

Primary Cutaneous Large B-Cell Lymphoma, Leg Type, Localized on the Dorsum

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Key Words

B lymphocytes · Histopathology · Immunohistochemistry · Lymphoma · Nodules · Skin · Primary cutaneous large B-cell lymphoma, leg type

Abstract

Primary cutaneous large B-cell lymphoma, leg-type (PCLBCL-LT), is a large B-cell lymphoma primarily involving the skin. It is distinguished from the other 3 subsets of this lymphoproliferative disorder by its immunohistopathological features, configuring confluent sheets of medium-sized to large B lymphocytes with round nuclei provided with evident nucleoli, resembling centroblasts or immunoblasts, which express Bcl-6, Bcl-2. Prevalently appearing on the lower limbs, as a single or multicentric and frequently ulcerated skin nodule or plaque, PCLBCL-LT has a worse prognosis than the other large B-cell lymphomas. Moreover, the age of onset is delayed (7th decade) compared to those of the other 3 subtypes (6th decade); it presents a slight female predominance (2:1), and a higher percentage of positivity to Bcl-2. We present a 52-year-old man who showed a 2-year standing, non-ulcerated, round, 4 cm in diameter, red plaque, medially located on the dorsum. After biopsy the diagnosis of PCLBCL-LT was made on histopathological and immunohistochemical studies, the latter showing positivity to CD20, Bcl-2, and Bcl-6. After treatment with radiotherapy the patient has shown a 4.4-year follow-up free of disease.

Introduction

In the early 1990s, the term primary cutaneous B-cell lymphoma (PCBCL) was introduced to indicate a heterogeneous group of lymphoproliferative disorders primarily involving the skin [1]. Nowadays, the new WHO-EORTC (World Health Organization-European Organization for Research and Treatment of Cancer) classification for

cutaneous lymphomas identifies four main types of PCBCLs: (1) primary cutaneous marginal zone B-cell lymphoma (PCMZL); (2) primary cutaneous follicle center lymphoma (PCFCL); (3) primary cutaneous large B-cell lymphoma leg-type (PCLBCL-LT); and (4) primary cutaneous large B-cell lymphoma, other (PCLBCL-other) [2]. The description of PCLBCL-LT as a subset of PCBCL was first reported in 1996 [1]; since then many cases have been recognized [3–5].

PCLBCL-LT is diagnosed by the presence of confluent sheets of medium-sized to large B lymphocytes with round nuclei provided with evident nucleoli, resembling centroblasts or immunoblasts, which express Bcl-6, Bcl-2. In this update of the classification, the localization on the leg is incidental to the immunohistological aspects, which represent the diagnostic criteria, irrespective of the site of onset. This explains the new term ‘leg-type’ instead of the previous ‘of the leg’. Locations other than the legs have been reported to be sporadic even in large series of patients [4]; in particular, trunk localization is found in 7.5–13.3% of all PCLBCL-LT [4–7]. Prognosis of PCLBCL-LT has an intermediate level severity and depends on pathological features, presence of multiple skin lesions (but not the spread of a single one), age of the affected patients and disease duration before diagnosis [2, 4–6, 8].

We describe a patient with a peculiar clinical presentation and an early age of onset with a single light red lesion, 4 cm in diameter, on the dorsum diagnosed as typical PCLBCL-LT on immunohistological grounds.

Case Report

In November 2004, a 52-year-old man was referred to us for a skin lesion that he had noticed 2 years before and which had been stable and asymptomatic until a sudden and rapid growth during the last 2 months (**fig. 1**). Family and personal history was negative for skin diseases and the patient had always been in good health.

Physical examination revealed a light red infiltrated round plaque located on the dorsum, medially to the scapulae, with a diameter of 4 cm, without signs of surrounding edema. This lesion was very firm, with a very compact consistency and a hard texture to the touch, such as to present a temporary difficulty in executing the external incision through a commonly used scalpel. Moreover, once the biopsy was performed, there remained a well demarcated lozenge cavity and the skin flaps were very hard to draw together.

The remaining dermatological examination was negative and superficial lymph nodes were not enlarged.

The biopsy was fixed in formalin and embedded in paraffin. Three-micron-thick sections were stained for hematoxylin-eosin (**fig. 2**), Giemsa and cut for immunohistochemistry, the latter being performed by applying previously reported antigen unmasking procedures [9] and the AAAP technique [10]. Histology showed a dense diffuse lymphoid infiltrate located in the papillary and reticular dermis, composed of sheets of large pleomorphic cells with multiple nucleoli and variably basophilic cytoplasm, resembling centroblasts and immunoblasts. No epidermotropism was evident. Immunohistochemistry demonstrated positivity for CD20, Bcl-2 (**fig. 3**) and Bcl-6, and negativity for CD10, with high proliferation index. MUM1/IRF4 test was performed on the bioptic paraffined specimen on May 2008 and was negative.

The staging procedures excluded an extra-cutaneous involvement of the disease. On the basis of the clinical and immunohistological features a diagnosis of PCLBCL-LT was made. The patient underwent localized radiotherapy with good response and after a 4.4-year disease-free follow-up, no signs of relapse are present.

