Case Report

DOI: 10.7860/JCDR/2023/58606.17911

Pathology Section

Primary Cutaneous Diffuse Large B Cell Lymphoma, Leg Type: A Rare Neoplasm Masquerading as Squamous Cell Carcinoma

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ABSTRACT

Primary Cutaneous Diffuse Large B Cell Lymphoma, Leg Type (PCDLBCL, LT) comprises 4% of all cutaneous lymphomas, and it presents as an aggressive form of lymphoma. Rarely do pathologist/cytologists find specimens of PCDLBCL, LT on Fine Needle Aspiration Cytology (FNAC). The mimickers on FNAC are metastatic small cell carcinoma, Merkel Cell Carcinoma (MCC), Malignant Melanoma (MM), Cutaneous Alveolar Rhabdomyosarcoma and Primary Cutaneous Ewing's Sarcoma (PCES). A 75-year-old female patient presented in the Department of Surgery with multiple nodules on the leg for three months. On cytology small round cell tumour with possibility of non hodgkin lymphoma was given and biopsy was advised. The confirmation of PCDLBCL, LT on cytology is not recommended however, it is emphasised that it can be picked up on FNAC and distinguished from its mimickers. Because of the aggressive nature and poor prognosis with the frequent relapses and tendency for extracutaneous spread, it is considered to be a distinct type of cutaneous lymphoma which needs to be diagnosed and treated as early as possible.

Keywords: Dusky nodule, Extracutaneous spread, Fine needle aspiration cytology

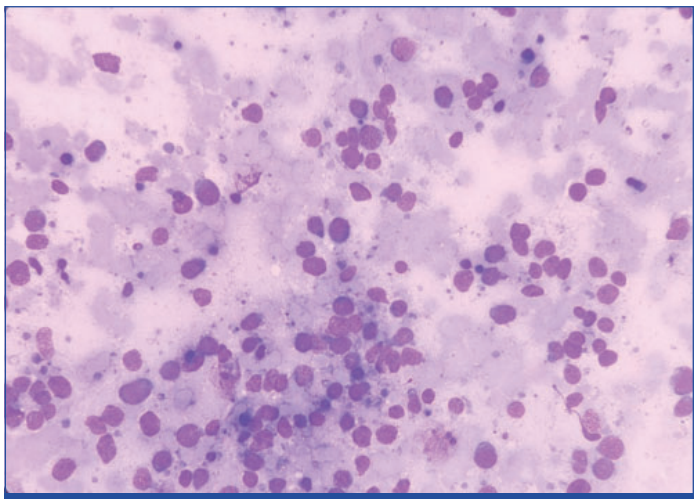
CASE REPORT

A 75-year-old female patient presented in the Department of Surgery with multiple nodules on the left leg for three months which were increasing in size and subsequently getting ulcerated. She had no significant past medical history or family history and was not taking any medications.

On clinical examination multiple coalescing erythematous and dusky nodules with ulceration at places, ranging from 2-3 cm in size were noticed over the anterior left lower leg [Table/Fig-1]. A clinical suspicion of squamous cell carcinoma like lesion was raised and FNAC from nodules was advised. FNAC was done with 24-gauge needle and 10 mL syringe and smears prepared were stained with Giemsa.

[Table/Fig-1]: Clinical photograph showing multiple coalescing erythematous and dusky nodules with ulceration over extensor aspect of left leg.

On microscopy [Table/Fig-2], smears were moderately cellular showing singly scattered round cells. These cells were monomorphic, medium to large size with scant cytoplasm, had finely dispersed nuclear chromatin, inconspicuous nucleoli. Background showed few lymphoglandular bodies. Cytomorphological diagnosis of small round cell tumour with the possibility of non hodgkin lymphoma was offered and biopsy was advised for histological diagnosis and correlation. Suspicion of a lymphoproliferative disorder on cytology prompted us to rule out visceral or lymph node involvement. CT scans of chest, abdomen, and pelvis were normal. Bone marrow aspiration and biopsy were normal. CBC, PS, LFT, KFT were within normal limits.

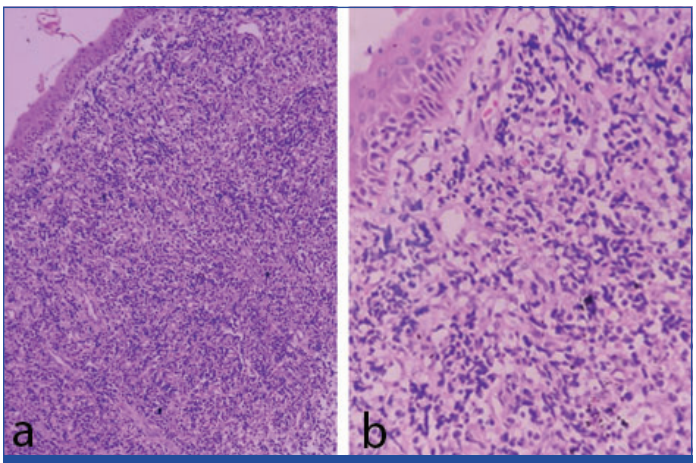


[Table/Fig-2]: Giemsa stained smears showing singly scattered round cells. These cells were monomorphic, medium to large size with scant cytoplasm, had finely dispersed nuclear chromatin, inconspicuous nucleoli. Background showed few lymphoglandular bodies. (Giemsa; X400).

