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SEZARY SYNDROME IN ADULTS: EPIDEMIO-CLINICAL AND BIOLOGICAL STUDY OF 6 CASES

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ABSTRACT

Sezary syndrome (SS) is a rare subtype of cutaneous T-cell lymphoma (CTCL) marked by erythroderma, circulating neoplastic T cells, and poor prognosis. Its belongs to the group of non-Hodgkin's lymphomas (NHL) resulting from malignant proliferation of skin-homing T cells. We report through a series of 6 cases, the experience of the hematology laboratory in the diagnosis of the syndrome of Sezary. Methods: This is a retrospective study of 6 cases of Sezary syndrome collected in the dermatology and hematology Departments Mohammed VI University Hospital of Marrakech. Results: six patients were identified with the clinicopathological criteria of SS. At the time of diagnosis, 5 patients had erythroderma and generalized lymphadenopathy in both superficial and deep stations. The white blood cell count was elevated (>10,000 WBC/mm3) in 3 patients. The blood smear showed the presence of small to medium-sized cells with a high nucleo-cytoplasmic ratio and cerebriform nuclei typical of Sezary cells and suggests the diagnosis of SS in all cases. Conclusions: The diagnosis of SS remains a challenge in many situations; the pathophysiology and definition of SS have evolved significantly over the past decades.

Keywords: Sezary Syndrome, Lymphoma, T-cell, Blood Smear

INTRODUCTION

Sezary syndrome (SS) is a rare subtype of cutaneous T-cell lymphoma (CTCL) traditionally defined by the triad of pruritic erythroderma, generalized lymphadenopathy, and clonally related neoplastic T cells with cerebriform nuclei (Sezary cells) in the skin, lymph nodes, and peripheral blood [1, 2]. Its belongs to the group of non-Hodgkin's lymphomas (NHL) resulting from malignant proliferation of skin-homing T cells [2]. SS and mycosis fungoides (MF) are the most common forms of CTCL, accounting for approximately 65% of cases, while SS accounts for approximately 2% of all CTCL [1, 3]. CTCLs are assumed to be predominantly male and the median age of onset is between the fifth and sixth decade and carries a poor prognosis, with a reported 5-year disease-specific survival of 36% [4, 5].

We report through a series of 6 cases, the experience of the hematology laboratory in the diagnosis of the syndrome of Sezary.

MATERIALS AND METHODS

This is a retrospective study of 6 cases of Sezary syndrome collected in the hematology laboratory of Arrazi Hospital in Marrakech. Data were collected from registers and patient files of the dermatology and hematology departments. A complete blood count and a blood

smear stained with the May-Grunwald-Giemsa (MGG) staining method were performed in the Hematology Laboratory of the Mohammed VI University Hospital of Marrakech- Morocco.

RESULTS

Six patients were identified with the clinicopathological criteria of SS. There were 4 males and 2 females (M/F=2), mean age at diagnosis of SS was 55,6 years (31-80).At the time of diagnosis, 5 patients had pruritic erythroderma, nodular lesions were found in one patient at diagnosis and generalized lymphadenopathy in both superficial and deep stations in 3 cases. The white blood cell count was elevated (>10,000 WBC/mm3) in all 3 patients with Hyperlymphocytosis in 50% and hypereosinophilia in 2 cases.
The blood smear showed the presence of small to medium-sized cells with a high nucleocytoplasmic ratio and cerebriform nuclei typical of Sezary cells (Fig. 1), and the percentage was higher than >10% suggests the diagnosis of SS in all patients.

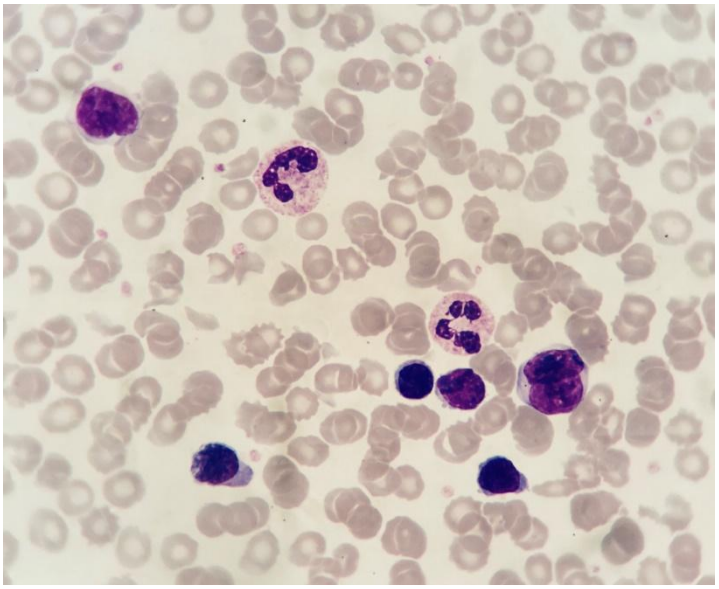

Figure 1.Sezary cell on peripheral blood smear, MGG staining (x1000).

The immunopheno type of abnormal peripheral T cell population in all cases is CD3+, CD4+, CD30 -.Cytological examination of the skin biopsy showed malignant lymphocytic proliferation. Thoraco abdominopelvic CT scan showed lymphadenopathies in 4 cases.

DISCUSSION

In 1938s, Albert Sezary described several patients who presented with erythroderma, unique “monster cells” in the skin, blood, and occasionally the lymph node; one patient also had generalized lymphadenopathy [6, 7]. It was not until the 1970s that the neoplastic “monster cells” of SS were determined to be T lymphocytes3 and therefore SS determined to be a cutaneous T-cell lymphoma [8].

