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Cutaneous Involvement as a First Sign of CD5(-) Blastoid Mantle Cell Lymphoma

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INTRODUCTION

Mantle cell lymphoma (MCL) is a subtype of B-cell non-Hodgkin's lymphoma and is cytomorphologically divided into several subtypes: blastoid, pleomorphic, small-cell, and marginal zone-like.[1] The blastoid variant has an aggressive course, and skin involvement is seen in about 2% of cases. Skin involvement is associated with poorer prognosis and extremely rarely found as the first clinical manifestation of blastoid MCL.[2] In this report, a 69-year-old male patient who presented with cutaneous nodules and was subsequently diagnosed with blastoid MCL is presented. Therefore, cutaneous signs and the disease course should be considered as any delay in the diagnosis that could lead to significant consequences.

CASE REPORT

A 69-year-old male patient presented with subcutaneous firm and fixed nodules on the scalp, face, and trunk. The lesions first appeared on the trunk and spread to the face and scalp in the last 1.5 months. Nodules were slightly livid brown, nonulcerated, and fixed to the underlying tissues (Figures 1a-d). Simultaneously with trunk lesions, ptosis developed in the left eyelid. Ultrasonography of the superficial lymph nodes revealed multiple lymph nodes with an irregular cortex and preserved hilus, the largest of which was 40 x 18 mm in the left axillary region. On neck ultrasonography, multiple lymphadenopathies were observed with a pathological and conglomerated appearance on both sides, the largest of which was 32 x 16 mm.

A selected cutaneous nodular lesion in the left suprascapular region was completely excised. Histopathological examination revealed perifollicular and perivascular dense nodular infiltrations in the dermis, sparing the epidermis and a zone in the papillary dermis. The subcutaneous fat tissue and the striated muscle were heavily infiltrated. The infiltration was composed of CD20, cyclinD1, and SOX11 positive and CD5 negative medium-sized cells with dispersed chromatin, frequent mitoses, and a high Ki67 proliferation index. Neoplastic cells were negative with TdT, MUM-1, CD10, Bcl2, Bcl6, and CD56, excluding acute lymphoblastic leukemia and diffuse large B-cell lymphoma. Morphologic and immunohistochemical findings were consistent with that of blastoid-type MCLs (Figures 2a-g).

Whole-body positron emission tomography imaging revealed multiple hypermetabolic foci in the subcutaneous tissues and internal organs, the fimdings consistent with foreground lymphoma involvement (Figures 3a-g).

Based on the results of these examinations, the patient was diagnosed with blastoid MCL and secondary skin involvement and was referred to the hematology department. The rituximab-cyclophosphamide-doxorubicin-vincristineprednisone (R-CHOP) protocol was planned for the treatment of the patient with 3-week intervals. After the first course of chemotherapy, the skin lesions

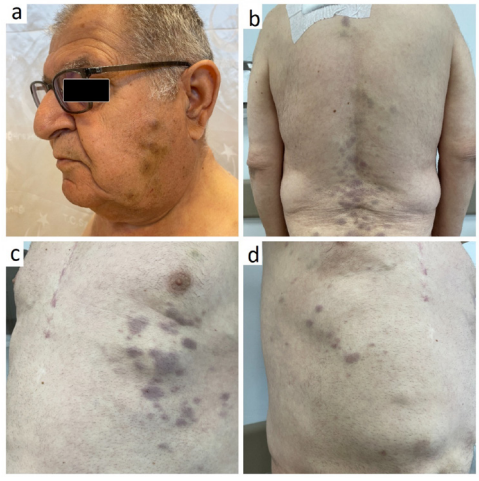


FIG. 1. a-d) Tissue-fixed, livid-colored nodules on the face, back, and anterior trunk.

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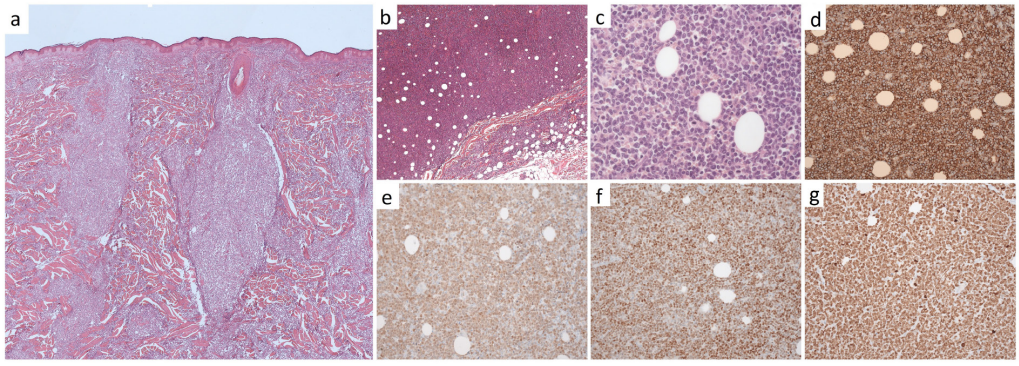


