapy followed by stem cell transplant are also in practice. The next available treatment is targeted therapy with brentuximab vedotin (anti-CD30), or ALK inhibitors (e.g., crizotinib). In immunotherapy, checkpoint inhibitors (e.g., nivolumab) are under trial. Last but not the least, radiotherapy can also be applied on the affected sites.[8-12]

CONCLUSION

The number of cycles and the exact type of chemotherapy depends on several factors like age, the stage of your lymphoma and whether it is ALK-positive or ALK-negative. Some people with early-stage ALK-positive ALCL might also have radiotherapy to the affected area. If patients have ALK-negative ALCL and respond to chemotherapy (like our patient), a self (autologous) stem cell transplant is further recommended. That may give a better chance of staying in remission (no evidence of lymphoma).

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