Ulcerated cutaneous Richter syndrome

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Abstract

Richter syndrome or Richter transformation comprises the conversion of chronic lymphocytic leukemia into an aggressive type of large cell lymphoma. Classically, patients have diffuse and abrupt lymphadenopathy and organomegaly, in addition to fever, weight loss, and fatigue. Cutaneous involvement is rare and often nonspecific. We report a patient with chronic lymphocytic leukemia who presented with a large and rapidly evolving ulcer, revealed to be a high-grade cutaneous lymphoma.

Keywords: lymphoma, non-Hodgkin, leukemia, lymphocytic, chronic, B cell, transformation, neoplastic

Introduction

Richter syndrome (RS) is a rare transformation of chronic lymphocytic leukemia/small cell lymphocytic lymphoma (CLL) into a high-grade lymphoma such as diffuse large B-cell lymphoma, Hodgkin lymphoma, or histiocytic sarcoma. This occurs in 5-10% of the cases and is generally associated with an aggressive clinical condition and worse prognosis [1,2].

The progression of low-grade lesions to transformed tumors follows different biological patterns depending on the hematologic neoplasia. Linear evolution, which explains most cases of RS, corresponds to the cumulative acquisition of new mutations by the aggressive subclones of early neoplasia so that transformed cells retain the original mutations of low-grade cells. However, in the minority of cases, the development of indolent and aggressive neoplastic cells occurs from progenitor cells without clonal relationship, which reflects the state of immunosuppression inherent to the leukemic condition [3].

Case Synopsis

A 76-year-old woman complained of a four-month duration of an erythematous nodule in the left cervical region that evolved into a painful ulcerated nodule with centrifugal growth that was refractory to antibiotic therapy. On admission, she had a relevant clinical history of CLL, diagnosed three years prior. She had not had regular follow up with a hematologist. She also noted loss of appetite and an 8kg weight loss in the period. She denied cough, fever, night sweats, or regular use of medication. She was a smoker and reported exposure to a rural environment and domestic animals since childhood. On physical examination, she exhibited an ulcer of approximately 10cm in the largest diameter and 2cm

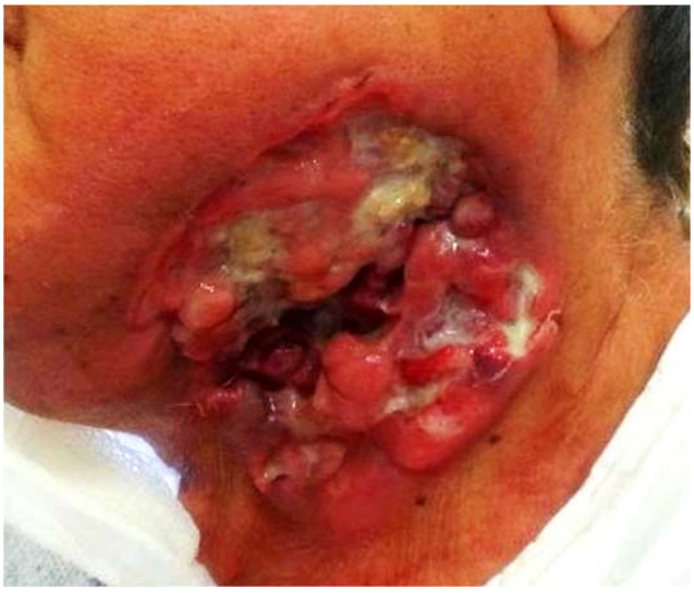

Figure 1. *Ulcer of approximately 10cm with erythematous, infiltrated, and irregular borders and fibrinous base located in the cervical region.*

