ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 72

ARCHIVES OF HELLENIC MEDICINE 2025, 42(6):859–862
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2025, 42(6):859–862

G. Vrachiolias,
C. Misidou,
S. Papadakis,
I. Liapis,
E. Panagiotopoulos,
L. Inglezou,
B. Malkoc,
I. Stamatiou,
S. Karavasilis,
D. Grigoriadou,
E. Charitaki,
T. Bounta,
P. Kolovos,
C. Roubakis,
M. Papoutselis,
Z. Bezirgiannidou,
E. Spanoudakis,
I. Kotsianidis,
K. Liapis

Department of Hematology, University Hospital of Alexandroupolis, Democritus University of Thrace, Alexandroupolis, Greece

A 72-year-old man with a 12-year history of mycosis fungoides presented to the haematology clinic with worsening thrombocytopenia, five weeks after treatment with chlorambucil. He had previously received UVA phototherapy (PUVA), methotrexate, bexarotene, and small doses of prednisolone. He also reported having worsening alopecia. Clinically, he had a pruritic, erythematous, and scaly rash over his extremities, including palms and feet as well as several plaques over the torso and neck (figures 1–3). There was no lymphadenopathy or hepatosplenomegaly. A full blood count showed a white blood cell count of 9.7×10^9/L, a hemoglobin level of 12.1 g/dL (MCV 101 fL), and a platelet count of 22×10^9/L. A peripheral blood smear showed no abnormal cells. A bone-marrow aspiration was done for evaluation of the thrombocytopenia and representative fields are shown in figures 4–11.

Comment

The marrow cellularity was reduced, with almost complete absence of megakaryocytes. The majority of the cells in the aspirates comprised abnormal small to medium sized lymphoid cells, with irregular or convoluted ("cerebriform") nuclei, condensed chromatin and moderately abundant cytoplasm was with faint to moderate basophilia (so-called Sézary cells). The mechanism underlying thrombocytopenia in this case is a combination of bone marrow infiltration with mycosis fungoides/Sézary syndrome, i.e. disease progression and prolonged myelosuppression from previous cyto-

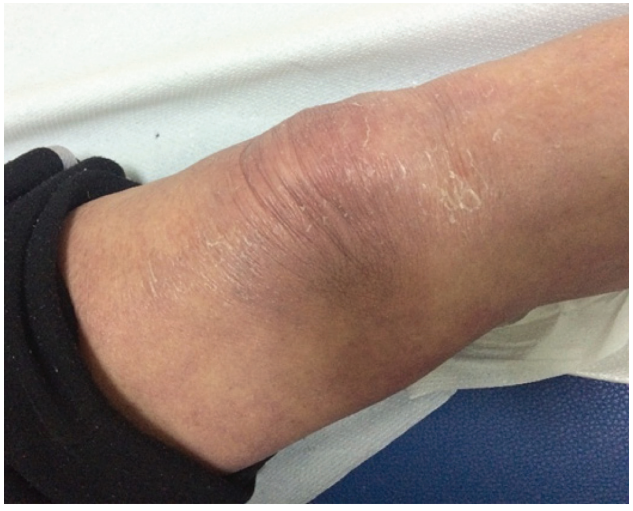

Figure 1.

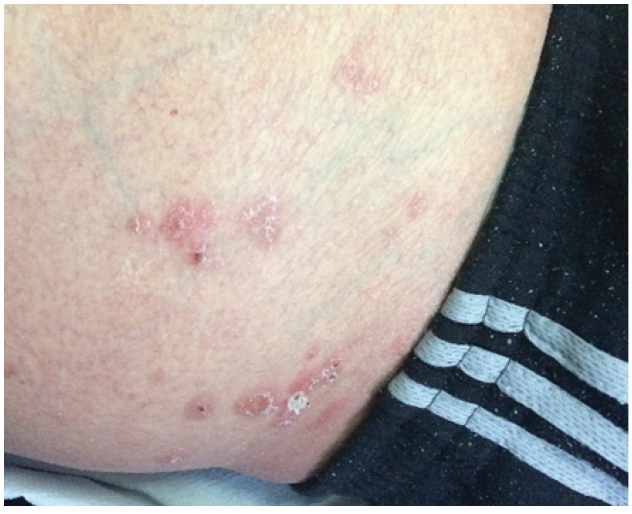

Figure 2.

