CLINICAL CASE

A RARE CASE OF ANAPLASTIC LARGE-CELL LYMPHOMA

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ABSTRACT

Anaplastic large cell lymphoma (ALCL) represents a rare form of Non-Hodgkin lymphoma; ALCL also called Ki-1 lymphoma, is a morphologically and immunologically distinct subset of non-Hodgkin's lymphoma (NHL) originally described by Stein et al, which accounts for 2% to 8% of all lymphomas. We will present the clinical case of a one year old boy, brought by his parents to a dermatology consult with an eight weeks history of erythematous skin lesions, skin nodules with small superficial crusts. The lesions were visible on both his arms and legs, on his chest, abdomen and the inguinal area. The diagnosis of ALCL is difficult because of a non-specific onset of symptoms and a fluctuant evolution, and this is the reason why the clinical suspicion of the diagnosis is so important, in order to direct the patient towards specific tests, able to offer a fast-precise diagnosis and avoiding the delay of treatment. The histopathology exam and the phenotype tests are absolutely necessary for the diagnosis.

KEYWORDS: *anaplastic large cell lymphoma, skin lesions, blood tests, lymphadenopathy, histopathology exam, skin biopsy*

INTRODUCTION

Anaplastic large cell lymphoma (ALCL) represents a rare form of Non-Hodgkin lymphoma; ALCL also called Ki-1 lymphoma, is a morphologically and immunologically distinct subset of non-Hodgkin's lymphoma (NHL) originally described by Stein et al, which accounts for 2% to 8% of all lymphomas. This disease is characterized by the proliferation of pleomorphic large neoplastic lymphoid cells, which strongly express the CD30 antigen (Ki-1 antigen), usually growing in a cohesive pattern and preferentially spreading in the lymph node sinuses [1].

The morphology of this particular lymphoma (ALCL) is associated with a clinical syndrome of peripheral lymphadenopathy (>80%) and frequent extra-nodal disease (>40%) in children and young adults (median age <40 yrs.). Skin lesions occur in more than 20% of patients; other extra-nodal sites are bone, soft tissue, gastro-intestinal tract, lung and pleura [2].

The initial symptoms may include fever, night sweats, lack of appetite, non-painful lymphadenopathy, fatigue, weight loss. The primary cutaneous ALCL is usually less aggressive and with a better outcome than the systemic ALCL.

The typical cutaneous aspect (Primary Cutaneous ALCL) consists in one or multiple red patches, non-painful skin nodules, infiltrated plagues, with the tendency to ulcerate. Occasionally, these skin lesions can spontaneously regress, but new lesions appear.

The malignant cell identified in all the histopathologic types of malignant anaplastic large cell lymphoma is a large lymphoid cell with abundant cytoplasm and pleomorphic, often horseshoe-shaped nuclei, the aspect of an activated lymphocyte, the phenotype is necessary for the diagnosis.

Besides being CD30+, most cases also express cytotoxic granule-associated proteins and epithelial membrane antigen (EMA) [3].

MATERIALS AND METHODS

We will present the clinical case of a one year old boy, brought by his parents to a dermatology consult with an eight weeks history of erythematous skin lesions, skin nodules with small superficial crusts. The lesions were visible on both his arms and legs, on his chest, abdomen and the inguinal area. (photo no.1)

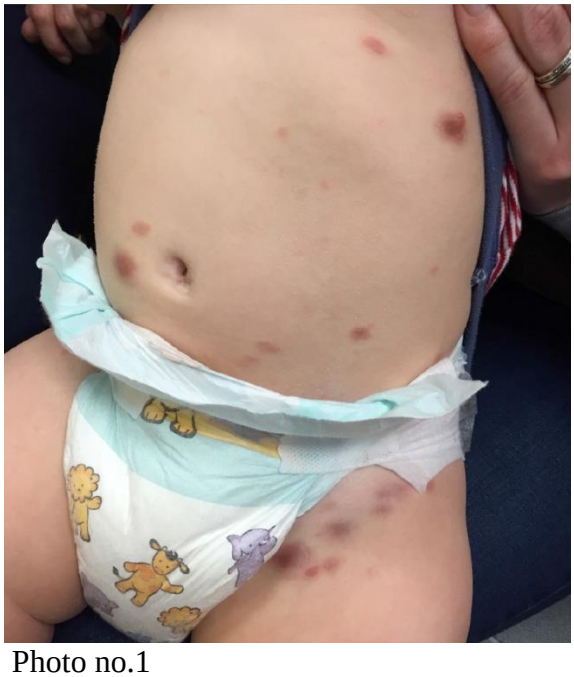

Photo no.1

Besides the skin lesions, the patient does not present other symptoms and the clinical examination does not reveal peripheral lymphadenopathy. His pathologic history includes 2 episodes of infectious respiratory disease, with one pneumonic episode, that were treated by the pediatrician. Every episode was treated with antibiotic (Amoxicillin). The skin lesions appeared 2 weeks after the second treatment ended.

The dermatologists initial different diagnosis were cutaneous mastocytosis vs psoriasis.

Action plan: Blood tests for serum tryptase

Local treatments with Elocon and Cetraben

7 days reevaluation

The usual blood tests came back normal.

