Dermatology Online Journal

Dermatology Online Journal
UC Davis

Sezary Syndrome presenting with leonine facies and treated with low-dose subcutaneous alemtuzumab

Ana Oliveira MD, Inês Lobo MD, Rosário Alves MD, Margarida Lima PhD, Manuela Selores MD
Dermatology Online Journal 17 (11): 6

Hospital de Santo António, Centro Hospitalar do Porto, Porto, Portugal

Abstract

Cutaneous T-cell lymphomas (CTCL) comprise a group of diseases characterized by the accumulation of malignant T cells within the skin. Sezary syndrome represents an aggressive form of CTCL, in which the skin is diffusely affected and the peripheral blood is involved. It is characterized by the triad of generalized erythroderma, lymphadenopathy, and neoplastic T cells (Sezary cells) in the skin, lymph nodes, and peripheral blood. Leonine facies is rare and corresponds to the morphologic manifestation of diffuse dermal infiltration of the face. It can occur in cutaneous T-cell lymphomas that progress during years without therapy. We present the case of a 54-year-old man with Sezary syndrome presenting with leonine facies, unresponsive to conventional therapies; he exhibited a promising response to subcutaneous low-dose alemtuzumab.

A 54-year-old male was observed in our department because of a four-year history of generalized pruritus and cutaneous lesions on the face. On physical examination he showed generalized erythroderma, lichenification, diffuse alopecia, madarosis, and diffuse infiltration of facial skin, particularly on the eyebrows and ears, giving the appearance of a leonine facies (Figures 1a and 1b). Small (<1 cm) axillary, supraclavicular, and inguinal lymph nodes were palpable. His physical examination was otherwise normal. His past medical history was irrelevant and he was not taking any prescribed or over-the-counter medications.

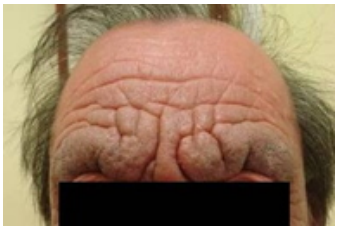

Figure 1

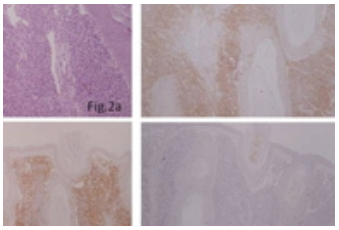

Figure 2

Figure 1a. Diffuse alopecia, madarosis and diffuse infiltration of facial skin giving the appearance of leonine facies
Figure 1b. Infiltration of the ear
Figure 1c. Third week of alemtuzumab: marked reduction of the facial infiltration

Figure 2a. Infiltration of the dermis by atypical lymphocytic cells. No epidermotropism (H&E, x4)
Figure 2b. Positivity for CD3 (x4)
Figure 2c. Positivity for CD4 (x10)
Figure 2d. Negativity for CD8 (x4)

A skin biopsy was made revealing an atrophic epidermis with follicular dilation and hyperkeratosis. The dermis was diffusely infiltrated with atypical lymphocytic cells, consisting of large cells with hyperchromatic and cerebriform nuclei (Figure 2a). There was no epidermotropism. The lymphoid infiltrate was characterized immunohistochemically by positivity for CD3 (Figure 2b) and CD4 (Figure 2c) and negativity for CD8 (Figure 2d). Flow cytometry showed a mixture of small and large CD4+ lymphocytic T-cells, with an aberrant CD3/TCRαβ+low, CD2+low, CD7- immunophenotype. Molecular biology studies revealed a monoclonal TCR γ-gene rearrangement.

The full blood count revealed 18.59x10^9/L leukocytes, 7.81 x10^9/L neutrophils, 1.39 x10^9/L lymphocytes, hemoglobin 15.2 g/dL, and platelets 395 x10^9/L, with 45.5 percent of atypical lymphocytes. Biochemistry studies were relevant for high LDH (430 UI/L) and high β2-microglobulin (2341 ng/mL) levels. Thoracic, abdominal and pelvic CT scans were unremarkable and the bone marrow biopsy revealed invasion of atypical lymphocytic cells. Flow cytometry and molecular biology studies confirmed the presence of the phenotypically abnormal monoclonal CD4+ T cells in the peripheral blood and bone marrow. The diagnosis of Sezary syndrome (SS) (T4NxM0B2) was made.

The patient started combined systemic chemotherapy with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) accomplishing four cycles with no response. A regimen of low dose subcutaneous (sc) alemtuzumab was then introduced, beginning with 3 mg in the first day, followed by 10 mg three times a week for twelve weeks. There was a transient interruption of the treatment at the fourth week, with a duration of six weeks, for asymptomatic reactivation of cytomegalovirus. We observed a marked reduction of

the erythema and of the facial infiltration beginning in the third week (Figure 1c). Sezary cells reached an absolute count of zero by the second week of treatment; by this time that the patient noted almost no pruritus. Currently, three months after the end of the treatment, there is a slight worsening of clinical and laboratory parameters.

