

CASE STUDY

AN ULCERO-PROLIFERATIVE LESION OVER LEFT CHEEK- A DIAGNOSTIC DILEMMA

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ABSTRACT: Primary cutaneous lymphomas (PCL) are defined as non-Hodgkin lymphomas presenting in the skin with no evidence of extra-cutaneous disease at the time of diagnosis and at 6-months follow up. Among these, primary cutaneous T cell lymphomas are more common than primary cutaneous B cell lymphoma (PCBCL). Primary cutaneous diffuse large B cell lymphoma commonly occurs on the legs (leg type), rarely at other sites of the body. The clinical manifestations are so complex that its diagnosis depends on histopathological and immune-histochemical examinations. We here present a case of 77-years old male who presented with an ulcero-proliferative lesion over left cheek.

KEYWORD: Primary cutaneous diffuse large B cell lymphoma, cheek, ulcero-proliferative lesion.

INTRODUCTION:

Primary cutaneous lymphomas (PCL) are non-Hodgkin lymphomas (NHL) which have cutaneous manifestation at the time of diagnosis. Primary cutaneous lymphoma must be followed up for atleast six months to exclude a NHL with secondary cutaneous involvement.^[1] It is the second most frequent extra-nodal lymphoma after gastrointestinal tract lymphomas with an incidence of around 10 cases per million in a year of which around 20-30% are primary cutaneous B-cell lymphomas (PCBCL).^[2]

Here, we present a case of primary cutaneous diffuse large B-cell lymphomas, leg type (PCDLBCL, LT) over left cheek in a 77-years-old male.

A 77-years-old male presented to Dermatology department with an ulcero-proliferative growth of 1.5x1.5 cm over upper part of left cheek for last 7 months which was progressively increasing in size. The growth was tender and fixed to the underlying soft tissue. There was no lymphadenopathy or organomegaly. Clinically a diagnosis of carcinoma was suspected in view of which an excision biopsy was done. Grossly, a skin covered soft tissue piece measuring 1.5x1.5x0.7 cm was received. Cut surface was grey white to yellow and solid. On microscopy, a skin covered lesion was identified with thinned out overlying stratified squamous epidermis. The underlying dermis was expanded by

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cellular tumor. The tumor was composed of large pleomorphic cells with round to oval nucleus having irregular nuclear membrane, vesicular nucleus and scanty to moderate amount of cytoplasm. Few cells were showing nuclear cleaving. Few multinucleated cells were also noted. There were frequent typical and atypical mitosis. All the resected margins were free of tumor. On immunohistochemistry the tumor cells were positive for LCA, CD20, bcl2 and bcl6 (Figure 1,2 and 3). Ki 67 index was more than 75% (Figure 4). The tumor cells were also positive for vimentin which indicates poor prognosis (Figure 5). These were negative for CD3, CD5, CD10, HMB45, MUM 1 and ALK. Bone marrow biopsy and aspiration were negative for tumor cells. Based on the clinical history, histopathological and immunohistochemistry a final diagnosis of PCDLBCL was made. A PET-SCAN was done to search for any primary. There was no evidence of any metabolically active lesion in whole body PET-SCAN. Thus, reaching to a final diagnosis of PCDLBCL, LT. Patient received R-CHOP chemotherapy followed by radiotherapy. He underwent plastic surgery after excision biopsy. On 9-months follow-up the patient is now symptom free and is doing well.

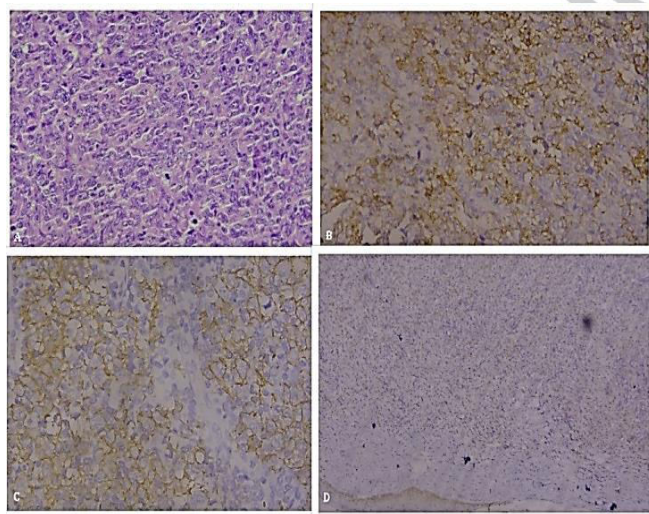


Figure 1. (A) section shows large pleomorphic cells with round to oval nucleus having irregular nuclear membrane, vesicular nucleus and scanty to moderate amount of cytoplasm. Few cells were showing nuclear cleaving. Mitotic figures are also seen.

