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Clinical and biological analysis of Sézary syndrome: A report of four cases

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Abstract

Background: Sézary syndrome (SS) is a rare and aggressive type of cutaneous T cell lymphoma characterized by an intensely pruritic, exfoliative rash, known as erythroderma, with cutaneous and systemic dissemination of clonal CD4+ T cells into the blood and lymph nodes. We report through a series of 4 cases, the experience of the hematology laboratory in the diagnosis of the syndrome of Sézary.

Methods: Four patients with SS were identified retrospectively among patients with cutaneous T-cell lymphoma followed up in the dermatology department and diagnosed in the hematology laboratory of the Avicenne military hospital in Marrakesh.

Results: Four patients with SS were described: three men and one woman, mean age at diagnosis 62 years (55-71). All the patients showed generalized dry erythroderma, pruritus and lymphadenopathy. Palmo-plantar hyperkeratosis, nail lesions and alopecia were also present. The white blood cell count was elevated (>10,000 WBC/ mm3) in all 4 patients with a mean value of 17,276 and one patient among these showed an elevation of eosinophils (> 500/ µl). The blood smear showed the presence of 65% of small to medium-sized cells with a high nucleocytoplasmic ratio and cerebriform nuclei typical of Sézary cells and suggests the diagnosis of SS.

Conclusion: Sézary syndrome is a rare subtype of cutaneous T-cell lymphoma characterized by erythroderma, circulating neoplastic T cells, and poor prognosis. Microscopic findings must be correlated with the clinical presentation to make the diagnosis.

Keywords: Sézary syndrome; Lymphoma; T-cell; Cerebriform lymphocytes; Mycosis fungoides

1. Introduction

Cutaneous lymphomas are a heterogeneous group of extra-ganglionic non-Hodgkin's lymphoma (NHL) that arise primarily from tropic T cells in the skin [1]. The overall incidence of cutaneous T-cell lymphoma (CTCL) is 10.2 per million people and increases with age, with a median age of disease onset between the fifth and sixth decade [2, 3]. The main subtypes of CTA are mycosis fungoides (MF) and Sézary syndrome, corresponding to approximately 55% and 5% of cases, respectively [4, 5].

SS is defined by a triad of signs namely erythroderma, generalized lymphadenopathy and the presence of neoplastic T cells in the skin, lymph nodes and peripheral blood [5]. Currently, the risk factors for SS are unknown and its etiology remains undetermined, preventing the development of targeted therapies [1, 5]. While MF has an indolent course, SS represents a leukemic form of erythrodermic T-cell lymphoma, which can be aggressive and associated with a poor prognosis [5].

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Given its rarity and the number of cases, we report 4 cases of SS diagnosed in the hematology laboratory of the Avicenne Hospital in Marrakesh.

2. Material and methods

A retrospective observational study of four patients affected by SS has been conducted. These patients were collected in the dermatology department of Marrakesh. The data collection was carried out from from registers and patient files of the dermatology department, the registers of the onco-hematology department and the anatomical-pathology department. Standard descriptive statistics were used to summarize the data.

3. Results

Four patients were identified as meeting the clinic-pathological criteria for Sézary syndrome. There were 3 males and 1 female (M/F= 3), mean age of SS diagnosis was 62 years (55-71).

At the time of diagnosis, all four patients had generalized dry erythroderma and generalized superficial and deep lymphadenopathies. At the same time none of the 4 patients presented visceral involvement.

Table 1 Clinical characteristics and staging

	Erythro-derma	**Lymph nodes**	**Pruritus**	**Palmo-plantar hyperkeratosis**	**Nail involvement**	**Alopecia**	**Immunophenotype of peripheral blood**
Patient 1	Yes	Yes	moderate	Yes	-	Yes	CD4/8 =10.4
Patient 2	Yes	Yes	moderate	Yes	-	-	CD4/8 = 22,1
Patient 3	Yes	Yes	moderate	Yes	Yes	-	CD4/8 = 18,7
Patient 4	Yes	Yes	Severe	Yes	-	Yes	CD4/8 =34,3

"Yes" indicated if present. CD4/8 for CD4+/CD8+ ratio

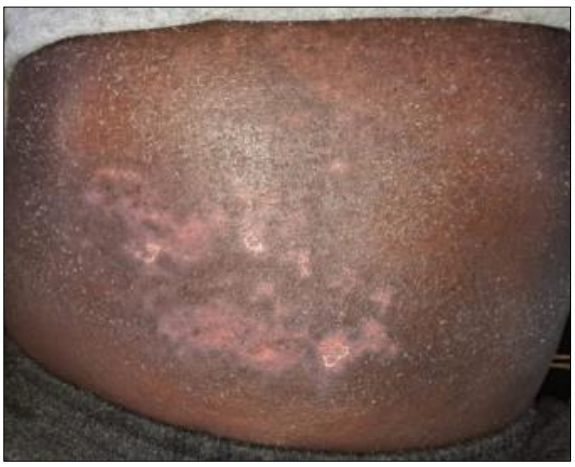

Figure 1 Generalized erythroderma

The white blood cell count was elevated (>10,000 WBC/ mm3) in all 4 patients with a mean value of 17,276 and one patient among these showed an elevation of eosinophils (> 500/ µl).