One week later, the skin lesions started to disappear and other new lesions did not appear (2nd photo)

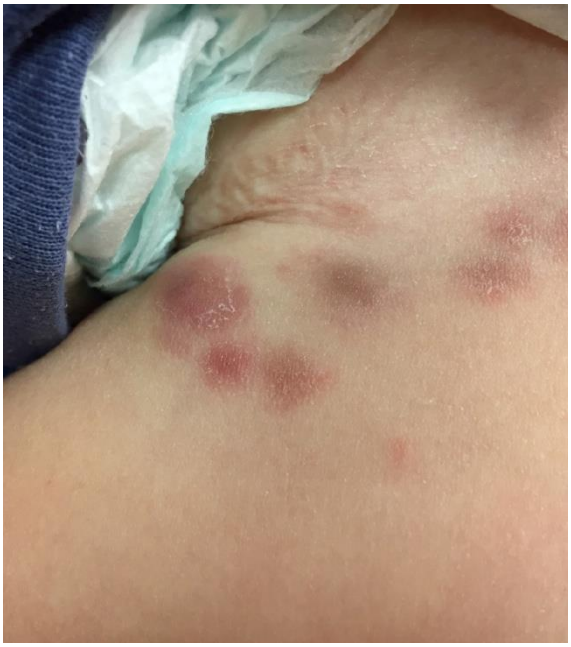

Photo no. 2

Amongst other suspected diagnosis, there was a high suspicion of the new-born acute hemorrhagic edema, and this is the reason the blood tests were repeated. All the blood tests came back normal (cell blood count, inflammation markers, RCP, liver function tests, renal function tests)

Approximatively 2 months after all the skin lesions disappear, the child was healthy looking and with no other symptom, only after this period of time the fever reappeared. He is brought back to the hospital by his parents, admitted with fever and similar new skin lesions. We suspect a rash as a reaction to

Ibuprofen treatment. The child was treated with Ibuprofen when the symptoms started, at home.

During physical exam, a left inguinal lymph-node and enlargement of the liver and spleen are noted. An ultrasound evaluation is requested at this moment.

The child was feeling well and was alert at that moment.

The blood tests show: WBC 6,1 109/L (N: 6-18), HB 10.3 g/L (N : 11.0-13.0), HTC 0,258 (N : 0,36-0,44), MCV 66.6 FL (N :77-101), MCHC 361 g/L (N :280-330), LDH 2276 UI/L (N :240-480), Calcium 2,32 mmol/L (N : 2,35-2,7), RCP 10mg/l. The rest of the blood tests were in between normal limits.

The screening test for glandular fever was negative.

Screening antibodies tests (pediatrics):

-anti-smooth muscle antibodies- negative

-kidney liver anti-microsomal antibodies – negative

-antinuclear antibodies- negative

-ant mitochondrial antibodies- negative

The i.v. antibiotics treatment was recommended and the viral screening tests were done.

The patient was seen again by the dermatologist and sent to the plastic surgeon for a skin biopsy.

We saw the patient for the first time the day he was sent to us by the dermatologist and because of the suspected lymphoproliferative disease, we took two skin biopsy probes from the skin lesions on right gluteal region, in emergency, with general anesthesia.

The ultrasound confirmed hepatosplenomegaly.

The child continued to have a fever and this is the reason the antibiotic treatment was not interrupted. The viral screening came back negative.

The heart ultrasound did not show any sign of endocarditis. The chest x-ray did not show any pathological modification.

The histopathology exam:

Skin biopsy, right gluteal region:

In the medium dermis, there was evidence of perivascular, per adnexal and nodular cell infiltration with both small lymphatic cells and large abundant eosinophilic cytoplasm cells. Non- characteristic aspect of lymphoid infiltration that cannot exclude a lympho-proliferative disease or a variety of histocytosis. The pieces were sent for a second opinion and supplementary tests to a secondary center lab.

The immunophenotype testing shows diffuse and strongly positive for CD4, CD43, CD 45Ro, CD163 and positive for cytotoxic perforin T, TIA 1 and granzyme markers. The lymphatic large cells were positive for CD30, ALK1 and EMA. A high proliferative index was identified for Ki67.

The second analysis was positive for a CD30 positive lymphoproliferative with a cytotoxic phenotype disease.

Final diagnosis: malignant lymphoma with large anaplastic cells (ALCL).

The child was admitted into a specialized clinic for the treatment of this disease.

RESULTS

The treatment plan:

5 mg/ m 2 of Dexamethasone, oral administration twice per day

3 Gm/m2 i.v. infusion of Methotrexate in the 1st day

15 mg/m2 i.v. Folic Acid starting at 24 h after the administration of Methotrexate, followed by 15 mg/m2 i.v. every 6 hours until reaching a level of Methotrexate lower than 0.1

200 mg/m2 i.v. Cyclophosphamide in the 1st and the 5th day

25 mg/m2 i.v. Doxorubicin in the 4th and 5th day

240 mg twice per day orally Cotrimoxazole (not the weekend before the Methotrexate infusion.

The patient tolerated the treatment well and at this moment he is in complete remission.

CONCLUSIONS

The ALCL ALK positive forms (ALK anaplastic lymphoma kinase is an abnormal protein on the cell surface) respond well to chemotherapy and the remission is a long-term result.

The diagnosis of ALCL is difficult because of a non-specific onset of symptoms and a fluctuant evolution, and this is the reason why the clinical suspicion of the diagnosis is so important, in order to direct the patient towards specific tests, able to offer a fast-precise

diagnosis and avoiding the delay of treatment. The histopathology exam and the phenotype tests are absolutely necessary for the diagnosis.

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