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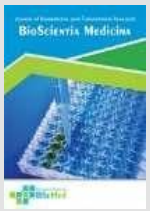

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Histopathological Features of Primary Cutaneous Diffuse Large B-Cell Lymphoma Leg Type: A Case Report

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A B S T R A C T

Background: Primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT), is a rare and aggressive lymphoma with poor prognostic. It is difficult to diagnose PCDLBCL-LT at an early stage due to its nonspecific manifestations that overlap with other lymphomas. A histopathological examination can be performed to establish the diagnosis. **Case Presentation:** A 74-year-old female presented with itchy red, swollen patches accompanied by a burning sensation on both her legs. Clinical examination revealed a hard ping pong ball-sized lump palpable on her left inner thigh. Haematoxylin eosin staining demonstrated the proliferation of diffused neoplastic cells, homogenous cells with atypical nuclei, and mitoses. Immunohistochemical examination revealed positive for CD 45 as well as CD 20 and negative for CD3. These findings were consistent with a diagnosis of PCDLBCL-LT. **Conclusion:** The presented case demonstrates that skin lesions in patients with diagnosed PCDLBCL-LT may have a variable clinical presentation. Histologically is characterized by a diffuse dermal infiltrate mostly consisting of activated B-cell (centroblast) and activated lymphocyte (immunoblast), with high mitotic activity and a minimal T-reactive component. Immunohistochemical analysis is necessary for establishing the diagnosis of PCDLBCL-LT which shows positive markers for CD 45, CD 20, CD79a, Bcl-2, MUM-1, FOX-P1, CD10, IgM, CD 138, Ki-67, CD 30 and MYC.

1. Introduction

Primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT) is one of the major types of primary skin B-cell lymphoma with distinctive clinicopathological and immunohistochemical features.[1-3] PCDLBCL-LT cases are estimated at 10-20% of all primary cutaneous B-cell lymphoma (PCBCL) and show an increasing trend in frequency.[4]

The obvious causative factor associated with the disease has not yet been found, but there are some conjectures that it may be a lymphoproliferative response to antigen stimulation in the skin.[3] In addition, the positivity of Human Herpes Virus (HHV)-6 and HHV-8 in neoplastic B cells have been reported recently to be the etiology.[5]

Primary cutaneous diffuse large B-cell lymphoma, leg type mainly affects elderly people in their seventies, especially women, with the ratio of men to women ranging from 1:2 to 1:4.[1,6,7] Usually, patients complain of rapidly growing nodules or tumors, solitary or clustered, red or bluish red in color located on one or both legs, which can ulcerate.[8] However, in 10-20% of patients, the lesions may appear in other parts of the body as an initial manifestation.[2,6] The clinical

manifestations of this lymphoma are commonly limited to the skin.[1] However, the most frequent sites are lymph nodes, bone marrow, and the central nervous system.[6,7] Primary cutaneous diffuse large B-cell lymphoma, leg type is an intermediate level of B cell lymphoma with a 5-year survival rate of approximately 41% to 73%.[8]

This study aimed to present a case of PCDLBCL-LT in a 74-year-old woman and focused on the clinical and histopathological features of PDCLBCL-LT.

2. Case Presentation

A 74-year-old Javanese woman presented to our dermatology & venereology outpatient clinic with reddish, swollen, itchy, and hot spots on both limbs, which became more widespread a month ago. A week prior to admission, a hard lump as big as a ping pong ball appeared on her left inner thigh, reddish and tender, followed by itching and pain. The patient also complained of severe pain and difficulty walking when she was hospitalized. The patient has neither history of similar complaints nor a history related to malignancy, hypertension, diabetes mellitus, and history of food and drug allergies. None of her family experiences similar complaints or has malignancy, hypertension, diabetes mellitus, and allergies to food and medicine.

On physical examination, erythematous patches and swell of both lower limbs were obtained. A lump was also found with a ping pong ball sized on the inner left thigh with a slightly hard, reddish, and secreted clear, odorless liquid accompanied by itching and pain (Figure 1). A histopathological examination was performed in order to make a definitive diagnosis. Hematoxylin-Eosin staining (HES) revealed neoplastic proliferation and diffused monotonous cells of the atypical nucleous with mitosis in the dermal layer and nodular features in some parts of the dermis (Figure 2).

