ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

# Hematology Quiz – Case 11

ARCHIVES OF HELLENIC MEDICINE 2009, 26(2):285–286
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2009, 26(2):285–286

**J. Meletis,**[1]
**A. Sarantopoulos,**[1]
**A. Giakoumis,**[1]
**J.V. Asimakopoulos,**[1]
**E. Papakostas,**[1]
**P. Kouzis,**[1]
**T. Chatzileonida,**[1]
**E. Bazani,**[1]
**E. Variami,**[1]
**N. Viniou,**[1]
**E. Terpos**[2]

*[1]First Department of Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, "Laiko" General Hospital, Athens*
*[2]Department of Medical Research, 251 General Air Force Hospital, Athens, Greece*

A 62-year-old man presented with easy fatigue, extended erythroderma in both palms which has not responded to local vitamin and steroid administration for two months (fig. 1). The medical history of the patient included hypertension treated with daily atenolol and hypercholesterolemia treated with daily rosuvastatin. His family medical history was unremarkable.

The physical examination revealed the erythroderma in both palms along with small oval and digitate patches on the inner sides of both arms, patches of different size and shape ("non-digitate") on the trunk, a small plaque on the upper part of the left arm, and limited erythematous, scaly patches on the abdomen and right thigh. There were no enlarged peripheral lymph nodes. The patient otherwise was in good health; the results of routine laboratory studies including the peripheral blood analysis were all normal. However, the study of the peripheral blood smears revealed the presence of abnormal lymphocytes (2% in the differential counts; fig. 2).

Skin biopsy specimens were taken from the elongated patch on the right arm and from the plaques on the abdomen. Histological examination of the patch revealed mild acanthosis, discrete scale-crusts atop a basket-woven cornified layer. There was a single focus of epidermotropism of lymphocytes into the epidermis, with few lymphocytes aligned as solitary units in the basal layer. The dermis contained a sparse perivascular infiltrate of small non-atypical lymphocytes. Immunohistochemically, the majority of lymphocytes expressed CD3, CD5, CD7, and CD45RO antigens. CD4 antigen was expressed by 80% of lymphoid cells, whereas CD8 labelled 20% of the lymphocytes; all CD8-positive cells were located in the dermis.

Histological examination of the erythroderma of the palms revealed an eroded epidermis, prominent irregular acanthosis and a dense lymphoid infiltrate composed of small cerebriform lymphocytes, medium-sized lymphoid cells, and occasional large hyperchromatic cells that infiltrated the basal layer of the epidermis and formed small collections of 3 to 5 cells (Pautrier microabscesses). There were atypical mitotic figures, especially

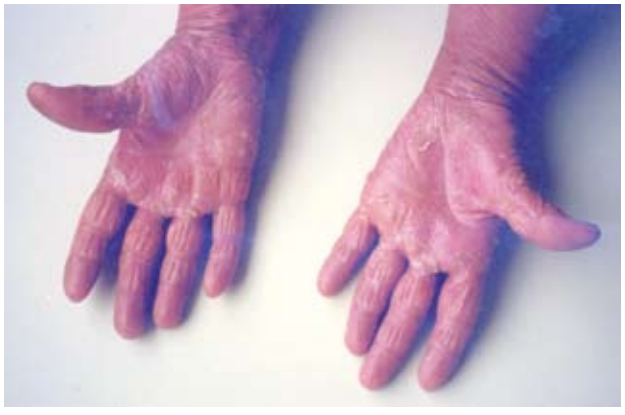

**Figure 1**

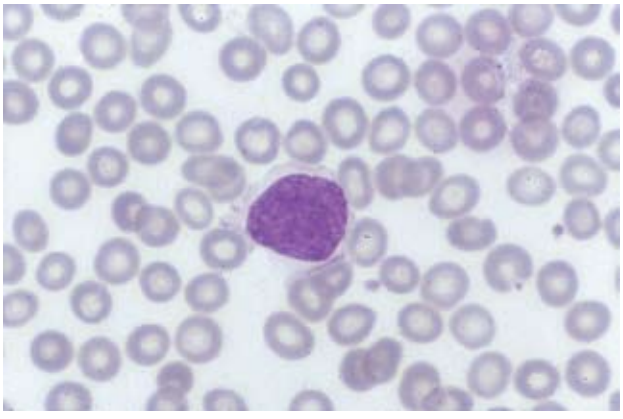

**Figure 2**

among the large cell population found in the deep dermis. Immunohistochemically, the majority of lymphoid cells expressed CD3, CD4, CD45RO antigens. Most of them also stained positive for CD7 antigen but were negative for CD5. Additionally, few scattered large cells in the deeper dermal portion of the infiltrate expressed CD30 antigen; these were ALK-1 and EMA negative. There was an admixture of small lymphoid cells that stained positive for CD8 antigen. All cells tested negative for CD56, granzyme B, and perforin. The proliferation index (Ki-67) was approximately 30%. B-cell population as detected with antibodies against CD20 and CD79a comprised an insignificant minority.