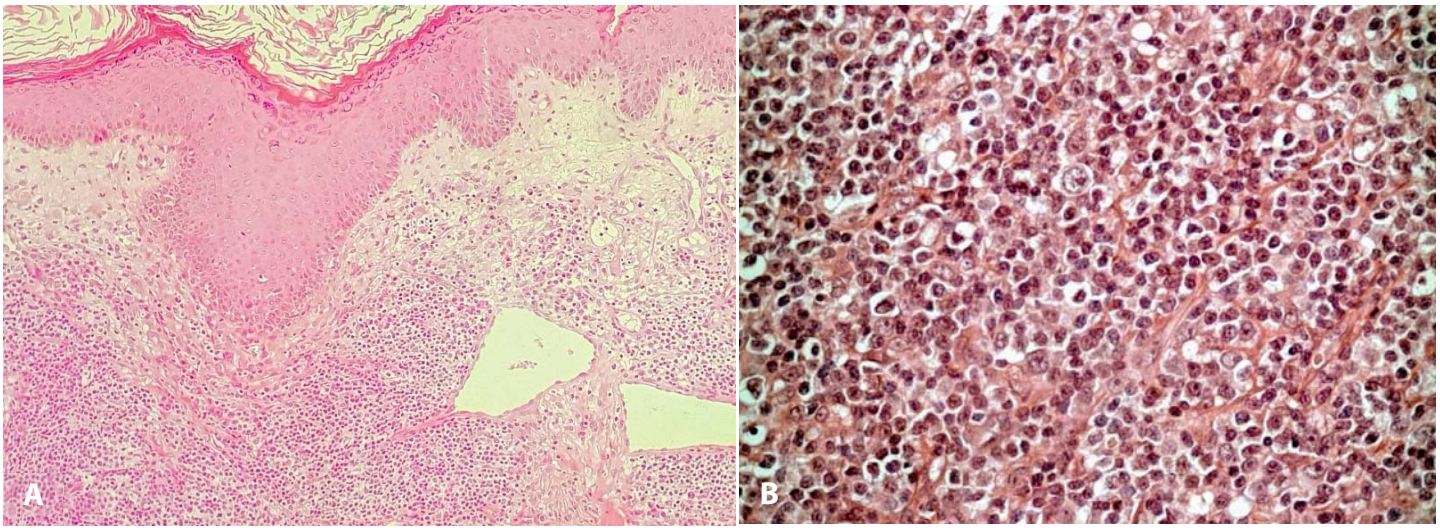

Figure 2. *Skin showing diffuse dermal infiltration by atypical lymphoid cells with high mitotic index. H&E,* ***A)*** *40×,* ***B)*** *400×.*

deep, with erythematous, infiltrated, and irregular edges and a fibrinous base located in the left cervical region (**Figure 1**). She also exhibited bilateral cervical, supraclavicular, axillary, and inguinal lymphadenopathy in addition to hepatosplenomegaly and diffuse skin xerosis.

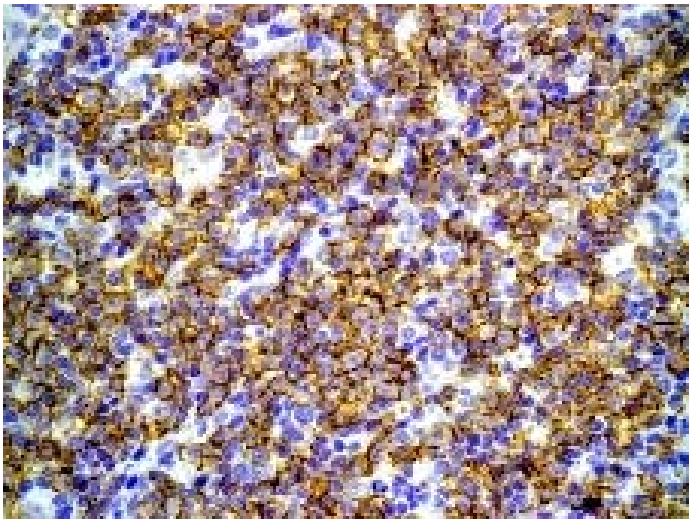

Figure 3. *CD20 immunostaining in atypical lymphocytes, 400×.*

The laboratory tests revealed microcytic anemia, increased C-reactive protein, hypogammaglobulinemia, and white blood cell count of 75.06×10^3/µL (reference: 4-$11x10^3$/µL). Lactic dehydrogenase, uric acid, and hepatic and renal function tests were normal. Peripheral blood immunophenotyping showed lymphocytes with co-expression of CD19, CD5, and CD23. In addition, there was a weak clonal expression of kappa light chain surface immunoglobulin. Computed tomography revealed infiltrative neoplasia in the left lateral cervicofacial region, associated with significant lymphadenopathy in the cervical, supraclavicular, retropectoral, axillary, and mediastinal chains.

The histopathological study of the tumor demonstrated diffuse cutaneous infiltration by atypical lymphoid cells, from intermediate to large size and with high mitotic index, showing a very large cell population on the surface (**Figure 2**). Immunohistochemistry demonstrated positivity for CD20 (**Figure 3**), CD30, EBV, p53, and Ki67 (60%), as well as negativity for CD3, CD15, and ALK. The skin cultures and stains were negative for mycobacteria, fungi, and amastigotes. Considering the previous condition of indolent leukemia, as well as clinical and histopathological findings, the final diagnosis of CLL with transformation to diffuse large B-cell lymphoma or cutaneous RS was determined. The patient underwent chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP), radiotherapy, and surgery. Remission of the cutaneous and systemic disease was achieved.

Case Discussion

Richter syndrome is classically characterized by sudden onset of fever, night sweats, weight loss, worsening of lymphadenopathy, and hepatospleno-

megaly. There is variable presence of anemia, thrombocytopenia, elevated lactic dehydrogenase, and hypercalcemia [3]. Cutaneous involvement in RS is uncommon, totaling 22 cases described since 1980. It presents abruptly with papules, plaques, nodules, and cellulitis-like lesions that may affect the face, scalp, upper limbs, lower limbs, and trunk. Ulceration is uncommon [1].

Owing to the humoral and cellular immunodeficiency inherent in CLL and chemotherapy treatment, the differential diagnosis is broad and requires differentiation from infectious and parasitic diseases, solid neoplasms, and cutaneous CLL [1,4,5]. In the histopathology of cutaneous infiltration of CLL, malignant lymphocytes are small and hyperchromatic, with delicate nucleoli. The lymphocytes are distributed in a diffuse, perivascular, or nodular pattern. In contrast, in large cell lymphoma, atypical lymphocytes present with abundant cytoplasm and ovoid or rounded nuclei, as well as evident nucleoli and mitotic figures [1].

Conclusion

This case illustrates an unusual presentation of cutaneous Richter syndrome. Skin lesions can be heterogeneous and are often consistent with a broad differential diagnosis given the context of immunosuppression and polypharmacy. Owing to the worsened prognosis and the need to adjust the therapeutic approach, careful dermatological examination and biopsy is required to detect the first signs of transformation in patients with chronic lymphocytic leukemia.

Potential conflicts of interest

The authors declare no conflicts of interests.

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