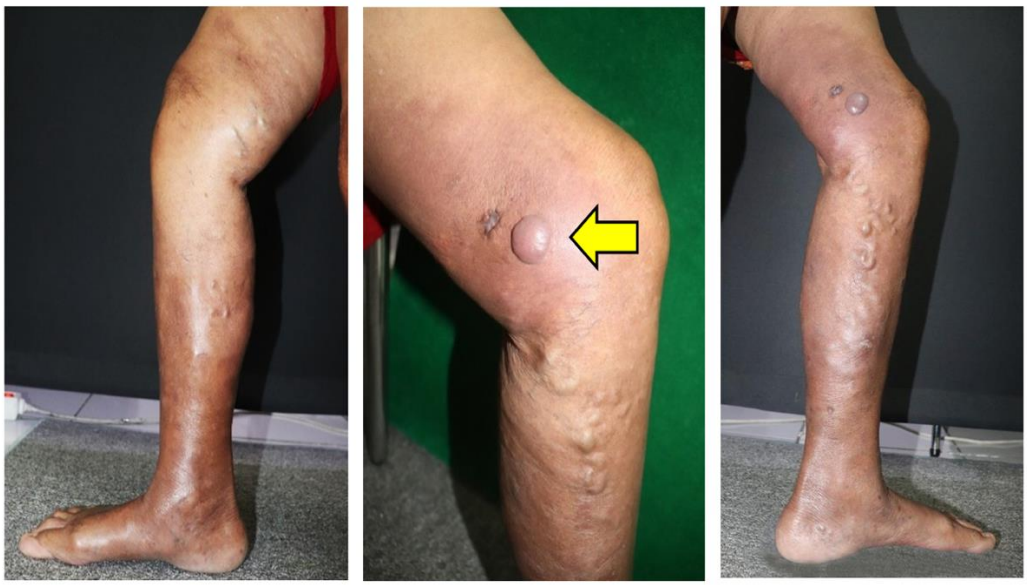

Figure 1. Erythematous patches with unclear boundaries on both limbs. A ping-pong ball-sized lump with hard consistency and a reddish color on the medial left limb region (yellow arrow).

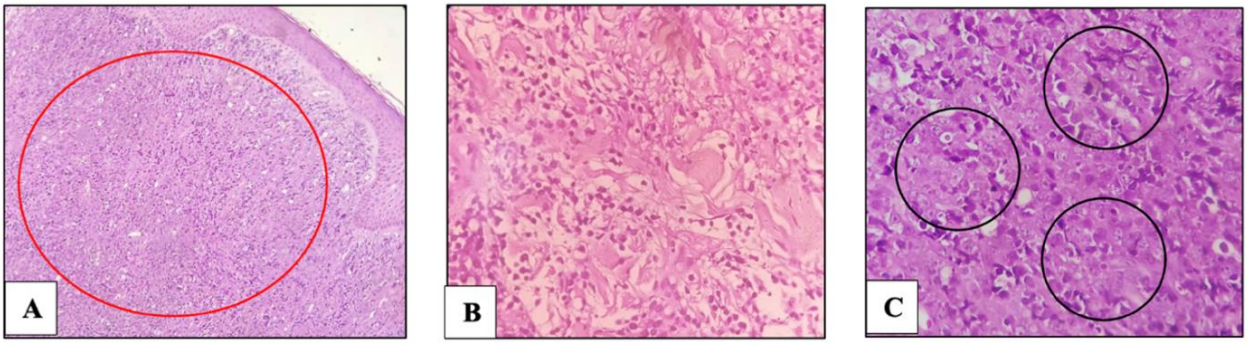

Figure 2. (A) Tumor cells appear in the layers of the dermis (red circle, H&E staining, 40x magnification); (B) Tumor cells composed of diffuse, cellular infiltration of the surrounding connective tissue (H&E staining, 10x magnification); (C) Homogenous tumor cells of medium to large size, slightly cytoplasm, oval rounded core, irregular edges, and hyperchromatic nuclei (dark circles, H&E staining, 100x magnification).

