SPANDIDOS PUBLICATIONS

Primary cutaneous follicular center lymphoma of the upper arm: A case report

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Abstract. Primary cutaneous follicle center lymphoma (PCFCL) is unique in its biological behavior and molecular features, and it is also relatively rare. The present study reports a case of PCFCL in a young male patient, aged 32 years, whose primary skin lesion was located in the left upper arm. A skin biopsy confirmed that the dermal tissue of the patient's skin was affected by PCFCL. The patient was treated with radiation therapy and the mass was significantly reduced, with a resultant good prognosis. This case of a young patient with PCFCL is reported in order to provide a reference for the diagnostic segment of this disease.

Introduction

Primary cutaneous B-cell lymphomas (PCBCLs) are low-grade malignant extranodal B-cell non-Hodgkin's lymphomas that are confined to the skin without extracutaneous manifestations (1). The three main subtypes of PCBCL include primary cutaneous follicle center lymphoma (PCFCL), primary cutaneous marginal zone lymphoma (PCMZL) and primary cutaneous diffuse large BCL (PCDLBCL) (2). Although PCFCL is the most common type among them, accounting for ~55% of all PCBCL cases, it accounts for <1% of cases of B-cell lymphoma (3). PCFCL is an indolent lymphoma with an incidence rate that has been increasing exponentially over the past few decades (4).

PCFCL usually presents as limited skin damage to the head or trunk (5), with no extracutaneous involvement of lymph nodes, bone marrow or internal organs at the time of diagnosis (6). Clinically, the limited skin lesions in PCFCL appear morphologically as single or multiple slow-growing pink or purplish-red plaques, papules, nodules or tumors (7). The present study reports the case of a young patient with PCFCL and no extracutaneous manifestations.

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Case report

In August 2024, a 32-year-old man presented to The Affiliated Yantai Yuhuanding Hospital of Qingdao University (Yantai, China) with a skin swelling on the left upper arm that had been present for 2 years. The patient experienced occasional itching without night sweats, pain or fever. The swelling was hard and was gradually increasing in size. A physical examination showed a purplish-red nodule of the skin of the left upper arm that was hard and measured ~4x3 cm, with poor mobility and no obvious redness, swelling or pressure pain (Fig. 1A). The superficial lymph nodes were not palpably enlarged. Ultrasound revealed a subcutaneous hypoechoic mass in the left upper arm, measuring ~4.0x1.6x3.7 cm, with poorly defined borders, irregular morphology, heterogeneous internal echogenicity, grid-like internal changes, unclear demarcation from the skin and a longitudinal to transverse ratio of <1 (Fig. 1B). A rich blood flow signal was seen within the mass on color Doppler flow imaging (CDFI) (Fig. 1C); lymph nodes were detected bilaterally in the axillary and inguinal areas with clear borders, acceptable morphology, clear corticomedullary demarcation and a gated blood flow signal (Fig. 1D and E). The diagnosis from the ultrasound was a subcutaneous solid mass on the left upper arm, with possible malignancy. Bilateral axillary and inguinal lymph nodes exhibited no obvious swelling. Positron emission tomography-computed tomography (PET-CT) showed an irregular mass-like soft-tissue density shadow with abnormally high fluorodeoxyglucose uptake, a maximum standardized uptake value of 12.3, a size of ~4.0x1.9 cm and poor demarcation from the adjacent skin in the subcutaneous area of the left lateral upper arm. The mass was considered to be a lymphoma. Blood biochemistry indicated lactate dehydrogenase levels within the normal range.

A skin biopsy was performed. Tissues were fixed in 4% neutral buffer formaldehyde solution at room temperature for 24 h, and then sectioned to a thickness of 3 μm. The sections were stained with hematoxylin and eosin at room temperature for 3 min and then observed using an optical microscope.