Sezary syndrome (SS) is one of the cutaneous lymphomas whose pathophysiology remains poorly understood. It is a primary cutaneous T-cell lymphoma, which means that the skin is the first or only organ affected. These lymphomas are composed of memory T cells with cutaneous tropism, which is conferred by the expression on their surfaces of specific markers such as CLA (cutaneaous lymphocyte antigen) which interacts with the E-selectin receptor present in the post-capillary venules of the dermis. These mature T cells are usually recruited to the skin during skin infections to prepare a specific immune response [9].

SS and MF are the most frequent forms of CTCL. It is a rare syndrome that represents between 3 and 5% of primary cutaneous T lymphomas. It generally affects adults aged 50 years on average. It is a rare and aggressive lymphoma, characterized by the triad of erythroderma, generalized polyadenopathy, and the presence of Sezary cells in the blood[10]. It is a primary cutaneous T-cell lymphoma that develops primarily in the skin, without extracutaneous involvement at diagnosis, i.e., no lymph node, visceral, or bone marrow involvement.

The diagnosis of SS must be suspected in any patient presenting with erythroderma (Figure 2). Though the skin involvement is diffuse in Sezary syndrome, it is not as dense as it is in mycosis fungoides. Therefore, a skin biopsy should be performed without any interventions for the lesions, and the site with the greatest induration should be biopsied [11].

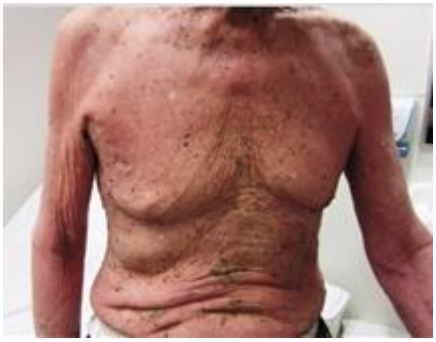

Figure 2. Generalized erythroderma in a 95 years-old man [12]

The biological workup includes a blood count, which is a non-specific test and most often shows normal hemoglobin, platelets, and leukocytes at the time of diagnosis. Hyperlymphocytosis and hypereosinophilia may be present and are most often associated with a poor prognosis. In patients with suggestive clinical signs, even a moderate lymphocytosis should prompt the diagnosis of SS. In some cases, signs of bone marrow involvement, such as normocytic normochromic anemia and severe cytopenia, may be found [13, 14].

Sezary cells (SCs) have a characteristic morphology (Fig 3): They are small to medium sized cells approximately 10 to 12 µm in diameter, with a high nucleo-cytoplasmic ratio, a very irregular nucleus with fairly dense, clear, mature chromatin without a nucleolus, and which has one to two "nail-bitten" grooves giving it a cerebriform appearance, sometimes described as a "wet sheet" appearance. [15, 16]

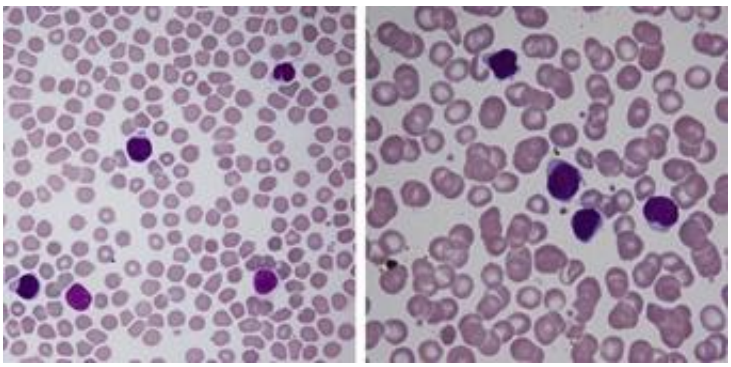

Figure 3.Sezary cell on blood smear stained with May-Grünewald Giemsa

A precise microscopic examination of the blood smear is essential for any patient presenting clinical signs suggestive of SS. Other more efficient techniques have been developed and allow a more objective diagnosis, in particular the immunophenotyping technique by flow cytometry [18].

Immunophenotyping confirming T-cell origin (CD3+ and CD4+) and lack of expression of CD2, CD5 and CD7 (mature T-cell antigens) are supportive of Sezary syndrome [19].

The diagnosis is made by erythroderma involving greater than 80% BSA (body surface area), clonal TCR rearrangement confirmed by PCR or Southern blot, and absolute Sezary cell count of at least 1000 cells/microL, or one of the following 2 criteria:
Increased CD4+ or CD3+ with CD4/CD8 ratio of 10 or more.

Increased CD4+ cells with abnormal phenotype: CD4+CD7- ratio of 40% or more or CD4+CD26- ratio of 30% or more.

The treatment options are based on the stage of the disease. Given the leukemic involvement in Sezary syndrome, the treatment is generally systemic (interferons, retinoids, low-dose methotrexate and histone deacetylase inhibitors). It can be given alone or in a combination of skin-based therapy.

CONCLUSION

The diagnosis of SS remains a challenge in many situations; the pathophysiology and definition of SS have evolved significantly over the past decades. Research continues to develop better management of this syndrome. The performed study showed the complementarity between biological analyse and clinic information in the process of SS diagnosis.

CONFLICTS OF INTEREST

The authors have nothing to disclose

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