Leonine facies is rare and corresponds to the morphologic manifestation of diffuse dermal infiltration of the face. It can occur in a variety of conditions [**1**], although it is more frequent in association with lepromatous leprosy and cutaneous T-cell lymphomas. Most of the time it occurs as the diseases progress without therapy.

Sezary syndrome is a rare disease, corresponding to 5 percent of all primary cutaneous T cell lymphomas [**2**]. Classically, it is characterized by the triad of erythroderma, generalized lymphadenopathy, and neoplastic T cells (Sezary cells) in the skin, lymph nodes, and peripheral blood [**3**]. Besides the erythroderma, it presents with generalized exfoliation, palmoplantar keratoderma, alopecia, and onychodystrophy [**3**].

The histological features in SS may be similar to those in mycosis fungoides, although in SS the cellular infiltrates are more often monotonous and epidermotropism may sometimes be absent. Usually, the neoplastic T cells have a CD3+, CD4+ and CD8− phenotype [**1**].

In 2002, the International Society of Cutaneous Lymphoma proposed new criteria for SS diagnosis, including one or more of the following parameters: an absolute Sezary cell count of least 1000 cells/mm^3; demonstration of immunophenotypic abnormalities (an expanded CD4 T-cell population resulting in a CD4/CD8 ratio more than 10; loss of any or all of the T-cell antigens CD2, CD3, CD4, and CD5); or the demonstration of a T-cell clone in the peripheral blood by molecular or cytogenetic methods [**2**].

The prognosis is in general poor and the median survival rate at 5 years is 24 percent [**4**]. Patients frequently die of opportunistic infections related to the immunosuppression that is inherent to the therapy [**3**].

Conventional treatment relies on systemic combined chemotherapy, alpha interpheron, photochemotherapy, and extracorporeal photopheresis, usually with partial, clinically unsatisfactory and transient responses [**3**].

Alemtuzumab is an anti-CD52 recombinant DNA-derived humanized monoclonal antibody that has been used in the last years for treatment of chronic lymphocytic leukemia and T-cell lymphomas, including primary cutaneous T-cell lymphoma, though never as first-line. In a study conducted in 2009 by Querfeld et al [**5**], 19 patients with advanced erythrodermic cutaneous T-cell lymphomas were treated with alemtuzumab intravenously using an escalating dose regimen with a final dose of 30 mg three times a week for 4 weeks, followed by subcutaneous administration for 8 weeks, with a response rate of 84 percent.

Bexarotene has been used in these patients, but the major complication, is the reactivation of cytomegalovirus, especially if used in the standard dose regimen of 30 mg intravenously or subcutaneously (sc), three times a week. In 2007 Bernengo et al [**6**] studied the efficacy of sc low-dose alemtuzumab (3 mg on day 1, then 10 mg on alternating days) in the treatment of fourteen SS patients. They concluded that the alemtuzumab given sc at very low doses has a good toxicity profile, high response rate, and causes durable remissions in SS patients with high tumor burden in the peripheral blood.

We applied this knowledge to our patient and found that by the beginning the second week there was already a significant decrease of atypical T cells in the peripheral blood and a waning of erythema and pruritus.

With this report we intend to present a rare manifestation of cutaneous T-cell lymphoma that particularly arises in patients untreated over years of evolution. Treatment with low-dose sc alemtuzumab seems to be useful in controlling the symptoms and progression of SS.

References

1. Willemze R. Cutaneous T-Cell Lymphoma. In: Bolognia J L, Jorizzo J L, Rapini R L, eds. *Dermatology*. Mosby Elsevier 2008;1870-84

2. Vonderheid EC, Bernengo MG, Burg G et al. Update on erythrodermic cutaneous T-cell lymphoma: report of the International Society for Cutaneous Lymphomas. *J Am Acad Dermatol* 2002;46(1):95-106. [**PubMed**]

3. Willemze R, Jaffe ES, Burg G et al. WHO-EORTC classification for cutaneous lymphomas. *Blood* 2005;105(10):3768-85. [**PubMed**]

4. Whittaker SJ, Marsden JR, Spittle M et al. Joint British Association of Dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas. *Br J Dermatol* 2003;149(6):1095-1107. [**PubMed**]

5. Querfeld C, Mehta N, Rosen ST et al. Alemtuzumab for relapsed and refractory erythrodermic cutaneous T-cell lymphoma: a single institution experience from the Robert H. Lurie Comprehensive Cancer Center. *Leuk Lymphoma* 2009;50(12):1969-76. [**PubMed**]

6. Bernengo MG, Quaglino P, Comessatti A et al. Low-dose intermittent alemtuzumab in the treatment of Sezary syndrome: clinical and immunologic findings in 14 patients. *Haematologica* 2007;92(6):784-94. [**PubMed**]