Primary cutaneous T-cell-rich B-cell lymphoma: a case report and literature review

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SUMMARY

T-cell-rich B-cell lymphoma (TCRBCL) is a recently recognized B-cell lymphoma variant, characterized by a minor population of neoplastic B-cells existing in a background of predominant reactive T-lymphocytes. It is a rare entity, accounting for approximately 1 to 2% of all non-Hodgkin's lymphomas. It has both nodal and extranodal presentation. Primary cutaneous TCRBCL is an extremely rare lymphoma and only 16 cases have been documented thus far in the medical literature. We report the case of a 46-year-old man that presented with a slowly-growing, painless skin nodule on the left temporofrontal region of the scalp. A complete surgical excision was performed and histological examination revealed diffuse infiltration of the dermis by TCRBCL. A complete surgical excision of the skin lesion and systemic chemotherapy seems to have been effective because the patient is disease-free 2 years after the initial diagnosis was made. This study reports a very rare case of TCRBCL presented primarily in the skin. Because of its rarity, it is especially important to make the correct diagnosis using the appropriate immunohistochemical stains and apply the proper therapy.

KEY WORDS

lymphoma, cutaneous, T-cell-rich, B-cell

Introduction

Primary cutaneous T-cell-rich B-cell lymphoma (TCRBCL) is a rare B-cell lymphoproliferative disorder. Only 16 cases have been described in the English-language literature so far (1–12) (Table 1). Although the histologic appearance is similar to its nodal counterpart, the clinical behavior is different and it appears to have a better prognosis (9).

This study reports an additional case of primary cutaneous TCRBCL in a 46-year-old man. Diagnosis is frequently difficult because the neoplastic B-cell population may be quite sparse, and immunohistochemical analysis is necessary to identify the B-cell origin and clonality of the cells.

Case report

A 46-year-old man presented in our hospital due to a painless nodular lesion on the left temporofrontal region of the scalp that had grown slowly over the last 8

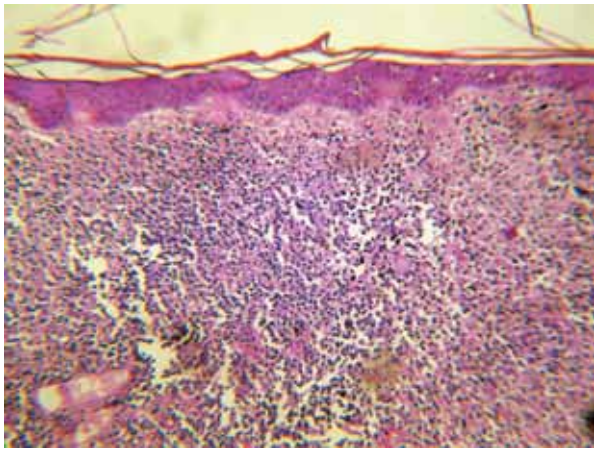

Figure 1. Diffuse infiltration of the dermis by TCRBCL (hematoxylin and eosin × 100).

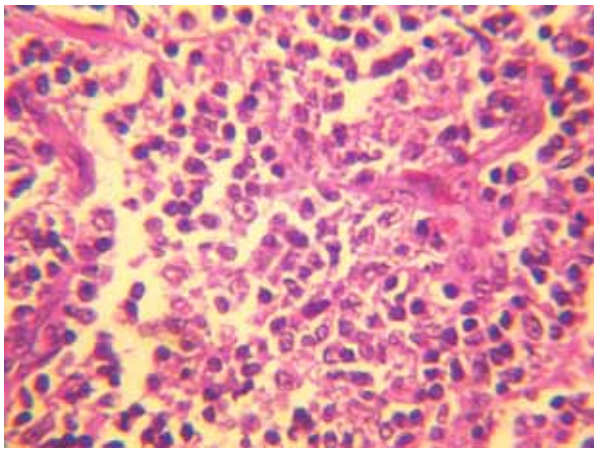

Figure 2. Higher magnification showing a few large lymphoma cells surrounded by small lymphocytes (hematoxylin and eosin × 400).

months. He had no fever, night sweats, weight loss, or other symptoms. The lesion measured 2 cm in maximum diameter and was firm. On physical examination no hepatosplenomegaly, no peripheral lymphadenopathy, and no other skin abnormalities were identified. Hematological and biochemical tests were normal. A complete surgical excision was performed. Histological examination revealed a TCRBCL according to the World Health Organization classification (13).

A work-up for metastases, including chest X-ray, CT-scan of the abdomen, bone scan, and bone marrow aspirate and biopsy revealed no evidence of disease. The patient received six courses of systemic chemotherapy with Mabthera (rituximab) and CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) and 2 years later is in good condition, without evidence of local recurrence or metastatic disease.

