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LONG-TERM EVOLUTION OF AN UNTREATED PRIMARY CUTANEOUS FOLLICLE CENTER LYMPHOMA OF THE SCALP.

Maria Teresa Fierro, MD, Federica Marenco, MD, Mauro Novelli, PhD, Paolo Fava, MD, Pietro Quaglino, MD, Maria Grazia Bernengo, MD.

I[st] Dermatologic Clinic, Dept. of Biomedical Science and Human Oncology, Turin University, Turin, Italy.

Corresponding Author: Fierro Maria Teresa - Dept. of Biomedical Sciences and Human Oncology, Section of Dermatology, University of Turin - via Cherasco 23, 10126, Torino, Italy. tel. +39-11-633 5816; fax +39-11-674034 - e-mail: mariateresa.fierro@unito.it

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ABSTRACT

Among primary cutaneous B cell lymphomas, follicle center lymphomas (FCL) represent, according to the WHO-EORTC classification, a subgroup with a favorable prognosis. We describe the case of a 45 year-old man who presented with large infiltrated tumors and nodules coalescing into a wide ulcerated plaque of the scalp, extending from the frontal to the occipital region. At the vertex two large ulcerations were present, reaching the subcutaneous tissues and the underlying bone structures with osseus infiltration and erosion and consequent meningeal exposure. A left retroauricular lymphadenopathy was also present. Histology and immunohystochemistry diagnosed a relapse of primary cutaneous follicle center lymphoma with multilobated histomorphology and lymph node involvement. The histological picture was unchanged from the first sample of 1989. Due to a refusal to treatment, the lesion progressively grew until now. After 6 courses of chemotherapy (CHOP-Rituximab) the tumor displayed an impressive complete regression, with persistence of a 4 cm occipital ulceration and underlying bone erosion. The adenopathy disappeared as well. This case gave us the opportunity to observe the natural development of the disease, leading to local mutilating and destroying lesions but with low tendency to systemic spread and an impressive response to chemotherapy.

INTRODUCTION

Primary cutaneous B-cell lymphomas (CBCL) are defined as malignant B-cell proliferations arising in the skin without evidence of extracutaneous involvement at the time of diagnosis. According to the WHO-EORTC (2005)[1] and the latest WHO classifications (2008), [2] primary cutaneous B-cell lymphomas (CBCLs) are divided in three major groups:1) marginal zone B-cell lymphoma (MZL), 2) follicle center lymphoma (FCL), 3) diffuse large B-cell lymphoma, leg-type (DLBCL). In addition more rare subtypes are represented by anaplastic or plasmablastic lymphoma, T-cell rich large B-cell lymphoma, intravascular large B-cell lymphoma, categorized as primary cutaneous diffuse large B–cell lymphoma, other. FCL and MZL account for about 80% of all primary CBCLs and share a mostly regional extension and an indolent clinical behaviour [3,4]. Conversely, primary DLBCL leg-type are characterized by a rapid growth of skin lesions, predilection for the elderly and much less favorable prognosis[3,4].

Herein we describe a case of primary cutaneous follicle center lymphoma of the scalp where the patient's refusal of any treatment led to the development of mutilating lesions with bone erosion, thus allowing us to observe the clinical evolution over a long period of time.

CASE REPORT

A Caucasian 45 year-old man presented in April, 2008 with large deeply infiltrated tumors and nodules coalescing into a wide ulcerated plaque of the scalp, extending from the frontal to the occipital region, involving the parietal regions bilaterally; at the vertex the tumor showed two large ulcerations, of 5 and 13 cm in diameter respectively, reaching the subcutaneous tissues and the underlying bone structures with osseus infiltration and erosion and consequent meningeal exposure (figure 1a,b). The whole lesion was covered with purulent exudate and serum hematic crusts. A palpable left retro-auricular lymphadenopathy of 5 cm in diameter was also present. In striking contrast with the condition of the lesions on his head the patient was in good general health and did not complain about pain, fever, night sweats nor weight loss. In 1989 the patient was firstly referred to our institution due to the onset of a single papulo-nodular lesion of the scalp diagnosed as "centroblastic B cell lymphoma with multilobated aspects" according to the "updated Kiel classification"[5], for which the patient was treated in another institution with surgery and chemotherapy with complete regression. At that time no extracutaneous lesions were documented. The patient suffered a relapse in 1994, but he refused any further biopsy or treatment. The lesion underwent indeed a progressive growth, until reaching the current dimensions. Episodes of depression and alcoholism were also reported in his past medical history.