The results showed a partial proliferation of oversized sheets of heterogeneous lymphoid cells in the dermis of the skin tissue (Fig. 1F). Incubation with primary antibodies was performed at 37˚C for 8 min. Horseradish peroxidase-conjugated secondary antibodies (ultraView Universal HRP; cat. no. SN 2884795; 1:500; Roche Diagnostics) were added and incubated at 37˚C for 8 min. All antibodies were supplied by Beijing Zhongshan Jinqiao Biotechnology Co., Ltd. A pathological slide scanner was used to obtain the following immunohistochemistry results: Bcl-6(+) (cat. no. ZM-0011; clone LN22), Bcl-2(some weak +) (cat. no. ZA-0536; clone OTIR1H2), CD10(+) (cat. no. ZM-0283; clone UMAB235), CD20(+) (cat. no. ZM-0039; clone L26;), MUM1(-) (cat. no. ZA-0583; clone OTIR1D1O), Ki-67(hotspot area 60% +) (cat. no. ZM-0166; clone UMAB107) and c-MYC(30% weak +) (cat. no. ZA-0555; clone EP121) (Fig. 2). Using *in situ* hybridization, the sample was determined to be negative for Epstein-Barr virus-encoded small RNAs (EBER) (Fig. 2). The EBER *in situ* hybridization kit (cat. no. ISH-7001UM) was developed by Beijing Zhongshan Jinqiao Biotechnology Co., Ltd. The EBER probe is a single-stranded DNA probe that binds specifically to EBER sequences, and can detect EBER1 and EBER2 at the same time. The detection method for gene rearrangement was PCR combined with fragment analysis. Detection was performed using the InVivoScribe Lymphocyte Gene Rearrangement Detection Kit (InVivoScribe Co., Ltd.). Analysis was performed using the ABI3500 Dx Genetic Analyzer (Thermo Fisher Scientific, Inc.). Positive gene rearrangement was detected in B lymphocytes. Immunoglobulin gene rearrangement testing revealed positivity for IGK (VK-JK) (cat. no. 4-088-0370) and IGK (VK-Kde+intron-Kde) (cat. no. 4-088-0370), and negativity for IGH (Fr1-JH, cat. no. 4-088-1750; Fr2-JH, cat. no. 4-088-1750; and Fr3-JH, cat. no. 4-088-1090) and IGL (cat. no. 4-088-0550). Combined with the immunohistochemistry and immunoglobulin molecular rearrangement results, the lesion was consistent with PCFCL. A bone marrow aspiration biopsy showed hypoproliferative subcortical myelopoiesis (<5%) and no lymphoma involvement. Ultrasound-guided puncture biopsy of the bilateral axillary and inguinal lymph nodes showed that the samples were consistent with reactive hyperplasia of lymphoid tissues, and no lymphoma involvement was observed.

Due to the limited extent of the lesion, the patient underwent radiotherapy combined with chemoimmunotherapy (700 mg rituximab on day 0, 1.5 g cyclophosphamide on day 1, 4 mg vincristine on day 1 and 100 mg prednisone on days 1-5). Low-dose radiotherapy was administered with a total dose of 30 Gy in 15 fractions (2 Gy per fraction, once daily) and with a treatment field margin of 1-1.5 cm. Four cycles of R-CVP were completed. At post-treatment follow-up, the lesion size had reduced to 2x1 cm.

Discussion

PCFCL is predominantly found in male patients. The age of onset for PCFCL patients is usually middle-age and older (>50 years), and it is less common for patients to be young males. The patient in this case was a young male. The lesion in this case, a slow-growing purplish-red nodule on the patient's left upper arm, matched the typical clinical presentation of PCFCL.

In the present study, ultrasound of the PCFCL lesion showed a nodular lesion with extremely low echogenicity and a raster-like pattern, no necrosis, no calcification, and posterior unaccompanied acoustic shadows within it. CDFI revealed an abundant blood supply. The possibility of a lymphatic origin should therefore be considered (8,9). A diagnosis also requires a combination of complete histopathological and immunohistochemical analyses after a skin biopsy to determine the nature of the nodules at the lesions. This is combined with a thorough general examination, medical history review, biochemical tests (lactate dehydrogenase), PET-CT and ultrasound-guided puncture biopsy to rule out extracutaneous organ and lymph node involvement.

Histologically, the tumors of PCFCL are composed of large central cells derived from B cells in the germinal center and include three growth patterns: Follicular, diffuse and mixed. Immunohistochemistry shows positive CD20 and BCL-6 expression, and mostly negative results for BCL-2 and MUM1.Rarely, co-expression of CD10 and BCL-2 indicates a high likelihood of recurrence and poor prognosis. Co-expression is also strong in an alternative diagnosis of systemic follicular lymphoma (FL) involving the skin (10). In this case, BCL-2 did not show strong positive expression, which was consistent with the common manifestations of PCFCL.