Pathological findings

The lesion showed a diffuse dense polymorphous infiltration involving the upper and deep dermis (Fig. 1) as well as the subcutaneous adipose tissue. There was no epidermotropism. The neoplastic infiltration consisted of large lymphoid cells with round to oval or sometimes abnormal nuclei with prominent nucleoli and

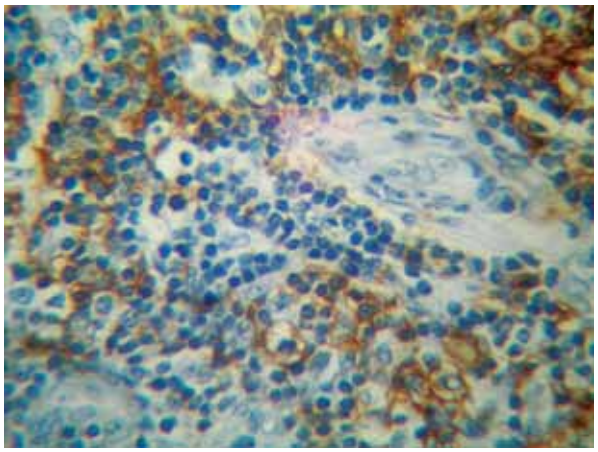

Figure 3. Lymphoma cells, positive for CD20; immunostaining (× 400).

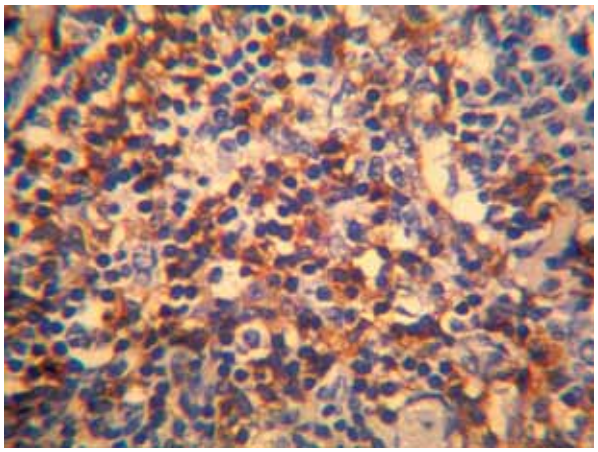

Figure 4. Small lymphocytes positive for CD45RO; immunostaining (× 400).

Table 1. Clinical summary of reported cases of primary cutaneous T-cell-rich B-cell lymphoma.

Reference	Age, Sex	Location	Treatment	Follow-up
Osborne et al. (1)	50, M	Not specified	Chemotherapy	Remission 3 months
Arai et al. (2)	61, M	Axillae	Excision	Remission 21 months
Krishnan et al. (3)	30, M	Face	Radiation	Died at 8 months
Dommann et al. (4)	18, M	Preauricular	Excision and radiation	10 year remission
Take et al. (5)	74, M	Neck	Chemotherapy	Remission 15 months, died
Sander et al. (6)	41, F	Ear	Excision	Remission 15 months
	58, M	Back	Excision	Remission 20 months
Wollina et al. (7)	45, M	Upper leg	Interferon-a perilesional	Remission 1 year
Dunphy et al. (8)	72, F	Scalp	Radiation	Remission 12 months
	33, M	Scalp	Radiation, chemotherapy	Remission 7 months
	71, M	Chest	Excision	Remission 10 months
Li et al. (9)	51, M	Lip	Radiation, chemotherapy	Remission 4 months
	62, M	Scalp	Radiation, chemotherapy	Remission 66 months
Watabe et al. (10)	86, M	Abdomen	Not applied	Same clinical status
Gogstetter et al. (11)	52, F	Arm	Chemotherapy	Relapse at 2 months
Kamarashev et al. (12)	50, M	Arm	Excision	Remission 4 years
Present case	46, M	Scalp	Excision, chemotherapy	Remission 2 years

pale cytoplasm, in a proportion < 10%, surrounded by small, mature lymphocytes in excess of 90% (Fig. 2). Plasma cells and eosinophils were also present.

Immunohistochemistry was performed and the large neoplastic cells showed strong positivity for CD20 (Fig. 3) and CD79a, whereas they were negative for CD15, CD30, EBV-LMP, CD45RO, CD3, EMA, and BCL-2. The small lymphocytic cell population showed CD45RO and CD3 positivity. (Fig. 4). Accordingly, the diagnosis of cutaneous TCRBCL was made.

