**Case Presentation:**

This peripheral blood smear is from a 78-year-old man presenting with leukocytosis and recent progression of skin tumors. Laboratory data include: WBC = 35.6 × 10E9/L; RBC = 4.44 × 10E12/L; HGB = 13.3 g/dL; HCT = 40.0%; MCV = 91 fL; and PLT = 423.

**Case Discussion: Sézary syndrome**

Mycosis fungoides (MF) is a primary cutaneous lymphoma characterized by epidermotropic neoplastic T-cells with characteristic morphologic features (cerebriform nuclei). Sézary syndrome (SS) is defined by the presence of neoplastic T-cells (“Sézary cells”) in the peripheral blood of patients with erythroderma and generalized

lymphadenopathy. Similar to SS, patients with advanced stage MF demonstrate circulating neoplastic cells (Sézary cells) in the peripheral blood and, in the absence of any clinical history, peripheral blood smears from both conditions show similar morphologic findings.

From an epidemiologic standpoint, MF is the most common type of cutaneous T-cell lymphoma (approximately 50%), and occurs mostly in adult to elderly patients, with a male:female ratio of 2:1. In contrast, SS is a rare disease (5% of cutaneous T-cell lymphomas) and it also has a predilection for affecting older male adults,

characteristically over the age of 60.

Clinically, MF has an indolent, protracted clinical course (years or decades) characterized by skin lesions evolving through different stages (patches, plaques and, eventually, tumors). Only patients with advanced stages of MF show extracutaneous dissemination, including lymph nodes, liver, spleen and blood. Patients with SS have a

more dramatic clinical picture with generalized disease, including general skin rash and leukemic presentation.

The characteristic morphology of the neoplastic cells (Sézary cells) is that of small to medium-sized lymphocytes, with irregularly convoluted (“cerebriform”) nuclei, powdery chromatin, and small amount of cytoplasm.

The diagnosis of MF/SS is based on clinical findings, morphology, immunophenotyping (by flow cytometry or immunohistochemistry) and genetic/molecular analysis.

In recent years, it has been recognized that the degree of peripheral blood involvement by lymphoma cells is an important prognostic indicator in patients with MF/SS. Even

though there is consensus on the importance of assessing circulating neoplastic T-cells, there is no universally accepted method to characterize and quantify the number of Sézary cells in peripheral blood. Morphologic identification of abnormal lymphocytes with cerebriform nuclei was previously the standard approach for disease detection and quantification. However, this method is compromised by several drawbacks, including high interobserver variability and difficulty in reliably identifying small Sézary cells. Flow cytometric immunophenotyping has proven to be more reliable than morphology in the detection of circulating Sézary cells, as these cells often have an aberrant immunophenotype, including typically expression of CD2, CD3, CD4, and

CD5, and absence of CD8, CD7, and CD26.

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