Primary cutaneous diffuse large B-cell lymphoma-other type; a report of a rare case

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Introduction

Primary cutaneous lymphomas are a group of lymphoproliferative disorders, which arise primarily from skin homing lymphocytes. The majority of primary cutaneous lymphomas are T-cell lymphomas (65%). B-cell lymphomas are usually less common and only account for about 25%[1]. According to WHO-EORTC classification, primary cutaneous B-cell lymphomas (CBCLs) divides into four distinct types and they are primary cutaneous marginal zone B-cell lymphoma (PCMZL), primary cutaneous follicular centre lymphoma (PCFCL), primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT), and PCDLBCL-other type[2]. These subtypes can be differentiated by histopathology and immunohistochemical evaluation. We report a case of PCDLBCL-other type, which presented as rapidly enlarging cutaneous nodules on the face. This type is very rare and needs the correct diagnosis and early treatment due to poor prognosis.

Case report

A 64-year-old previously healthy male presented with multiple, rapidly enlarging, asymptomatic erythematous skin nodules on the face for four months duration. He did not complain any other systemic symptoms. On examination, there were two firm, non-tender skin nodules of 3x2 cm in size, on left side of the face (Figure 1). There was no regional lymphadenopathy and rest of the systemic examination was unremarkable.

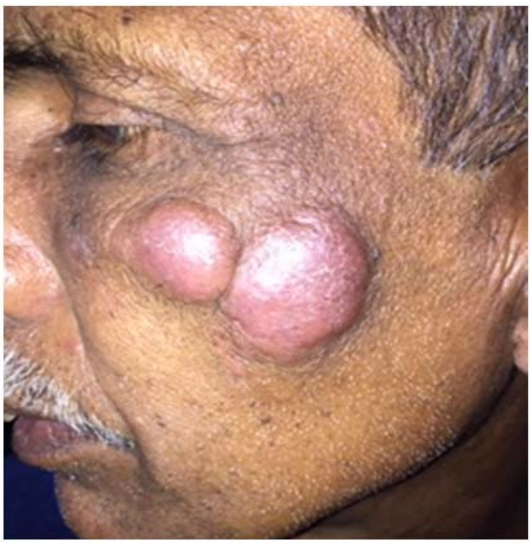
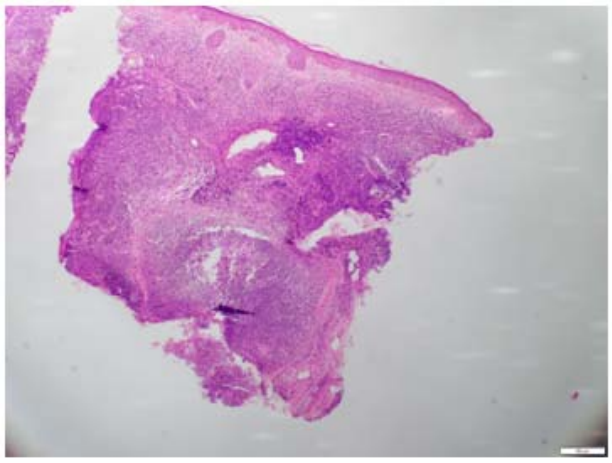


Figure 1.

Incision biopsy from a skin nodule revealed a diffuse dense infiltration of large lymphoid cells in the dermis. Scattered centroblast like cells and plasma cells are also noted but there was no epidermotrophism or granulomas (Figure 2,3).



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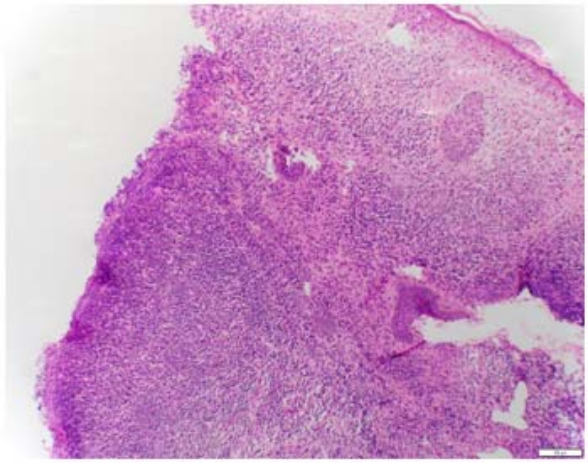

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Figure 2 and 3.

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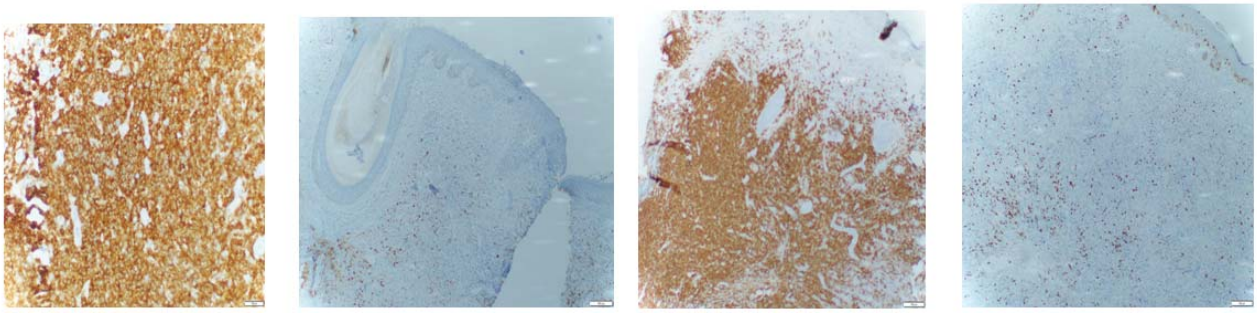

Figure 4, 5 and 6.