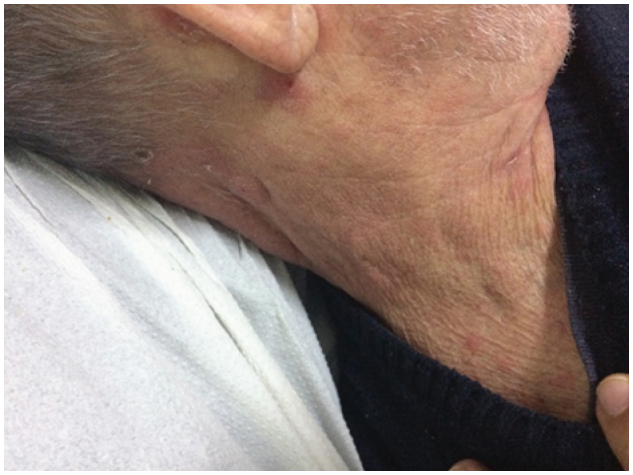

Figure 3

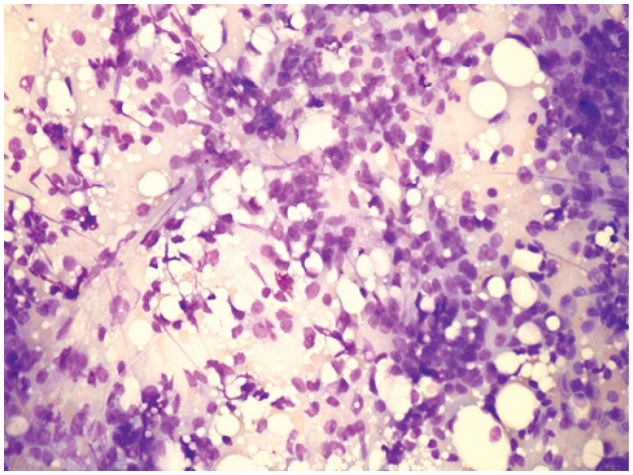

Figure 4

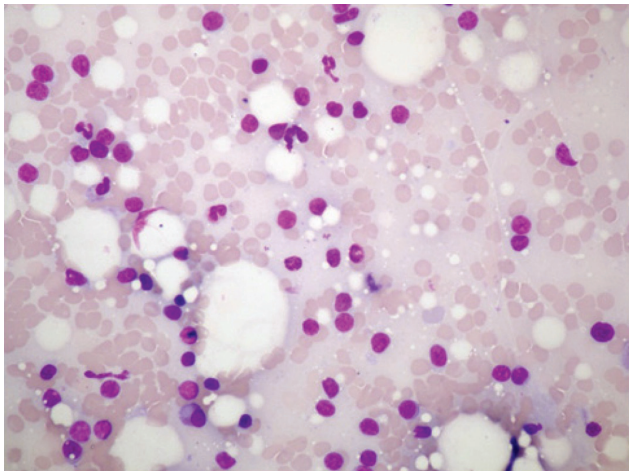

Figure 5

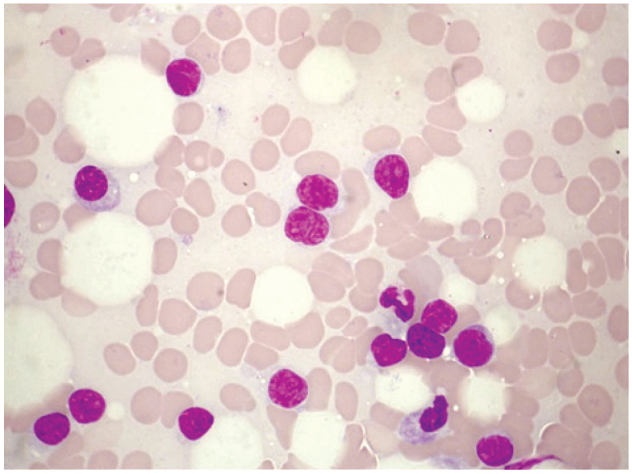

Figure 6

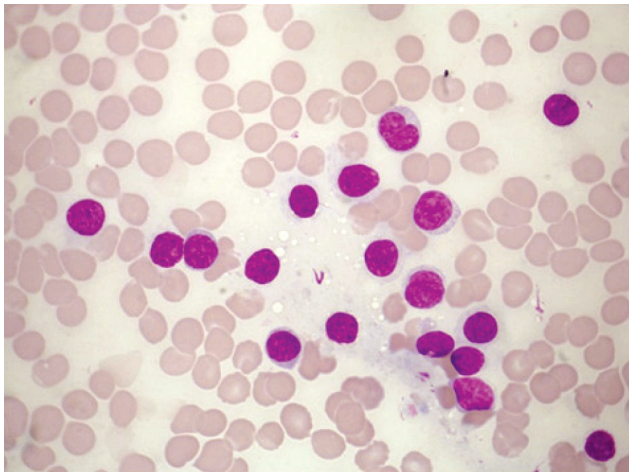

Figure 7

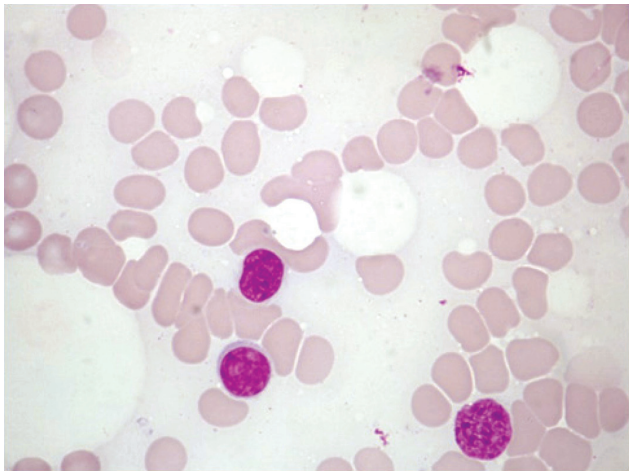

Figure 8

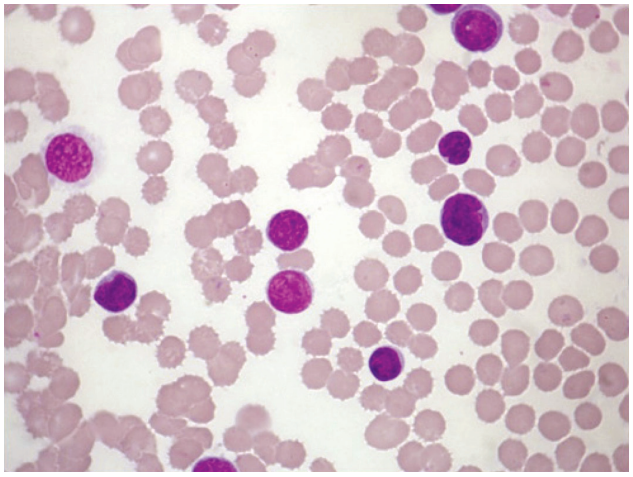

Figure 9

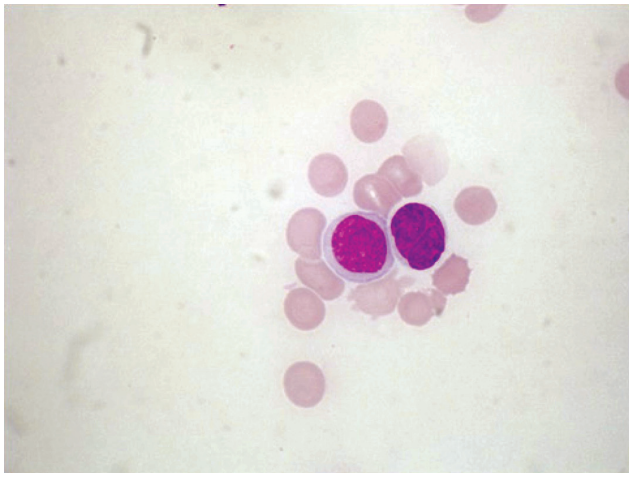

Figure 10

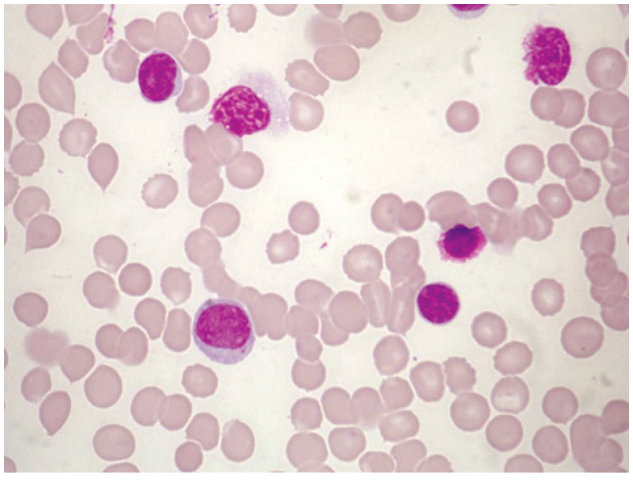

Figure 11

toxic treatment. Morphologically, Sézary cells are small, medium or large sized atypical lymphoid cells with characteristic irregular, folded or "cerebriform" nucleus. The nucleus occupies at least four fifths of the cell, reducing the amount of cytoplasm. The cytoplasm is relatively scanty (peripheral rim) or moderately abundant with variable basophilia (faint to moderate), occasionally with a necklace of vacuoles around the nucleus. These cells are CD4+ T-helper cells of the Th2 subset that home to skin, and their presence in the circulation in counts more than 1,000 cells per μL or >10% defines Sézary syndrome.

There are three morphological variants: Large cell variant (>20% of Sézary cells are very large cells with near tetraploid chromosome number), small-cell variant (>80% of Sézary cells are small cells), and mixed-cell variant. Most cases demonstrate small-cell variant or a mixed population. Small cells (Lutzner cells) are more common than large cells and may have a periodic acid Schiff (+) collarette of cytoplasmic vacuoles. Flow cytometry will identify Sézary cells as aberrant T-cells expressing CD3 and CD4, but commonly lacking CD7 and/or CD5.