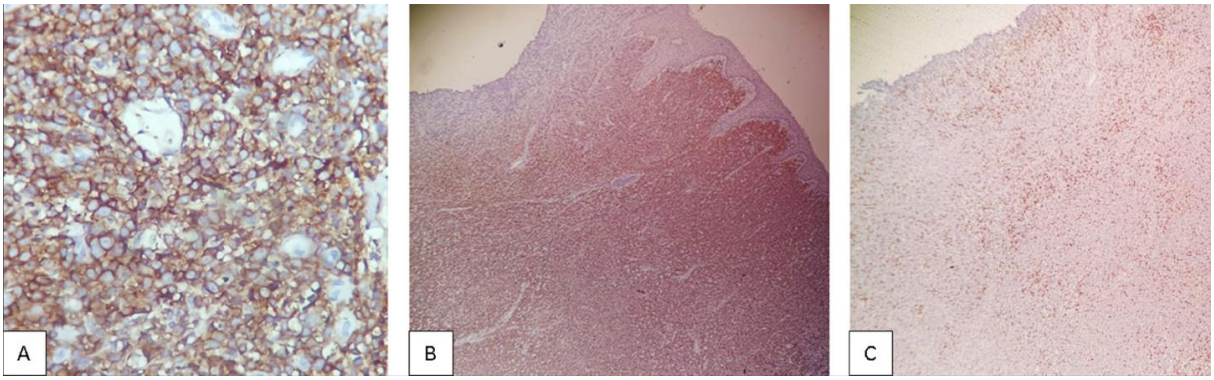

Figure 3. (A): CD 45 immunohistochemistry examination at a positive 40x magnification; (B). Immunohistochemical staining of CD 20 at a positive 4x magnification; (C) Immunohistochemistry examination of CD 3 at a negative 4x magnification.

Immunohistochemistry examinations of CD45, CD20, and CD 3 were conducted and revealed positive results for CD 45 as well as CD 20 and negative for CD 3 (Figure 3). All these findings supported the diagnosis of PCDLBCL-LT. Accordingly, based on history taking, physical examination, and histopathological examination, the patient was diagnosed with PCDLBCL-LT. She was referred to internal medicine for further management.

3. Discussion

Primary cutaneous B-cell lymphoma (PCBCL) belongs to a different group of lymphoproliferative disorders of B-cells determined by their presentation in the skin, without evidence of the spread of extracts at the time of diagnosis.[3] Primary cutaneous B-cell lymphoma includes 25% of all skin lymphoma and is classified into three main subgroups: primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous follicle center lymphoma (PCFCL), and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT).[8,9]

Primary cutaneous B-cell lymphoma is a rare disease with an incidence rate of 0.5 to 1 case per 100,000 people per year. It accounts for about 25% of all primary skin lymphoma. It is more common in men

than women.[9,10] This case report discusses PCDLBCL, LT, occurring in a 74-year-old woman.[11]

Primary cutaneous diffuse large B-cell lymphoma leg type primarily affects elderly women and has rapidly progressive clinical manifestations of tumors involving the lower leg, with about 10% of cases possibly involving other skin areas.[12] On histopathological feature of lymphoma is described by diffuse sheets of activated B-cell (centroblast) and activated lymphocyte (immunoblast) that do not hit the epidermis but it often extends deep into the dermis and subcutaneous tissue. A similar case has been reported by Huang & Liu in an 88-year-old woman who had two painful erythematous nodules with unclear borders on both limbs. On histopathological examination, they found monotonous, diffuse, and non-epidermotropic infiltrations of the fused immunoblast and centroblast sheets, and in staining with Bcl-2, it showed positive for CD 20.[13] This is in line with this case which reported PCDLBCL-LT in a 74-year-old woman with reddish, swollen patches accompanied by an itchy and burning sensation. A painful ping-pong-sized lump was also seen on the inner left thigh, which secreted a clear, odorless fluid. In this case, the histopathological examination demonstrated the proliferation of neoplastic and diffuse homogenous cells of atypical nuclei with mitosis in the dermal layer with the nodular features in some parts of the dermis. The immunohistochemistry examination of our patient also revealed a positive for CD 20.