The histopathological and immunohistochemical phenotypes can be distinguished from FL by the fact that most PCFCLs do not show the t(14;18) translocation at the BCL-2 locus, and their immunohistochemistry will be consistent with tumors derived from germinal center B cells showing BCL-6 positivity, MUM1 negativity and varying degrees of CD10 expression (11,12). Positive immunoglobulin gene rearrangement results confirm the clonal nature of the infiltration and also differentiate it from reactive lymphoid tissue hyperplasia (13). PCFCL also needs to be differentiated from other subtypes of PCBCL. PCMZL occurs in adolescents (<20 years of age) without a sex preference, and histologically shows small centrocyte-like or mononuclear lymphocytes surrounding reactive germinal centers. Immunohistochemistry shows positive results for CD20, CD79a and BCL-2 expression, and negative results for CD10 and BCL-6 (14). PCDLBCL usually shows high expression of BCL-2, MUM1 and MYC (15).

The International Society for Cutaneous Lymphomas (ISCL) has established a Tumor-Node-Metastasis staging system (16) for primary cutaneous lymphomas, which is based on the number and extent of cutaneous lesions, lymph node involvement and the presence or absence of organ involvement, and can effectively assess the patient's prognosis and formulate the correct treatment plan (16). Since PCFCL is an inert lymphoma and low-dose radiotherapy reduces toxicity to achieve better outcomes with remission rates approaching 100%, localized low-dose radiotherapy is recommended for patients with single lesions or single irradiated fields. Patients with multiple localized lesions can be treated with multiple fields and patients with generalized lesions can be treated extensively with systemic rituximab. Although the complete remission rate of surgical resection is also close to

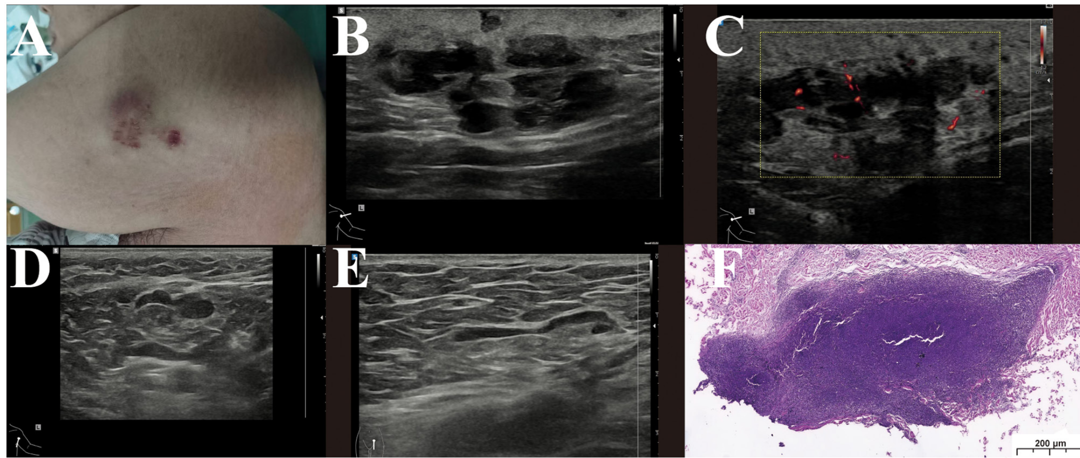

Figure 1. (A) A skin nodule on the left upper arm, measuring ~4x3 cm and purplish in color. (B) Two-dimensional ultrasound imaging and (C) color Doppler flow imaging of the patient's skin lesions. Two-dimensional ultrasound images of the patient's (D) axillary and (E) inguinal lymph nodes. (F) Histopathological examination (dermis) revealing partial proliferation of large, heterogeneous lymphoid cells arranged in sheets, with nuclear atypia (hematoxylin and eosin; x50 magnification).