Tissues for fungal studies, TB PCR were negative. Immunehistochemistry studies revealed (Figure 4,5,6), tumour cells, which were positive for CD79a and CD20 and negative for CD3, CD10, BCL2, and MUM-1. Ki 67 index was 45% suggesting a significant mitosis.

Therefore, based on infiltration by CD20 and CD 79a positive large lymphoid cells, which were negative for bcl2, MUM-1, and CD10 expression, a final diagnosis of PCDLBCL-other type was made. Blood picture, LDH level, CXR, USS abdomen, CT chest, abdomen and pelvis were done for staging and all were negative. Patient was referred to oncology unit and started on CHOP-R (cyclophosphamide, doxorubicin, vincristine, and prednisolone + rituximab) regime. A satisfactory response with a significant resolution of skin nodules was noted at 4th month of the treatment (Figure 7).

Figure 7.

Discussion

Cutaneous B-cell lymphomas can be either primary, which originally arises from the skin, or, secondary that has a systemic disease with subsequent development of skin lesions[3]. This distinction is vital because primary cutaneous lymphomas are less aggressive with an overall better prognosis than the secondary category. Primary cutaneous B lymphomas are rare with an annual incidence of 0.5/100,000 and represent only for 22.5% of all cutaneous lymphomas[4].

According to the WHO-EORTC classification primary cutaneous B-cell lymphomas (PCBCL) can be classified as follows.

- Marginal zone B-cell lymphoma (MZBCL)
- Follicle center B-cell lymphoma (PCFCL)
- Diffuse large cell B-cell lymphoma-leg type (PCDLBCL-LT)
- Diffuse large cell B-cell lymphoma-other type (PCDLBCL-other)
- Intravascular large cell B-cell lymphoma

Usually, first two types have a better prognosis and an indolent clinical behaviour, compared with the diffuse large cell types (leg and other), which have a poor prognosis and therefore, need more aggressive systemic therapy. There are evidences to say that Borrelia infection is a possible aetiological association of cutaneous B-cell lymphomas and it is recommended to investigate with PCR analysis and treat with a course of antibiotics such as doxycycline at the early stage of disease to those who are from endemic areas. Diagnosis needs careful histological analysis and immunohitochemical studies. All types show positivity for B-cell markers such as CD20, CD79a and negativity for T-cell markers like CD3. Determination of the specific type is done by analysis of other specific markers like CD10, bcl-2, bcl-10, MUM-1.

PCFCL is the most common variety and involves scalp, forehead and trunk in middle-aged patients[2,6,7]. The prognosis is satisfactory with >95% of 5 year survival[9]. Histopathology shows dermal infiltrate of centrocytes and centroblasts in a follicular, or diffuse pattern. Immunohistochemically **PCFCL does not express bcl-2, MUM-1, but express CD10** in contrast to PCDLBCL-LT. The distinction is important because PCFCL needs less aggressive treatment such as surgical excision, intralesional interferon or local radiotherapy due to better prognosis compared to PCDLCL-LT[10].

PCDLBCL-LT classically presents as rapidly growing red-purple-colored nodules on legs in elderly females. However, in 10%-20% of patients, other areas of the body can be affected[6]. Histopathologically, there is diffuse, monotonous proliferation of large cells in the dermis. Immunohistochemical studies characteristically show **positivity for bcl-2, and MUM-1** B-cell markers. PCDLBCL-LT also commonly expresses bcl-6 but **lacks CD10 expression**[7, 8].

PCDLBCL-other is a very rare type which does not meet the diagnostic criteria for either PCDLBCL-LT or PCFCL[2]. This variety usually presents as solid nodules involving the leg (50%), head, trunk, or arms. Our patient presented with skin nodules on the face. This type morphologically and clinically identical to PCDLBCL-LT but d**oes not express bcl-2**[2,6]. But they can show **positivity for bcl-6, MUM-1** (67%), and FOX-P1 (72%) but almost all lack bcl-2 expression[8]. The 5-year survival rate is around 50% and due to the poor prognosis. The therapeutic modalities are similar in both PCDLBCL-LT and PCDLBCL-other type[9]. These types usually need more aggressive therapy using chemotherapy with CHOP regime, which includes cyclophosphamide, doxorubicin, vincristine, and prednisolone or/and rituximab, which is an anti CD20 monoclonal antibody. Depending on the size and the number of lesions, excision or local radiotherapy may be necessary to be combined in certain cases.

Our case, there was diffuse dermal and subcutaneous infiltrate by large non-cleaved B-cells which are diffusely positive for CD20 and CD79a. The differentials considered were PCDLBCL-LT, PCDLBCL-other, and PCLFCL type. Due to absence of CD10 expression, a diagnosis of PCFCL type was excluded. The large cells were also negative for bcl-2 and MUM-1 markers, which are positive in the majority of PCDLBCL-LT. Ki 67 index was 45% and it was suggestive of significant mitotic activity. Hence, due to characteristic histology, IHC and absence of extra cutaneous involvement at the time of presentation, we finally arrived to a diagnosis of PCDLBCL-other type.

Patient was referred to oncology unit for chemotherapy (CHOP regimen) and currently he is responding well. We presented this case due to the rarity of PCDLBCL-other type and to highlight the importance of correct diagnosis and early chemotherapy to obtain a satisfactory outcome.

Conclusion

PCDLBCL-other is a very rare type of primary cutaneous B cell lymphomas and usually presents as solid nodules involving the leg, head, trunk, or arms. Histology shows diffuse, monotonous proliferation of non-cleaved large B cells in the dermis, which does not express bcl-2, CD 10 and show positivity for B cell markers like CD20 or CD79a. This type has a poor prognosis and therefore, aggressive treatment with chemotherapy is necessary following the accurate diagnosis.

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