TCR-gamma gene rearrangement studies detected clonal populations in the skin specimens and in the peripheral blood.

## Comment

*Primary cutaneous lymphomas constitute a heterogeneous group of diseases characterized by clonal accumulation of lymphocytes with initial restriction to the skin. Mycosis fungoides (MF) is the most common form of cutaneous T-cell lymphoma. Sézary syndrome is considered by some authors to be an erythrodermic leukemic variant of MF, but it is classified separately in the WHO-EORT classification of cutaneous lymphomas. MF usually occurs in old adults with a 2:1 male to female ratio.*

*Typically, the neoplastic cells are of the mature T-helper memory phenotype, that is, $CD3^+$, $CD4^+$, $CD8^-$, $CD30^-$, $CD45RO^+$, $CD56^-$, with a T-cell receptor of the alpha/beta heterodimer type. $CD8^+$ cytotoxic primary cutaneous T-cell lymphomas are subdivided into an aggressive form with marked epidermotropism and a more indolent form resembling $CD4^+$ MF. Furthermore, a few early cases of MF with a CD4/CD8 double-negative immunophenotype are described.*

*MF prognosis is variable and strongly conditioned by the extent and type of skin involvement and presence of extracutaneous disease. Patients with stage IA-disease have an excellent prognosis with an overall long-term life expectancy that is similar to an age-, sex-, and race-matched control population. Almost all patients with stage IA MF will die from causes other than MF, with a median survival >33 years. Only 9% of these patients will progress to more extended disease. Patients with stage IB or IIA have a median survival greater than 11 years. These patients have a likelihood of disease progression of 24% and nearly 20% die of MF. Subgroups with stage IB or IIA have similar prognosis. Patients with cutaneous tumors or generalized erythroderma have a median survival of 3 and 4.5 years, respectively. The majority of these patients will die of MF. Extracutaneous dissemination is observed in less than 10% of patients with patch or plaque disease and in 30–40% of patients with tumors or generalized erythrodermatous involvement. Extracutaneous involvement is directly correlated to the extent of cutaneous disease. The most commonly involved organs are lung, spleen, liver, and gastrointestinal tract. Patients with extracutaneous disease at presentation involving either lymph nodes or viscera have a median survival of <1.5 years. Patients with plaque-type or erythrodermic MF may develop cutaneous tumors with large cell histology, often expressing CD30, which share a common clonal origin as observed in their preexisting MF and are associated with a less favourable outcome.*

*For patients with T1 without extracutaneous involvement (stage IA) and for patients with T2 without extracutaneous involvement (stage IB–IIA), the standard treatment plan is limited to topical therapeutic measures. The main therapeutic options for these patients are local or total-skin topical mechlorethamine hydrochloride (HN2), psoralen and ultraviolet A (PUVA), or total-skin electron-beam radiotherapy (EBRT). Standard therapeutic option for patients with stage IIB disease depends on the entity of tumors. Local EBRT combined with topical HN2 or with PUVA are the first choice treatments for patients with few discrete tumors. In patients with generalized tumors three effective combinations are available: Total-skin EBRT plus topical HN2, PUVA plus interferon-alfa, and PUVA plus retinoids. Standard therapeutic option for patients with stage III disease is low-dose PUVA with a low and cautious increase of the UVA dose to avoid phototoxic reactions. Standard therapeutic option for patients with stage IV disease is conventional doses' systemic chemotherapy. In MF, most chemotherapy regimens result in temporary palliative control only. Chemotherapy is used alone, or in combination with radiation or interferon alfa. In spite of a complete response rate of 80–100%, the median duration of response to chemotherapy is shorter than 1 year. The most effective and commonly used combinations are CHOP and CVP regimens. Methotrexate, etoposide, bleomycin, vinblastine, fludarabine, and 2-deoxycoformycin are the most commonly used single agent chemotherapy regimens in MF.*

*Corresponding author:*

J. Meletis, First Department of Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, "Laiko" General Hospital, Athens, Greece, Tel.: +30 210 74 66 206, Fax: +30 210 7788830
e-mail: imeletis@cc.uoa.gr