Primary cutaneous diffuse large B-cell lymphoma, leg type usually appears as tumors or erythematous nodules measuring 2 to 5 cm to violaceus of the legs or nodules on the legs, with 10% to 15% at locations other than the feet. Patients generally have a single lesion or grouping of lesions upon diagnosis, with the involvement of the foot having a higher rate of spreading compared to another region (33% vs. 18%).[14]

The histopathological feature of PCDLBCL-LT consists of large and often homogenous sheets of lymphoid cells with an activated B cell phenotype, infiltrates filling the dermis, can involve subcutaneous, and sometimes extend to the ulcerated epidermis. The absence of small lymphocytes and granulocytes supports the diagnosis of PCDLBCL-LT compared to PCFCL cases with many centroblasts, cells consisting of PCDLBCL-LT show an immunoblastic, centroblasts appearance, or a mixture with frequent mitosis.[15]

Commonly supporting examinations perform to establish the diagnosis by skin biopsy, which is staining by H&E as well as immunohistochemical with antibody panels against B cell antigens including CD20, CD79a, CD5, CD10, BCL-2, BCL-6, kappa/lambda, and MUM/IRF4.[16,17] A histopathological features of PCDLBCL-LT type which showed dense lymphocyte infiltration of the entire dermis and subcutaneous fat (A); another finding that can be found in neoplastic B lymphocyte epidermotropism that forms an indistinguishable intraepidermal group of Darier's nest (Pautrier microabscesses) (B); infiltration of mild perivascular lymphocytes (C).[18] Immunohistochemistry analysis of PCDLBCL-LT are positive results on CD 20, CD79a, Bcl-2, MUM-1, FOX-P1, CD10, IgM, CD 138, Ki-67, CD 30 and MYC.[19,20] In this case, a skin biopsy was performed on the lesions in both lower limbs. Based on immunohistochemical staining, CD 45 and CD 20 showed positive results.

The differential diagnoses of this patient are primary cutaneous follicle center lymphoma (PCFCL) and cutaneous T cell lymphoma (CTCL). Primary cutaneous follicle center lymphoma is an indolent PCBCL and covers 60% of the overall PCBCL, and has an excellent prognosis. It mostly affects people in 50's men tend to get PCFCL 1.5 times greater than women.[17,20] PCFCL is characterized by slow growth, measuring 2 cm to 5 cm, hard, smooth, plaque, nodules, or erythematous-violaceous tumors and rarely ulcerates and often telangiectasis.[10,21] Tumor mainly occurs in the head and neck (61%), upper extremities (23%), and body (16%). Most patients have local or regional diseases, with 20% with single lesions and 80% with multiple lesions. Although untreated

lesions continue to grow, the spread is rare (<10%).[9,14,17]

The standard treatment of PCDLBCL-LT is based on intravenous rituximab and combination chemotherapy. Patients treated with a combination of chemotherapy and radiation may have better clinical outcomes than patients treated with chemotherapy alone.[21] The combination of multiagent chemotherapy and rituximab has been shown to have a response rate of 60% to 90% and a disease-specific survival rate for 3 years of 80% to 90%.[12,17,19]

4. Conclusion

A 74-year-old woman came up with a reddish, swollen spot, which was itchy and hot on both limbs. A ping-pong-sized lump on the left inner thigh, hard palpable, reddish in color, then the lump secreted a clear, odorless liquid, itchy and painful. The histopathological finding showed the proliferation of neoplastic and diffuse cells, with homogenous cells of the atypical nucleus with mitosis. In addition, most of the dermis with a nodular picture is obtained. In the immunohistochemical staining, positive results were obtained on CD 45 and CD 20 but showed negative results on CD 3.