A new biopsy showed a massive diffuse infiltrate involving the whole dermis and sparing the epidermis, with a partial follicular component. The infiltrate was composed of a population of follicle center cells, predominantly with multilobated nuclei, associated with large centroblasts and scattered centrocytes intermingled and surrounded by a large amount of small reactive T lymphocytes (figure 2a,b). The neoplastic population was CD20 (+), BCL2(-), BCL6(+), MUM-1(-) (figure 2c,d), with a proliferation index of 15% (Mib-1). The follicular dendritic cell meshworks of residual lymphoid follicles were highlighted by positive staining with CD21+ and CD35+. The histopathological and immunophenotypical pattern was therefore consistent with a diagnosis of cutaneous follicle center lymphoma. PCR analysis confirmed a clonal IgH gene rearrangement (FR2 and FR3 regions). A comparison with the specimens collected in 1989 showed a similar histological and immunopathological picture, thus demonstrating the local relapse of the primary cutaneous lymphoma previously diagnosed. Biopsy of the palpable node documented a nodal involvement. Subsequently, the patient was properly staged with bone marrow biopsy, total body computed tomography (CT) scans, esophagogastroduodenoscopy and pharyngeal fibroscopy; no other tumor localizations were found. LDH value was in the normal range. CT scan revealed that the tumor mass at the vertex caused a bone erosion measuring 9 x 4,5 cm wide, with pathologic tissue appearing not separable from the dura mater while subarachnoideal space seemed to be uninvolved (figure 3).
The final staging according to the revised ISCL-EORTC TNM classification was T2bN1M0[6].
The patient underwent 6 courses of CHOP-Rituximab (CHOP: Cyclophosphamide, Vincristine, Liposomal Doxorubicin, Prednisone). During chemotherapy the tumor displayed an impressive regression, with complete re-epithelization of the parietal ulceration; the occipital ulceration was still present but superficialized and reduced to 4 cm in diameter (figure 1c,d), completely covering the meninx, although cranial bones were not completely repaired. CT scan at the end of treatment confirmed a reduction of the bone erosion to 5 x 3,5 cm in diameter without appearance of new lesions. No signs of infection were present, and the retroauricolar lymphadenopathy was no longer identifiable. At the time of writing the patient has completed chemotherapy and is undergoing a strict follow-up.

DISCUSSION

Primary cutaneous B-cell lymphomas (PCBCL) are a well-defined group among cutaneous lymphoproliferative disorders[1-3, 7]. It is widely known that FCL are characterized by an excellent prognosis, with an overall and disease-free 5-years survival of 87% and 95% respectively[8], nevertheless no data are available as to the natural history in absence of treatment. The peculiarity of the case herein described consists in the progressive tumor growth over a 20 years period, showing an impressive loco-regional aggressiveness with capacity to destroy bones in contrast with low tendency to systemic spread. The patient felt good and continued to work. The availability of the first skin biopsy allowed us to compare the two skin samples (1989 and 2008): as the clinico-pathological picture was similar we diagnosed a relapse of the known primary cutaneous follicle center lymphoma with nodal invasion instead of a concurrent lymphoma.

The wide extension of the tumor made difficult the classification according to the new ISCL/EORTC TNM system[6,8]. Even if the lesion was single, it clearly originated from the coalescence of multiple tumors and nodules extending for less than 30 centimetres, thus we considered it a T2b PCBCL with a regional node involvement (N1). The bone erosion was considered as an invasion by contiguity, and not as a metastatic involvement. This feature is very unusual, being reported to our knowledge only one case of PCBCL with invasion of the cranial vault and orbit[9].

From an histological point of view, a peculiar finding in this case is the multilobated morphology of the cells. Large multilobated lymphoma, originally described by Pinkus et *al* in 1979[10] as T-cell lymphoma and later recognized also as B-cell lymphoma, is now considered as a rare morphologic variant both of nodal and extranodal T- and B-cell lymphomas, sometimes reported also among primary cutaneous follicle center lymphoma[1,7]. REAL classification (1994) considered multilobated B-cell lymphoma as a variant of large B-cell lymphoma[11], whereas the most recent EORTC (1997) [7] and WHO-EORTC classification (2005)[1] included it among follicle center cell lymphoma on the basis of its phenotypic characteristics. In literature, Korkopoulou et al.[12] collected only seventy well documented cases of B-cell multilobated lymphomas, forty with extranodal origin. Scattered multilobated lymphocytes are not unfrequently found in follicular lymphomas; the rarity of this case resides in the predominant multilobated morphology of neoplastic cells. Actually, also in our series, only two out of 403 primary cutaneous B cell lymphomas diagnosed since 1975 presented such histological pattern (unpublished data).

In FCL, considering the good prognosis and the low tendency of extracutaneous spread, radiotherapy is regarded as the first treatment choice; the efficacy of chemotherapy coupled or not with Rituximab is still poorly documented, while it has become standard treatment for DLBCL[3,4,13,14]. This unusual case indicate that, despite the high tumor burden, FCL are highly sensitive to chemotherapy coupled with Rituximab. At the time of writing the patient has just completed chemotherapy courses and obviously a strict follow-up is warranted.