The blood smear showed the presence of 65% of small to medium-sized cells with a high nucleocytoplasmic ratio and cerebriform nuclei typical of Sézary cells and suggests the diagnosis of SS.

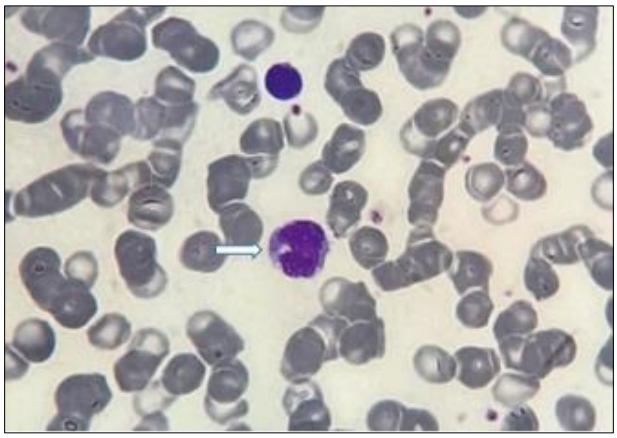

Figure 2 Sézary cell on peripheral blood smear, MGG staining (x1000)

Lymphocyte immunophenotyping was performed and showed a CD4 / CD8 ratio greater than 10 in all cases.(Table :1)

Cytological examination of the skin biopsy showed malignant lymphocytic proliferation.

4. Discussion

Sézary syndrome was described in 1938 by Albert Sézary (1880-1956). Like mycosis fungoides, SS belongs to a group of extra-nodal non-Hodgkin's lymphomas of cutaneous epidermotropic T-cell origin. They are distinguished from other CTCL by their unique clinical and histopathological features. This disease results from the malignant transformation of helper T cells with a characteristic tropism for the epidermis. SS is a systemic variant of MF, characterized by erythroderma, lymphadenopathy, pruritus and the presence of atypical cells in the peripheral blood [7]. SS is relatively rare. It generally affects middle-aged adults, with a peak age at presentation of 55 years [6]. The predominance is male and the disease is twice as common in blacks as in whites [7]. Black patients are diagnosed at an earlier age (median age of diagnosis 53 years, compared with 63 years for whites) and have poorer survival than white patients, regardless of age and stage of disease [8]. Environmental and occupational exposure to solvents, chemicals, and toxins, as well as the role of human T-lymphotropic virus type I (HTLV-I) [7] have been suggested but not proven.

The clinical picture of SS combines generalized erythroderma (dry or edematous), pruritus, polyadenopathy, palmoplantar keratoderma, and other major clinical features such as ectropion, onychodystrophy, alopecia and sometimes hepatosplenomegaly [9]. Patients may also experience non-specific signs such as fever, chills, weight loss and malaise.

The skin may sometimes be infiltrated and give rise to the formation of plaques. Usually at the time of diagnosis, SS develops mainly in the skin, without extra-cutaneous involvement. The main extra-cutaneous route is through the regional lymphatics and viscera [10]. Peripheral lymph nodes are the most common, followed by the spleen, lungs and liver. Despite circulating Sézary cells, the bone marrow is often negative. However, autopsy studies have shown that involvement of any organ can occur in the late stages of the disease.

World Health Organization (WHO) and European Organization for Research and Treatment of Cancer (EORTC) for cutaneous lymphomas was developed in 2005 and updated in 2018.Unlike mycosis fungoides, SS is classified as an aggressive lymphoma. [20].

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 [11,12], a CBC must be associated with a blood smear.

Sézary cells have a characteristic morphology: 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 [13,14].

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 [14, 15].

Immunophenotyping by flow cytometry 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 [15,16].

TNMB (tumor, node, metastasis, blood) staging remains the most important prognostic factor in MF/SS and forms the basis for a "risk-adapted," multi-disciplinary approach to treatment. For patients with disease limited to the skin, skin-directed therapies are preferred, as both disease-specific and overall survival for these patients is favorable. In contrast, patients with advanced-stage disease with significant nodal, visceral or blood involvement are generally approached with systemic therapies. These include biologic-response modifiers, histone deacetylase (HDAC) inhibitors, or antibody-based strategies, in an escalating fashion. In highly-selected patients, allogeneic stem-cell transplantation may be considered, as this may be curative in some patients [17].

Diagnosis of Sézary syndrome is often difficult and delayed, resulting in a poor prognosis due to the lack of effective therapeutic resources. The disease results in immunosuppression responsible for recurrent infections and decreased antitumor immune responses [18]. The five-year survival rate is only 24%, ranging from 55.8% when the number of circulating Sézary cells is less than 2,600 per cubic millimeter to 11.6% when the number of Sezary cells is greater than 2,600 per cubic millimeter [19].

5. Conclusion

Sézary syndrome is a rare subtype of cutaneous T-cell lymphoma characterized by erythroderma, circulating neoplastic T cells, and poor prognosis. Microscopic findings must be correlated with the clinical presentation to make the diagnosis. The goal of treatment is to minimize morbidity and limit disease progression. However, hematopoietic stem cell transplantation, considered for advanced patients, is the only therapy with curative intent.

Compliance with ethical standards

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Disclosure of conflict of interest

Authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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