5. References

1. Patsatsi A, Kyriakou A, Karavasilis V. Primary cutaneous diffuse large B-cell lymphoma, leg type, with multiple local relapses: Case presentation and brief review of literature. Hippokratia. 2013; 17(2): 174-6.
2. Sokol L, Naghashpour M, Glass, L. Primary cutaneous B-cell lymphomas: Recent advances in diagnosis and management. Cancer Control. 2019; 19: 236-44.
3. Thomas V, Dobson R, Mennel R. Primary cutaneous large B-cell lymphoma, leg type. Proc (Bayl Univ Med Cent) 2011; 24: 350-33.
4. Nakayama-Ichiyama S, Yokote T, Iwaki K. Co-infection of human herpesvirus-6 and human herpesvirus-8 in primary cutaneous diffuse large B-cell lymphoma, leg type. Br J Haematol. 2011; 155: 514-16.
5. Nakayama-Ichiyama S. Co-infection of human herpesvirus-6 and human herpesvirus-8 in primary cutaneous diffuse large B-cell lymphoma, leg type. British Journal of Haematology. 2012; 55: 514–6.
6. Kempf W, Denisjuk N, Kerl K. Primary cutaneous B-cell lymphomas. JDDG - Journal of the German Society of Dermatology. 2012; 10: 12–23.
7. Hristov AC. Primary cutaneous diffuse large b-cell lymphoma, leg type: Diagnostic considerations. Archives of Pathology and Laboratory Medicine. 2012; 136: 876–81.
8. Wobser M, Kneitz H, Brocker EB. Primary cutaneous diffuse large B-cell lymphoma, leg-type, treated with a modified R-CHOP immunochemotherapy - Diagnostic and therapeutic challenges. J Dtsch Dermatol Ges. 2011; 9: 204–11.
9. Goyal A, LeBlanc RE, Carter B. Cutaneous B-cell lymphoma. Hematology/Oncology Clinics of North America. 2018; 33(1): 149–61.
10. Lang CCV, Ramelyte E, Dummer R. Innovative therapeutic approaches in primary Cutaneous B cell lymphoma. Frontiers in Oncology. 2020.10: 1–6.
11. Korgavkar K, Weinstock MA. Changing incidence trends of cutaneous B-Cell lymphoma. J Invest Dermatol. 2014; 134(3): 840–2.
12. Ryan AW. Cutaneous B-cell lymphomas: 2019 update on diagnosis, risk stratification, and management. Am J of Hematol. 2018; 93(11): 1427–30.
13. Huang SF, Liu WC. A rare case of primary cutaneous diffuse large B-cell lymphoma, leg type, presenting as cellulitis: A case report. J Surg Case Rep. 2021; (6).
14. Suárez AL, Querfeld C, Horwitz S. Primary cutaneous B-cell lymphomas: Part II. Therapy

and future directions. J Am Acad Dermatol. 2013; 69(3): 1-11.

15. Robson A, Shukur Z, Ally M. Immunocytochemical p63 expression discriminates between primary cutaneous follicle centre cell and diffuse large B cell lymphoma-leg type, and is of the TAp63 isoform. Histopathology. 2016; 69(1): 11-9.
16. Sokol L, Naghashpour M, Glass FL. Primary cutaneous B-Cell lymphomas: Recent advances in diagnosis and management. Cancer Control. 2012; 19(3): 236-44.
17. Hamilton SN, Wai ES, Alexander C. Treatment and outcomes in patients with primary cutaneous B-cell lymphoma: The BC cancer agency experience. Int J Radiat Oncol Biol Phys. 2013; 87(4): 719-25.
18. Aldarweesh FA, Treaba DO. Primary cutaneous follicle centre lymphoma with Hodgkin and Reed-Sternberg like cells: A case report and review of the literature. Case Rep Hematol. 2017; 2017: 1-5.
19. Hristov AC, Tejasvi T, Wilcox RA. Cutaneous T-cell lymphomas: 2021 update on diagnosis, risk-stratification, and management. Am J Hematol. 2021; 96(10): 1313–28.
20. Swerdlow SH, Campo E, Pileri SA. Review series the updated who classification of hematological malignancies the 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016; 127(20): 2375-90.
21. Rubio-Gonzalez B, Zain J, Rosen, ST. Clinical manifestations and pathogenesis of cutaneous lymphomas: Current status and future directions. British Journal of Haematology. 2017; 176(1): 16-36.