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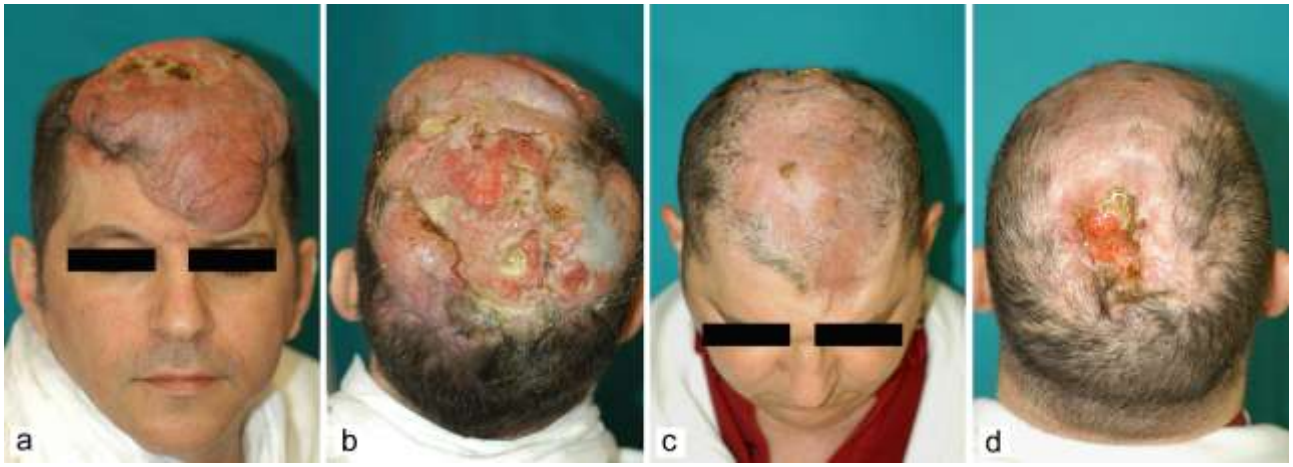

Figure 1a-d. Clinical appearance of the lymphoma before (a,b) and after (c,d) treatment

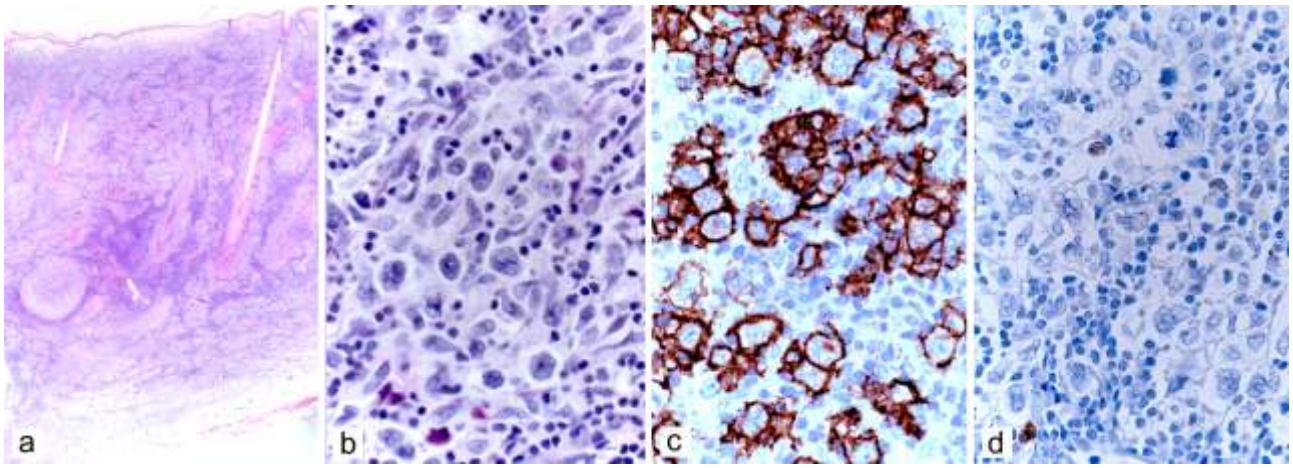

Figure 2a-d. Histological and immunohistochemical features of atypical multilobated cells, centroblasts and centrocytes. a,b) Hematoxylin-Eosin, (original magnification 20x, 600x), c) CD20 positivity of all large multilobated cells, d) Mum-1 staining: only few scattered medium-sized cells are positive (original magnification 600x).

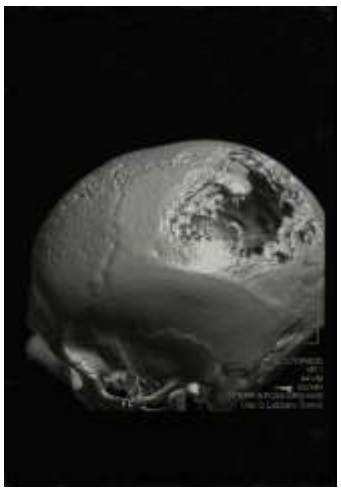

Figure 3. CT scan showing bone erosion before treatment.