Discussion

PCLBCL-LT usually affects elderly patients during the 7th decade of life and presents a female predominance [4, 5, 7, 11]. This subset encompasses approximately 1–3% of all cutaneous lymphomas and 5–10% of PCBCL [12]. PCLBCL-LT is classified as a cutaneous B-cell lymphoma with an intermediate clinical behavior and a 5-year survival of 41% [2]. The typical clinical presentation of PCLBCL-LT is a unique red or violaceous rapidly growing nodule, frequently ulcerated and located on the lower limbs. We believe our case to be interesting for its atypical clinical presentation and outcome. In fact, the lesion was located on the dorsum, which has only been sporadically reported [5] as an onset site, and presented as a firm light red plaque without ulceration; the latter aspect may be explained by the recent growth of the lesion, which had previously been stable for 2 years. Moreover, the age of the patient (52 years) is significantly lower than the mean age reported in the literature for PCLBCL-LT [2–5].

Despite this unusual clinical presentation, the case fits well into this category on histological and immunohistochemical grounds, by showing sheets of pleomorphic large B cells growing diffusely, with positivity for Bcl-6, Bcl-2, and CD20 as well as CD10 and IRF4 negativity, as reported [2, 13].

Regarding the clinical course, PCLBCL-LT is reported to behave more aggressively than the other PCBCLs with large cell component [1]. This is partly due to the Bcl-2 expression. In reality, cases of PCLBCLs occurring outside the legs, but with the same morphologic and immunophenotypic pattern, can also be indicated as PCLBCL of the ‘leg type’, meaning that they present similarly to the variant classically occurring in the leg. The adverse prognostic impact of the Bcl-2 expression has recently been substantiated by gene expression profiling studies showing high expression levels of apoptosis-inducing cytotoxic effector genes, which lead to the constitutive inhibition of apoptotic pathways in the neoplastic cells [14, 15].

To our knowledge, in all the reports written in English [4–7] involving large series of patients since the new WHO-EORTC classification for PCLBCLs, only 25 patients with a solitary trunk/dorsum involvement have until now been mentioned out of 209 patients with a diagnosis of PCLBCL-LT, thus confirming the extreme rarity of our patient’s case: the localization of the lesion, the behavior of the lesion before and after diagnosis (before: single, non ulcerated, slow growing lesion, not spreading; after: good response to radiotherapy with a 4.4-year follow-up free of disease), the age of the patient at disease onset (52 vs. more than 70 years), the fact that despite some unfavorable prognostic parameters (Bcl-2+; 2-year old lesion, pathological features) the disease-free follow-up is long. Our case might underline the lack of reports on this rare subclass of patients with non-leg PCLBCL-LT, while in future analyses of such patients the parameters and clinical behavior of non-leg PCLBCL-LT should be extrapolated and pondered.

Fig. 1. Plaque on the dorsum, light red, firm and infiltrated.



Fig. 2. Diffuse lymphocytic infiltrate in the papillary and reticular dermis. HE. Original magnification $\times 40$.

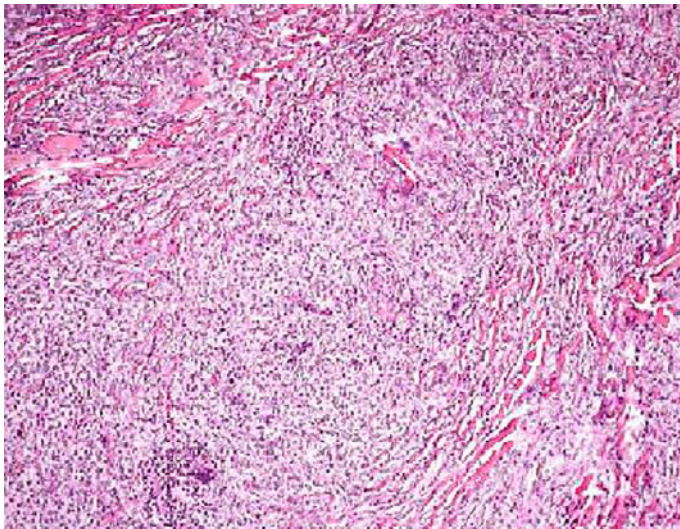
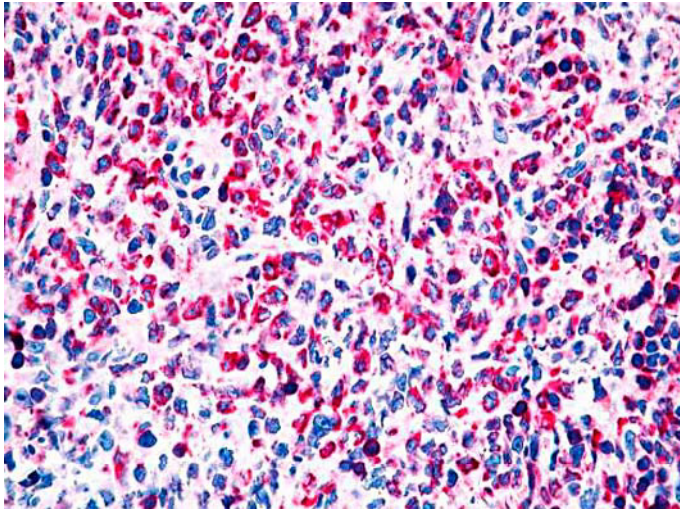


Fig. 3. Tumor cells contain cytoplasmic Bcl-2 staining. Bcl-2 immunoperoxidase. Original magnification $\times 64$.



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