[H & E stain, (A) 40X]. (C, D & E,) Immunohistochemistry showing cytoplasmic positivity of LCA, CD 20 and BCL 6 respectively. (40X).

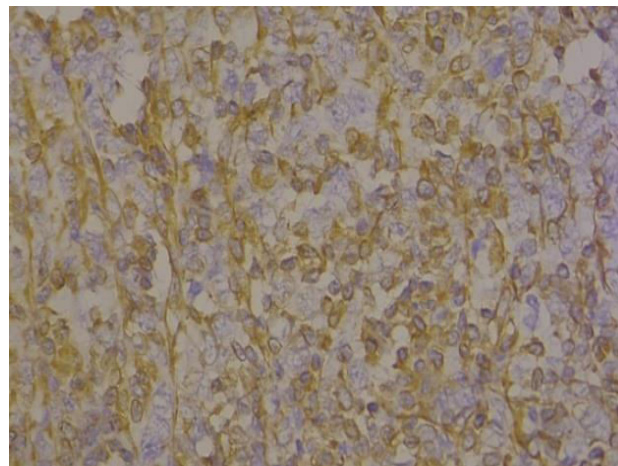


Figure 2. Immunohistochemistry shows cytoplasmic positivity of vimentin in tumor cells respectively. (IHC, 40X)

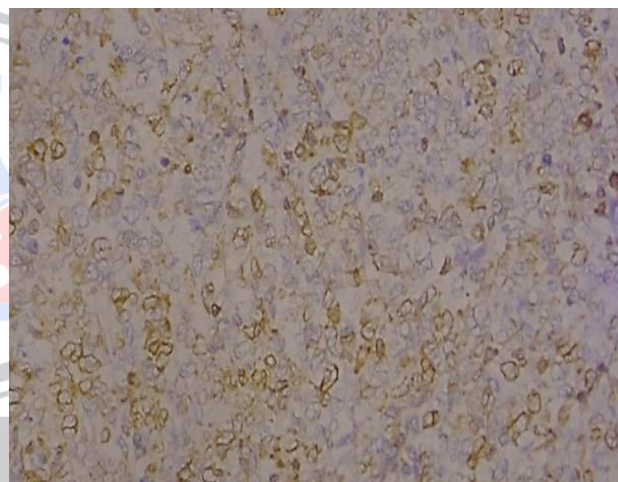


Figure 3. Immunohistochemistry shows nuclear positivity of Bcl6 in tumor cells. (IHC, 400X)

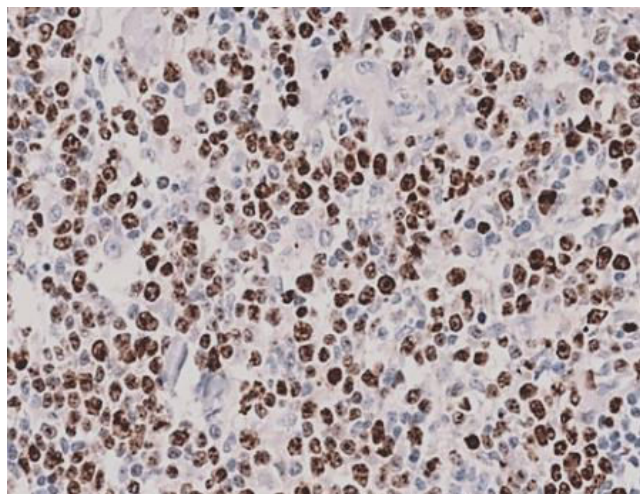


Figure 4. Immunohistochemistry shows nuclear positivity of ki67 in tumor cells (more than 75%). (IHC, 400X)

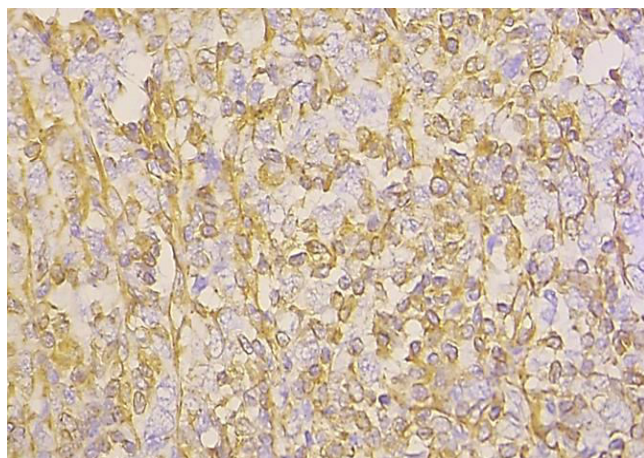


Figure 5. Immunohistochemistry shows cytoplasmic positivity of vimentin in tumor cells respectively. (IHC, 400X)

