Case Report

SYSTEMIC ANAPLASTIC LARGE CELL LYMPHOMA PRESENTING WITH CUTANEOUS MANIFESTATIONS IN A YOUNG MAN: A CASE REPORT

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ABSTRACT

Skin lesions can be a sign of internal disease. When they are associated with persisting systemic signs, the possibility of an internal malignancy should always be considered.

We describe a 25-year-old man who presented with weight loss, fatigue, subpyrexia, xerostomia and skin rash of 6 months duration. Physical examination showed a dry red skin, most prominent in the face, the palms of the hands and the soles of the feet. Laboratory investigations revealed signs of inflammation and a high level of antinuclear antibodies. Retroperitoneal lymph nodes were visualized on a CT scan of the abdomen. CT-guided biopsy of an abdominal lymph node revealed the presence of an anaplastic large cell lymphoma (ALCL), ALK-positive. A biopsy of the skin showed non-specific signs of inflammation. The patient underwent 8 cycles of chemotherapy according to the CHOP protocol. A complete remission was obtained.

Non-Hodgkin lymphoma can indeed be associated with skin lesions. They result from direct invasion by malignant cells or are of paraneoplastic origin, as was the case in this patient.

Key words: Anaplastic large cell lymphoma, cutaneous involvement, skin lesions

CASE REPORT

A 25-year-old man complained of a reddish dry skin with crackling at the hands and feet, dry eyes and a dry mouth since 6 months. He was also suffering from a loss of appetite with weight loss, general fatigue and persisting subpyrexia. There was no particular medical history except surgery for palatoschizis and allergy to dust mite. He worked for a travel agency and had visited Thailand and Crete in the previous year.

Physical examination revealed diffuse redness of the skin most prominent on the trunk and a heliotropic rash in the face, as well as palmar erythema and desquamation of the skin at the soles and edges of the feet (Figure 1). Opening of

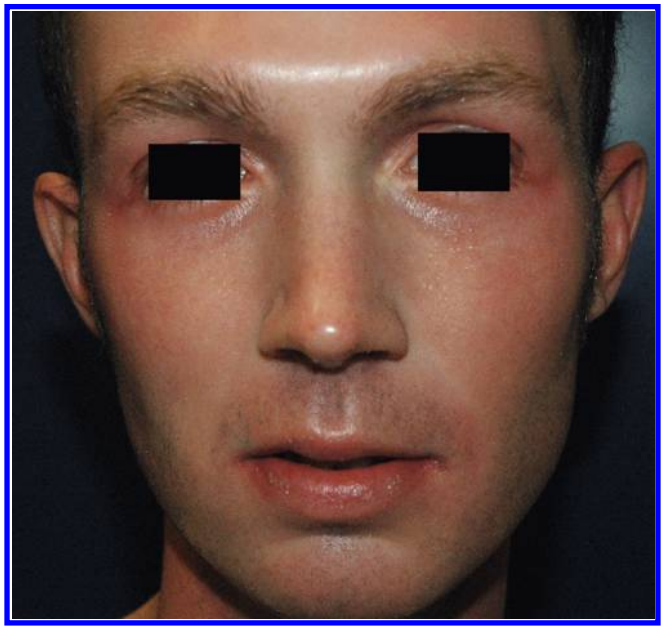

Figure 1: *Image of heliotropic rash in the face at admission.*

Table 1: Blood tests on admission

Parameter	Value	Reference
Albumin	2.71 g/dL	4,0-4,8
C-reactive protein	171 mg/L	< 5
Lactate dehydrogenase	486 U/L	241-549
Creatine kinase	24 U/L	< 145
White blood cell count	7.0 x 10^3/mm^3	3,6-9,6 x 10^3
Sedimentation rate	> 120 mm/h	0-10
Fibrinogen	1018 mg/dL	180-400
Antinuclear antibodies	1/2560	absent

the mouth was difficult as a result of skin dryness, but there were no mucosal ulcerations. Peripheral lymph nodes were not enlarged and auscultation of heart and lungs was normal. There was no hepatosplenomegaly.

Blood examination showed elevation of inflammatory parameters (table 1). Muscle enzyme levels were normal and all serologic tests (cytomegalovirus, Epstein Barr virus, toxoplasmosis, syphilis) were negative. A CT scan of the abdomen revealed multiple enlarged lymph nodes located retroperitoneally and around the common iliac and right external iliac vessels. Complementary PET–FDG scan was suggestive of lymphoma located in lymph nodes on both sides of the diaphragm with hot spots at the sternum, several ribs and the right side of the pelvis. A small submucosal mass was suspected at the level of the duodenum on gastroscopy.