FIG. 2. a) Nodular and diffuse dermal lymhoid infiltration separated from the epidermis by a grenz zone (hematoxylin and eosin [H&E] x 20), b) Muscle and subcutaneous fat tissue infiltration (H&E x 50), c) Mitotically active, medium-sized atypical cells with oval and irregular nuclei, finely dispersed chromatin, occasional small nucleoli, and scant cytoplasm (H&E x 400), d) Strong membranous expression of CD20 by immunohistochemistry (H&E x 200), e-f) Diffuse staining with Bcl1 and SOX11 antibodies (x 200), g) Staining with the Ki67 antibody demonstrates a proliferation score of nearly 100% (x 200)

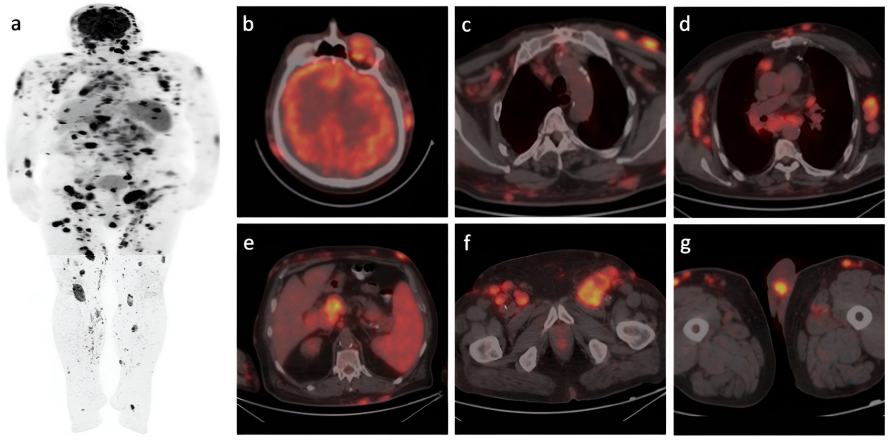


FIG. 3. a) Whole-body maximum intensity projection image, b) View inside the left orbit, c) Subcutaneous lesions at the level of the left pectoral muscles, d) Axillary and mediastinal lymph nodes, e) Portal hilar lymph nodes and spleen involvement, f) Inguinal lymph nodes, g) Involvement of the scrotum

started to disappear and the ptosis regressed. After eight cycles of chemotherapy, the patient's cutaneous lesions and internal organ involvement completely regressed. The patient follow-up was continued in the hematology department.

DISCUSSION

Hematological neoplasms may involve the skin, which may be either the primary site of the occurrence of hematological malignancies with blastic features or cutaneous lesions, and are the first manifestation of an underlying systemic malignancy.[3] MCLs rarely present with skin involvement. Cutaneous involvement is generally observed at an advanced age and is associated with a widespread disease.[4] The isolated cutaneous disease is more benign than the systemic forms but may evolve into a systemic form during follow-up. The disease may present with widely varied elementary lesions, ranging from petechial erythematous macules to subcutaneous nodules, and very atypical presentations, such as acneiform lesions have also been reported.[5,6]

Blastoid MCL is associated with a higher mitotic index and a poorer prognosis than classical MCL.[7] Cutaneous involvement is very rare, consisting of 17 patients who presented with cutaneous involvement in the literature to date. The female/male ratio of the reported cases was 2/16, with an average age of 70 years (Table 1). As extremity and trunk involvements are more frequently observed, cutaneous involvement can ocur throughout the body. Nodular lesions represent the most prevelant form of skin involvement and can manifest in various ways, ranging from erythematous macules to nodules. In this patient, the nodules started on the trunk and spread to the face and scalp.

In MCL involving the skin, the aggressive cytological subtypes were more common (72.9%) compared with the classic subtype.[8] Histopathological examination of the blastoid MCL in the skin reveals a diffuse and/or nodular growth pattern in the dermis that may extend into the subcutaneous fat tissues.[9,10] Immunophenotypically, it exhibits positivity for pan-B-cell markers, cyclin D1 positivity, and a high mitotic index, as observed in the current case. As MCL

TABLE 1. Patients who Initially Presented with Skin Lesions and were Diagnosed with Blastoid Mantle Cell Lymphoma.