DISCUSSION:

Primary cutaneous B cell lymphomas are rare in comparison to T cell lymphomas. According to 2018 WHO classification of skin tumors PCBCLs are classified into primary cutaneous marginal zone B - cell lymphoma (PCMZL), primary cutaneous follicle center lymphoma (PCFCL) and primary cutaneous DLBCL (PCDLBCL), leg type (LT). Previously used entity PCDLBCL, others have now

been removed from WHO 2018 classification to avoid confusions.^[3]

In 1987, PCDLBCL, LT was first identified as a subgroup of PCFCL based on its unique histological feature and more aggressive behavior.^[4] In 1996 Vermeer et al. used the term Primary cutaneous B-cell lymphoma of the leg.^[5]

Primary Cutaneous Diffuse Large B-cell Lymphoma, Leg Type (PCDLBCL, LT) is an aggressive type of PCBCL which is characterized by skin lesions predominantly but not exclusively and comprises of mainly diffuse sheets of Centro blasts and immunoblasts.

The clinical manifestations are not sufficient to make diagnosis of PCBCL. The location and type of lesions also provide some indications. Primary cutaneous follicle center lymphomas present are more frequently seen in head and neck regions, while PCMZL predominantly affects trunk and limbs. Presence of nodules and/or single or multiple tumors over the legs should raise a suspicion of PCDLBCL- LT, especially when the patient is an elderly female (M: F,1:3-4).^[6] The present case was an elderly male.

The etiology of PCDLBCL is not well described in the literature. It has been reported to be associated with Epstein-Barr virus, human herpes virus 6, human herpes virus 8, Borrelia burgdorferi infection, or systematic application of methotrexate. This indicates that infection and immunodeficiency both play an important role in its pathogenesis.^[7]

PCDLBCL, LT predominantly occurs in distal leg and the lesions can be solitary or multiple, involving one or both the legs. It is characterized by rapid growth of red to purple nodules or sometimes an ulcer. It is a relatively malignant tumor and extra cutaneous spread is quite common (such as the central nervous system, bone, liver, kidney, spleen, testis, pancreas, breast, pelvis, and brachial plexus nerve).^[8] The other relatively slow developing rare form of PCDLBCL, LT type may occur in head, trunk and limbs. It is a low-grade malignancy compared to the usual leg type.^[7,9] Patients have either no symptoms or have mild pruritis

irrespective of the site of the lesion. The present patient also had a history of slow growing ulceroproliferative lesion and was present over left cheek which is not the usual site as well as presentation of this lymphoma.

Histopathology is the gold standard for the diagnosis. PCDLBCL have same histopathological findings as of systemic DLBCL. The tumor cells diffusely infiltrate the dermis which consists of mainly centroblasts and immunoblasts. The overlying epidermis is usually spared. The tumor cells are positive for CD19, CD20, CD22, CD79a, Pax5 and are negative for CD5 as well as CD10. Most PCDLBCL are Bcl2 and Bcl6 are also positive. Bcl2 is positive in 100% of cases when the site of lesion is leg and is positive in 50% of cases when the lesion is present at some other site.^[10] CD10 positivity has been reported in 28 to 40 % cases and is associated with longer survival rate. About 25 % of these lymphomas show CD43 positivity and is considered as an independent poor prognostic factor. Vimentin positivity is also considered as a poor prognostic factor.^[11] The present case was positive for CD20, vimentin, Bcl2 and Bcl6.

The recommended treatment includes systemic treatment with R-CHOP combined with radiotherapy at a radiation dose of (36–40 Gy) for localized disease if the patient can tolerate multi-agent chemotherapy. A dose of 40Gy is recommended in absence of systemic treatment.^[12]

CONCLUSION:

PCDLBCL are rare tumors of skin. Due to lack of morbidity and specific clinical manifestation it is difficult to diagnose and distinguish this entity from other skin diseases and secondary lymphomas. However detailed clinical history, histopathology and immunohistochemistry can lead to an accurate diagnosis and timely treatment.

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