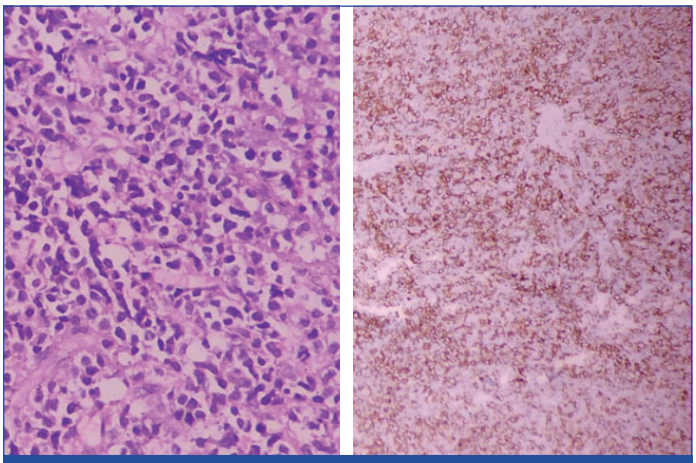
Biopsy specimen was done from the nodules on the leg. Haematoxylin and Eosin (H&E) stained sections of biopsy specimen done from the nodules on the leg showed unremarkable epidermis. There were diffuse sheets of monotonous non epidermotropic

infiltrate of atypical cells was seen in papillary and reticular dermis reaching the interface between dermis and subcutaneous tissue. Skin adnexal structures were not seen. The atypical cells were large round, non cleaved, had large nuclei with open chromatin and prominent nucleoli [Table/Fig-3,4]. Frequent mitotic figures were seen (2-3/HPF). Provisional diagnosis of non hodgkin's lymphoma was made.

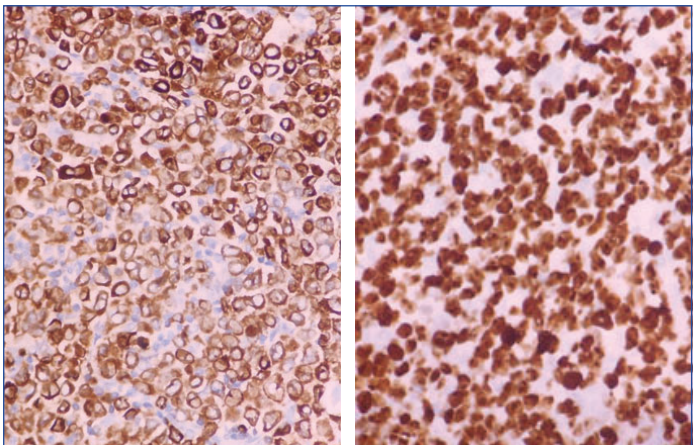
The atypical cells were positive for LCA, CD 20, BCL-2 and MUM1 [Table/Fig-5-7] confirming the B-cell lymphoid cell phenotype and negative for CK, CD10, CD 30, CD 3 and CD 5. A final diagnosis of PCDLBCL, LT was rendered. Patient was referred to a higher centre for treatment.



[Table/Fig-3]: (a) Haematoxylin and Eosin stain (X40) showing dermis and subcutaneous areas, (b) Haematoxylin and Eosin stain (X100)-Photomicrograph showing diffuse sheets of monotonous non epidermotropic infiltrate of atypical cells was seen in papillary and reticular dermis. Skin adnexal structures were not seen.



[Table/Fig-4]: Photomicrograph showing the large round atypical cells, non cleaved, with large nuclei, open chromatin and prominent nucleoli. (H&E, X 400).
[Table/Fig-5]: Photomicrograph showing CD20 positivity (cytoplasmic membrane) by tumour cells (×100). (Images from left to right)



[Table/Fig-6]: Photomicrograph showing Bcl-2 positivity (nuclear membrane and cytoplasmic positivity) by tumour cells (×400).
[Table/Fig-7]: Photomicrograph showing MUM1 positivity (nuclear positivity) by tumour cells (×400). (Images from left to right)

DISCUSSION

Primary Cutaneous Lymphomas (PCL) is extra nodal lymphomas of the skin. Most PCL cases are of T-cell origin, accounting for approximately 65%-75% of all cutaneous lymphomas [1,2]. The rest around 25%-35% of all PCL cases are Primary Cutaneous B-Cell Lymphomas (PCBCLs). According to the WHO classification 2017 and the updated WHO-EORTC 2018, PCBCLs consist of three distinct common subtypes: Primary Cutaneous Marginal Zone Lymphoma (PCMZL), Primary Cutaneous Follicle Centre Lymphoma (PCFCL), and PCDLBCL, LT. As a new provisional entity, EBV-associated mucocutaneous ulcers (EBV-MCUs) has also been added. PCDLBCL, LT is a unique rare aggressive diagnostic entity comprising only 4% of all cutaneous lymphomas [3]. Typically, it occurs in elderly women. In most cases, it affects the lower legs (characteristic rapidly enlarging red to purple nodules), but 10-15% occurs in other places. There is a greater tendency for this type to relapse and to disseminate to extracutaneous sites (regional lymph nodes and bone marrow are typical sites). The histopathology of PCDLBCL-LT has been described in many case reports [4,5].