As a rule, mycosis fungoides is limited to skin for a protracted period and follows an indolent course with slow progression over years (or sometimes decades) from: pruritic patches to (more infiltrated) plaques to (eventually) tumors. Patients with tumor-stage mycosis fungoides characteristically show a combination of patches, plaques and tumors which often show ulceration. Uncommonly, patients may develop an erythrodermic phase of disease. Occasionally, lymph nodes and visceral organs (liver, spleen, lungs, bone marrow) may become involved in the later stages of the disease. Extracutaneous dissemination may occur in advanced stages mainly to lymph nodes, liver, spleen, lungs and blood. Involvement of the bone marrow by mycosis fungoides is rare.

Typical, de novo Sézary syndrome is characterized by the triad: (a) erythroderma, (b) multiple small peripheral lymph nodes, and (c) circulating cerebriform cells (>1,000/μL or >10%). Other characteristic features include pruritus, alopecia, and palmoplantar keratoderma. It should be remembered that in Sézary syndrome, bone-marrow aspirates are either normal or show minimal infiltration in spite of significant peripheral blood involvement. Other conditions in which circulating cerebriform lymphoid cells may be seen include: (a) Cerebriform variant of T-cell prolymphocytic leukaemia (5% of cases of T-cell prolymphocytic leukaemia), (b) cerebriform adult T-cell leukaemia/lymphoma, (c) T-cell acute lymphoblastic leukaemia (mature or medullary subtype) and (d) angioimmunoblastic T-cell lymphoma.