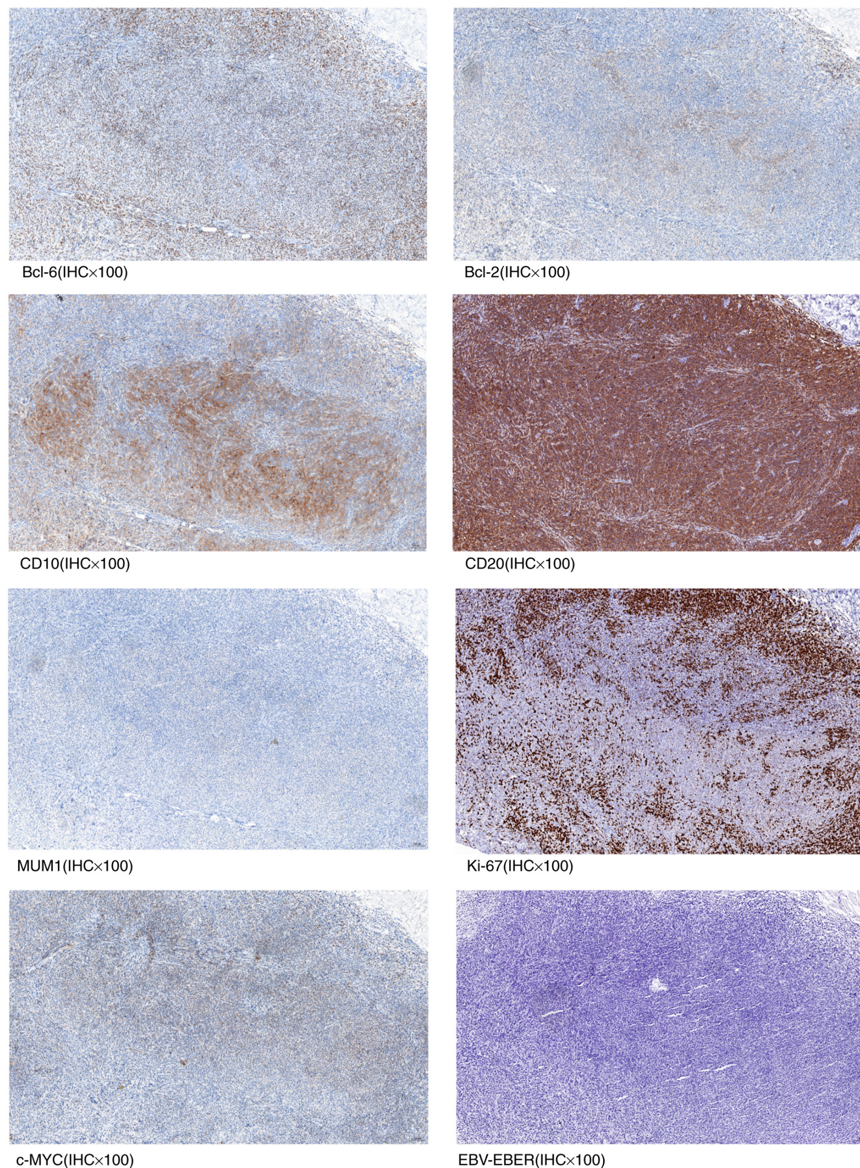

Figure 2. Skin biopsy IHC results: Bcl-6(+), Bcl-2(some weak +), CD10(+), CD20(+), MUM1(-), Ki-67(hotspot area 60% +) and c-MYC(30% weak +). Using *in situ* hybridization, the sample was determined to be negative for EBV-EBER. All images are x100 magnification. IHC, immunohistochemistry; EBV-EBER, Epstein-Barr virus-encoded small RNA.

100% for the treatment of small lesions, its recurrence rate is high compared with low-dose radiotherapy (11,17,18). In a retrospective study, Wang *et al* (19) reported a complete remission rate of 100% and a relapse rate of 20% in patients with PCFCL treated with chemoimmunotherapy (R-CVP). Rituximab-based chemoimmunotherapy is highly effective in treating and preventing relapse. In this case, the patient received low-dose radiation therapy combined with chemoimmunotherapy to prolong clinical remission and reduce recurrence risk. In conclusion, PCFCL is relatively rare among young individuals. The current report presents the case of a 32-year-old male patient with PCFCL, including its diagnosis and treatment, with the intention to inform the diagnosis and treatment of the disease.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XY was responsible for data collection and writing the manuscript. YW and YC were responsible for collecting images and data. XC made substantial contributions to conception and design, revising the manuscript critically for important intellectual content. All authors have read and approved the manuscript. XY and XC confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The studies involving human subjects were reviewed and approved by the Ethics Committee of the Affiliated Yantai Yuhuanding Hospital of Qingdao University (Yantai, China; approval no. 2025-616).

Patient consent for publication

The patient provided written informed consent for publication.

Competing interests

The authors declare that they have no competing interests.

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