Discussion

TCRBCL was first recognized as a separate entity by Ramsay et al. in 1988, who described a B-cell lymphoproliferative disorder in which the majority of the cells are reactive T-lymphocytes (> 90%) with large neoplastic B-cells accounting for < 10% of the overall infiltrating lymphoid cells (14). It is a rare entity, accounting for approximately 1 to 2% of all non-Hodgkins lymphomas, and is generally believed to be a subtype of diffuse large B-cell lymphoma in the World Health Organizations' classification (13).

Usually the lymph nodes are primarily involved (75%) with or without cutaneous involvement. It is an aggressive lymphoma that often presents as stage IV disease, with frequent bone marrow involvement and requiring systemic chemotherapy (15, 16).

Extranodal involvement has been reported in liver, soft tissue, spleen, nasopharynx, brain, tongue, mediastinum, and bone (1, 17–19). Primary cutaneous TCRBCL appears to be very rare because only 16 cases have previously been reported (1–12) (Table 1). Histologically, the lymphoid infiltration of the skin is diffuse or relatively well circumscribed, involving the dermis and the subcutaneous fat. It is composed of a mixture of small lymphocytes, some with irregular nuclear contours, representing > 90% of all the infiltrating cells, eosinophils, and sparse individual large lymphoid cells, accounting for less than 10% (9, 14). The large atypical lymphoid cells sometimes have clear cytoplasm and multilobated nuclei, but typical Reed-Sternberg cells are not seen. Prominent vascular proliferation is frequently present. Immunohistochemical stains reveal small T-lymphocytes, which express CD45RO, CD3, CD4, and large transformed B-cells that are positive for CD20. In addition, clonality of the neoplastic B-cell population can usually be demonstrated by immunohistochemical staining for immunoglobulin light-chain protein and molecular genetic study for rearrangement of the immunoglobulin heavy-chain gene (9).

Although the pathogenesis is not completely understood, it seems that more arguments speak in favor of biological heterogeneity. In some cases, bcl-2 rearrangements were found, strongly suggesting that the neoplastic B-cells are of follicle center-cell origin (18, 20). In our case, the immunohistochemical staining for bcl-2 protein was negative. Moreover, some studies suggest a possible histogenetic background on the basis of tumor progression from lymphocyte-predominant Hodgkin's disease, sharing common morphological features (12, 21). On the other hand, the massive T-cell

infiltration has been related to the cytokine milieu of the tumor, such as interleukine-4 (15). It has also been hypothesized that Epstein-Barr virus might participate in the pathogenesis of B-cell lymphomas, with a corresponding T-cell reaction (22, 23). However, Epstein-Barr virus infection has only been documented in a few cases of nodal TCRBCL and in two cases of primary cutaneous TCRBCL (3, 5, 10). In our case, there was no evidence of Epstein-Barr virus infection.

The main differential diagnosis of TCRBCL includes benign lymphoproliferative diseases, pseudolymphomas, cutaneous T-cell lymphoma, other B-cell lymphomas, and lymphocyte-predominant Hodgkin's disease (3, 9, 14–16). The histological appearance mimics that seen in pleomorphic peripheral T-cell lymphoma or Hodgkin's lymphoma, and the differential diagnosis particularly from lymphocyte-predominance Hodgkin's disease is very difficult. This suggests potential evolution from one process to the other, although cutaneous involvement is exceedingly rare in this disease (14, 16, 18). The B-cell phenotype of the blasts in TCRBCL is similar to that of lymphocyte-predominant Hodgkin's lymphoma, in which, however, the blasts often coexpress EMA (16, 24). It can also be differentiated by the lack of nodularity of the infiltrate, the absence of typical lymphohistiocytic cells, the large numbers of reactive small B-lymphocytes composing the nodules, and the absence of CD57-positive cells in the reactive infiltrate (23, 25).

The treatment regimens have primarily included surgery, chemotherapy with or without radiation therapy, and interferon-a (3–7). In our case, complete surgical excision seems to have been effective because 2 years later there is no evidence of local recurrence or metastatic disease.

Although the histological appearance of primary cutaneous TCRBCL is similar to its nodal counterpart, the clinical behavior is different. Nodal TCRBCL with or without secondary skin involvement usually presents as advanced-stage disease, with frequent bone marrow involvement and splenomegaly. The reported cases of primary cutaneous TCRBCL appear to have a better prognosis with early-stage disease at presentation, without evidence of recurrence and better overall survival, as in our case (1–12).

This study reports a very rare case of TCRBCL presenting primarily in the skin. Although rare, an accurate diagnosis is important for therapeutic and prognostic purposes.

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