A CT-guided needle biopsy of a para-aortic lymph node was performed and the skin was biopsied at the level of the neck. All microbiological cultures of the specimens remained negative. Histological examination of the lymph nodes revealed a non-Hodgkin's lymphoma of the anaplastic large cell type, anaplastic lymphoma kinase (ALK) positive, confirmed by immunohistological staining. A skin biopsy showed non-specific inflammatory changes and the biopsy of the submucosal lesion seen on gastroscopy revealed infiltration by lymphoma cells. Staging of the lymphoma was completed with a bone marrow biopsy which showed no invasion.

The diagnosis was anaplastic large cell non-Hodgkin's lymphoma stage IV_EB. The patient was treated with CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone). Initially six cycles were administered. A follow-up PET-CT scan showed residual subcentimetric lymph nodes in the mesenterium for which an additional 2 cycles were given. Finally, complete remission was achieved, with complete disappearance of all skin lesions.

DISCUSSION

We describe a patient who presented with systemic signs and a diffuse skin rash since several months. The protracted clinical course and the presence of a facial heliotropic rash led to consider the diagnosis of dermatomyositis, an autoimmune inflammatory disease involving muscles and skin. The pathognomonic skin signs of dermatomyositis consist of heliotropic rash and Gottron's papules on the hands (1). Other signs are weakness and tenderness of the proximal muscles with elevation of muscle enzymes in the serum. These signs were not present in our patient.

Dermatomyositis "sine myositis" or "amyopathic" dermatomyositis is a variant of dermatomyositis, characterized by the absence of muscle enzyme elevation in the blood and a seemingly normal muscle strength on physical examination for a prolonged period of time (6 months or longer) (1). There is positivity of antinuclear antibodies and an elevated erythrocyte sedimentation rate (1). This entity has also been described in association with a variety of malignant diseases such as breast carcinoma, lymphoma/leukaemia and lung carcinoma (2).

The findings on the abdominal CT scan in our patient oriented towards a diagnosis of lymphoma, subsequently confirmed by CT-guided needle biopsy.

The presentation of lymphoma can be atypical. Paraneoplastic cutaneous symptoms may be the initial presentation, as illustrated in the present case report. These symptoms are diverse and may include acquired ichthyosis and paraneoplastic pemphigus (3-4). Malignant lymphoma can also cause skin disease by direct invasion of the skin. Lymphoma types particularly prone to do so are the primary cutaneous T-cell lymphomas, mycosis fungoides being the most common subtype.

In this patient the diagnosis of ALK-positive anaplastic large cell lymphoma (ALCL) was made without histological proof of direct lymphomatous invasion of the skin.

ALCL was first described in 1985 as a neoplastic proliferation of lymphoid cells with anaplastic appearance (5). There are two subtypes, the primary systemic ALCL and the primary cutaneous ALCL. Primary systemic ALCL involves both lymph nodes and extranodal sites and consists of two subgroups. The first one is ALK-positive and is mostly seen in a young adult population. The second one is ALK-negative; it presents at older age and tends to have a poorer prognosis (5).

Primary cutaneous ALCL is mostly ALK-negative and usually presents with a nodular skin lesion instead of diffuse skin involvement. Skin lesions in primary cutaneous ALCL and systemic ALCL with secondary cutaneous involvement have overlapping histological and immunophenotypical features. The histological clue is the presence of large lymphoid cells, the so-called hallmark cells. They are characterized by horseshoe shaped nuclei and abundant cytoplasm (5). The difference between primary cutaneous and systemic ALCL is difficult to make on histopathological grounds alone. Clinical presentation and medical imaging allow to make a definite diagnosis.

The patient we describe had no specific abnormalities on skin biopsy. In particular, there was no invasion by lymphoma cells. Therefore the cutaneous symptoms in this case can be considered to be of paraneoplastic nature. The fact that the skin symptoms disappeared completely during chemotherapy seems to confirm this hypothesis.

To our knowledge an amyopathic dermatomyositis-like presentation has not been described previously in association with primary systemic ALK-positive ALCL.

We conclude that ALK-positive anaplastic large cell non-Hodgkin's lymphoma can be associated with skin lesions that are not caused by direct invasion of the skin by malignant cells. Furthermore, we believe that malignant lymphoma should be considered in the differential diagnosis in young patients presenting with persisting cutaneous symptoms and systemic signs.

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