Rarely, small numbers of circulating Sézary-like cells may be found in chronic dermatologic conditions, such as phenytoin hypersensitivity syndrome, discoid lupus erythematosus, erythrodermic follicular mucinosis, lichen planus, psoriasis, and particularly actinic reticuloid ("pseudolymphoma"). These are reactive T-cells, with no immunophenotypic abnormalities or clonal T-cell receptor (TCR) rearrangements.

The staging of mycosis fungoides and Sézary syndrome is complicated and is done according to the International Society for Cutaneous Lymphomas and the European Organization for Research and Treatment of Cancer (ISCL/EORTC) TNMB stag-

ing system. However, a more simple approach is the following: (a) Clinical stage 1: Patches/papules/plaques only (IA <10%, IB >10% total skin area); (b) clinical stage 2: One or more tumors (>1 cm); (c) clinical stage 3: Erythroderma with no or low blood circulating Sézary cells (<1,000/μL); (d) clinical stage 4: Sézary syndrome or overt lymph-node involvement (>1.5 cm) or visceral disease (liver, lung, bone marrow).

This patient has developed erythrodermic mycosis fungoides with spread to the bone marrow. CT scans are required to detect lymph node or other visceral organ involvement.

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Corresponding author:

C. Misidou, Department of Hematology, University Hospital of Alexandroupolis, Dragana, 681 00 Alexandroupolis, Greece
e-mail: xmisidou@yahoo.gr