Cytology of PCDLBCL shows immunoblasts that have the appearance of large cells with abundant basophilic cytoplasm and a large nucleus having a prominent central nucleolus; centroblasts which are lymphoid cells with oval to round nuclei and fine chromatin, ranging in size from medium to large. There are usually two to four nucleoli linked to the nuclear membrane. The cytoplasm is usually sparse and mildly basophilic; vacuolisation can also occur in some cells. Lymphoglandular bodies are found in the background indicating lymphoid origin [6].

Histologically, this type of lymphoma shows a dense diffuse infiltrate of a monotonous population of confluent sheets of B-cells (described as centroblasts and immunoblasts) with medium-sized to large round nuclei, prominent one to more nucleoli and coarse chromatin within the dermis and subcutis [5,7].

To distinguish from other PCBCL, IHC is essential. B-cell markers (CD19, CD20, CD22, CD79a) are generally expressed by neoplastic B-cells. In addition, the proteins Bcl-2, MUM-1/IRF4, IgM, and FOXP1 are all significantly positive. Furthermore, CD10 and CD138 are typically negative, however, IgH gene clonal rearrangement can be found in the majority of patients [5,7,8].

Huang S-F et al., reported a similar case of an 88-year-old woman who presented with two rapidly growing painful nodules on her right lower leg which mimicked skin cellulitis initially. On histopathological examination there was diffuse infiltration of large, atypical lymphocytes with centroblast and immunoblast features in the whole dermis without epidermal involvement. Immunohistochemical staining revealed the following results: CK AE1/AE3(-), CD3(-), CD20(+), CD30(-), BCL-2(+), CD10(-to dim,±), MUM1(+) which all were same as in our case. The results were compatible with a Diffuse Large B-Cell Lymphoma (DLBCL), either primary or secondary [9].

Mondal SK et al., also reported a case of 26-year-old male who presented with light red plaque on medial aspect of left leg of five months duration. Microscopical examinations revealed diffuse non epidermotropic infiltrares predominantly made up of large non cleaved cells with variable proportions of centroblasts and immunoblast-like cells which were similar as in our case. The cells had large nuclei with conspicuous nucleoli. The tumour cells were located in the papillary and reticular dermis and reaching the interface between dermis and subcutis. Immunohistochemistry (IHC) revealed expression of CD20, CD19, Bcl-2, Bcl-6 and MUM-1 by tumour cells, while they were negative for CD10, CD30, EMA, CD3, and CD5 as were in our case [10].

It is also necessary to know the cytological features of its other mimickers such as metastatic small cell carcinoma, MCC, MM, cutaneous alveolar rhabdomyosarcoma and PCES.

Metastatic small cell carcinoma has small round cells with scant cytoplasm. Nuclear moulding seen. There is no lymphoglandular bodies which are seen in our case. On IHC the cells are positive for neuroendocrine markers like synaptophysin, chromogranin A and CD 56. Also they will be negative for LCA [11,12].

MCC show highly cellular smears with small to medium sized atypical cells, arranged in cohesive disorganised groups with nuclear molding. On IHC, these cells are positive for CK-20 and neuroendocrine markers like synaptophysin, chromogranin A and CD 56 [13]. MM may also show singly scattered small round cells. Many of the cells with show black pigments. Lymphoglandular bodies are not seen [14].

Alveolar rhabdomyosarcoma shows large pleomorphic tadpole shaped tumour cells with eosinophilic cytoplasm and these cells are positive for the vimentin and desmin. Absence of nuclear molding, prominent nucleoli and pseudorosette excludes PNET [15]. PCBCL-LT is a relatively aggressive form of CBCL that requires more aggressive treatment. Most commonly used regimen is using cyclophosphamide, doxorubicin, vincristine, and prednisone plus rituximab. Local chemotherapy or radiation with rituximab is also used [10]. The prognosis for PCBCL-LT is not as favourable as other types of primary CBCL, with an estimated 5-year survival rate of approximately 50%.

CONCLUSION(S)

This report presented a rare case of PCDLBCL-LT. The presence of erythematous nodules on the lower limbs should raise the suspicion of PCDLBCL-LT. However, lesions can involve areas of the body other than the lower limbs. However this patient was referred to a higher centre and follow-up was not done but cases like these with aggressive nature as well as a tendency for extracutaneous spread, if delayed, can significantly affect prognosis. Thus, there is a need for increased clinical awareness to enhance the likelihood of prompt identification and early, aggressive management.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jun 24, 2022
- Manual Googling: Oct 06, 2022
- iThenticate Software: Feb 13, 2023 (10%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jun 22, 2022**
Date of Peer Review: **Sep 05, 2022**
Date of Acceptance: **Feb 16, 2023**
Date of Publishing: **Apr 01, 2023**