

Sezary Syndrome: A Clinico-biological Study of 5 Cases

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Abstract: *Background:* Sézary syndrome (SS) is a rare erythrodermic and leukemic variant of cutaneous T-cell lymphoma (CTCL) that 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 5 cases, the experience of the hematology laboratory in the diagnosis of the syndrome of Sézary. *Methods:* This is a retrospective study of 5 cases of Sezary syndrome collected in the dermatology department of Marrakech. *Results:* five patients were identified with the clinicopathological criteria of SS. At the time of diagnosis, all 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 all 5 patients with a mean value of $18,120$ WBC/mm³. The blood smear showed the presence of 75% (27 G/l) of small to medium-sized cells with a high nucleocytoplasmic ratio and cerebriform nuclei typical of Sezary cells and suggests the diagnosis of SS. *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

1. Introduction

Sézary syndrome (SS) is a rare erythrodermic and leukemic variant of cutaneous T-cell lymphoma (CTCL) that belongs to the group of non-Hodgkin's lymphomas (NHL) resulting from malignant proliferation of skin-homing T cells [1]. SS and mycosis fungoides (MF) are the most common forms of CTCL, accounting for approximately 65% of cases, while SS accounts for approximately 3% of all CTCL [2]. CTCLs are assumed to be predominantly male and the median age of onset is between the fifth and sixth decade [3].

In order to establish the diagnosis of SS, clinical signs, a blood smear with cerebriform atypical nuclei T cells, and evidence of T cell clones in the skin, lymph nodes and blood should be considered [4].

We report through a series of 5 cases, the experience of the hematology laboratory in the diagnosis of the syndrome of Sézary.

2. Material and Methods

This is a retrospective study of 9 cases of Sezary syndrome collected in the dermatology department of Marrakech.

The data collection was carried out from registers and patient files of the Dermatology Department. The patients were admitted in the Dermatology department. We have performed a blood sample for the purpose of complete blood count and blood smear with May-Grunwald-Giemsa (MGG) staining method. The blood analyse has been performed in the Military Hospital Inb Tofail in Marrakech – Morocco.

3. Results

Five patients were identified with the clinicopathological criteria of SS. There were 3 males and 2 females (M/F=1.25), mean age at diagnosis of SS was 62.1 years (52-73).

At the time of diagnosis, all 5 patients had erythroderma

and generalized lymphadenopathy in both superficial and deep stations.



Figure 1. Generalized erythroderma.

The white blood cell count was elevated ($>10,000$ WBC/mm³) in all 5 patients with a mean value of 18,120 WBC/mm³.

The blood smear showed the presence of 75% (27 G/l) of small to medium-sized cells with a high nucleocytoplasmic ratio and cerebriform nuclei typical of Sezary cells and suggests the diagnosis of SS.



Figure 2. Sezary cell on peripheral blood smear, MGG staining (x1000).

Lymphocyte immunophenotyping was performed and showed a CD4/CD8 ratio greater than 10 in all cases.

Cytological examination of the skin biopsy showed malignant lymphocytic proliferation.

Thoracoabdominopelvic CT scan showed bilateral iliac lymphadenopathies.

4. Discussion

The first description of Sézary syndrome (SS) was by Sézary and Bouverain in 1938. They described a disseminated form of cutaneous lymphoma associating erythroderma and the presence of "monstrous" cells in the blood. [5]

Sézary 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 (cutaneous 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. [6]

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 [7].

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 ISCL/EORTC system has well determined the diagnosis of SS, thus requiring a rigorous clinicopathological and molecular cohesion. Its diagnosis is based on clinical, biological, and histological criteria. [8]

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 [9, 10], a CBC must be associated with a blood smear.

Sézary cells (SCs) have a characteristic morphology:

They are small to medium sized cells approximately 10 to 12 μ m 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. [11, 12]

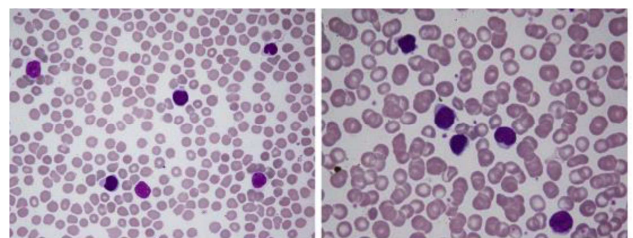


Figure 3. Sezary cell on blood smear stained with May-Grünwald Giemsa [13].

The blood smear distinguishes two types of Sezary cells:

1. Lutzner-Flandrin cells with a size of less than 12 μ m
2. Sezary-Lutzner cells whose size is greater than 12 μ m

These 2 cell types have the same nuclear characteristics described above. The existence of large Sezary cells is the majority of cases related to a poor prognosis. [12]

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 [4, 15].

Immunophenotyping by CMF during SS allows to find several abnormalities that are part of the diagnostic criteria defined by the International Society of Cutaneous Lymphomas (ISCL) and the EORTC since 2007. There is a T cell hyperlymphocytosis (>1750 CD3+/uL lymphocytes) composed of cells with the following phenotype: CD2+, CD3+, CD4+, CD5+, CD8-, CD45RO+, CD45RA-, associated with the increase of CD4/CD8 ratio that is greater than 10 that was found in 48% to 88% of SS patients [16, 17].

5. 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.

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