	Report	Age/ sex	Examination	Immunohistochemistry	FISH (BCL-1/ Cyclin D1)
1	Phelps et al.[13]	71/M	Erytematous papules on the right cheek	Cyclin D1+ CD5+ CD20+ bcl-2+ Ki-67 (> 90%)	Positive
2	Li et al.[14]	53/M	Nodules and plaques on the head, trunk, and lower extremities	Cyclin D1+ CD5- bcl-2+ Ki-67 (> 80%)	Positive
3	Hrgovic et al.[15]	55/F	Nodular mass of the right infraorbital region	Cyclin D1+ SOX11+ CD5+ CD20+	NA
4	Cao et al.[16]	55/M	Petechiae and ecchymosis on the face, neck, back, and chest	Cyclin D1+ CD5+ CD20+ BCL2+ Ki-67 (> 90%)	Positive
5	Péčová et al.[17]	71/M	Red papules, nodules, and tumors of the face and trunk	Cyclin D1+ CD20+	NA
6	Estrozi et al.[18]	72/M	Cutaneous nodules in the right temporal region	Cyclin D1+ CD5+ CD20+ Ki-67 (> 80%)	Positive
7	Cesinaro et al.[19]	75/F	Purplish nodules on the lower left leg	Cyclin D1+ CD5+ CD20+ bcl-2+ Ki-67 (> 90%)	Positive
8	Lynch et al.[20]	83/M	Nodular erythematous skin eruption on the thighs	Cyclin D1+ CD5+ CD20+	Positive
9	Wehkamp et al.[21]	68/M	Multiple skin lesions on both legs	Cyclin D1+ CD5+ CD20+ bcl2+ Ki-67 (42%)	NA
10	Wehkamp et al.[21]	74/M	Isolated lesion on the lower leg	Cyclin D1+ CD5+ CD20+ bcl2+ Ki-67 (90%)	Positive
11	Wehkamp et al.[21]	82/M	Multiple lower-leg lesions	Cyclin D1+ CD5+ CD20+ bcl2+ Ki-67 (60%)	Positive
12	Wehkamp et al.[21]	50/M	Isolated scalp lesion	Cyclin D1+ CD5+ CD20+ bcl2+ Ki-67 (90%)	Positive
13	Wehkamp et al.[21]	84/M	Isolated forearm lesion	Cyclin D1+ CD5+ CD20+ bcl2+ Ki-67 (80%)	Positive
14	Sen et al.[4]	85/M	Macular rash on the leg skin	Cyclin D1+ CD5+ CD20+ Ki-67 (42%)	NA
15	Sen et al.[4]	76/M	Nodular skin lesions on the thigh	Cyclin D1+ CD5+ CD20+ Ki-67 (51.6%)	Positive
16	Sen et al.[4]	57/M	Maculopapular lesions on the leg	Cyclin D1+ CD5+ CD20+	NA
17	Kazlouskaya et al.[6]	77/M	Elevated pink papules on both cheeks	Cyclin D1+ CD5- bcl-2+ Ki-67 (90%)	NA
18	Our case	69/M	Nodules on the scalp, face, and trunk	Cyclin D1+ CD5- CD20+ bcl2+ Ki-67 (99%) SOX11+	NA

NA, not available; F, female; M, male

is typically expected to be CD5 positive, CD5-negative cases are also reported as in this case. SOX11 positivity, which is observed in > 90% of MCL's, helps in identifying CD5 negative cases.[11] The immunophenotypic features of the MCL involving the skin are similar to the MCL at other sites, confirming the more frequent CD5 negativity in cases with aggressive morphology and a higher Ki67 proliferation rate (90%) compared with the classic variant (20%).[3] Immunophenotypic studies play a crucial role in the differential diagnosis, including acute lymphoblastic lymphoma and large B-cell lymphoma, providing valuable information for accurate classification.

The R-CHOP regimen is most commonly used for the disease treatment. However, the treatment response is not the same in all patients. The international prognostic index of the MCL and the Ki-67 index provide the most useful information for the disease prognosis.[12] The disease treatment and follow-up are managed by hematologists and oncologists.

Patients with blastoid MCL may initially seek evaluation at dermatology clinics. Given that blastoid MCL is a highly aggressive variant, avoiding any delays is crucial for its diagnosis. Dermatologists should therefore be awarene of the cutaneous manifestations of lymphoma to ensure timely recognition and appropriate management.

Informed Consent: Written informed consent was obtained from the patient.

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