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Case Report

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Secondary cutaneous diffuse large B-cell lymphomas: bad scenario

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ABSTRACT

Primary or secondary cutaneous involvement may occur in common diffuse large B-cell lymphomas. The secondary cutaneous involvement of diffuse large B-cell lymphoma is a condition that develops during the course of the disease and is associated with an aggressive course and shorter survival. The development of secondary cutaneous involvement shortly after the initial diagnosis of the primary disease predicts more aggressive clinical outcomes and is more likely to present with multiple skin lesions.

Keywords: Premature, sepsis, thrombocytopenia

INTRODUCTION

Primary cutaneous lymphomas (PCL) are composed of approximately 25% B-cell origin lymphomas. B-cell cutaneous lymphomas (B-PCL) are classified into three main categories: primary cutaneous follicle-center lymphoma (pcFCL), primary cutaneous diffuse large B-cell lymphoma, leg type (pcDLBCL-LT), and primary cutaneous marginal zone lymphoma (pcMZL).[1,2] While pcMZL and pcFCL are clinically indolent, pcDLBCL-LT is an aggressive lymphoma. Secondary cutaneous DLBCL (scDLBCL) is defined as lymphoma that demonstrates secondary spread to the skin after systemic involvement. Patients with both pcDLBCL and scDLBCL are older than those with pcFCL and pcMZL.[3] In scDLBCL, skin lesions emerge as a result of disease progression, leading to a significantly lower survival rate. Additionally, this may indicate an increase in tumor burden and/or the ability of the disease to spread through blood or lymphatic vessels.[4] We present this case to emphasize the appearance of secondary skin involvement and the poor prognosis associated with diffuse large B-cell lymphomas.

CASE

A 49-year-old male patient presented with complaints of cough, abdominal pain, sweating, and weight loss. Abdominal computed tomography (CT) revealed splenomegaly and a heterogeneous, lobulated mass in the left upper quadrant of the abdomen, approximately 20×17×16 cm in size, with central necrotic areas and heterogeneous contrast enhancement. A biopsy of the splenic mass confirmed the diagnosis of diffuse large B-cell lymphoma of the germinal center type (CD19 (+), C-MYC (+) BCL-6 (+), BCL2 (-)). The patient was staged as stage 2 bulky, with an International Prognostic Index (IPI) of high-intermediate risk and a high Central Nervous System International Prognostic Index (CNS IPI). The patient underwent 4 cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapy and 3 intrathecal methotrexate treatments. A follow-up positron emission tomography-computed tomography (PET-CT) scan showed stable disease. Due to an inadequate response to first-line therapy, salvage treatment with 3 cycles of rituximab plus gemcitabine and dexamethasone (R-GDP) was administered. However, progression was observed after 3 cycles of R-GDP. Subsequently, the patient received 2 cycles of rituximab plus dexamethasone, cytarabine, and cisplatin (R-DHAP) chemotherapy, but progression was again detected on PET-CT. On physical examination, erythematous, indurated, papular lesions were observed in a large area of the skin over the left abdominal quadrant (**Figure**). Punch biopsy of these lesions was performed, and the biopsy was evaluated as germinal center type diffuse large B-cell lymphoma. The patient was started on bendamustine, rituximab, and ibrutinib therapy. However, the patient passed away on the 3rd day of the new treatment, 9 months after the diagnosis.

DISCUSSION

The most common primary extranodal sites of diffuse large B-cell lymphoma (DLBCL) are the gastrointestinal system,

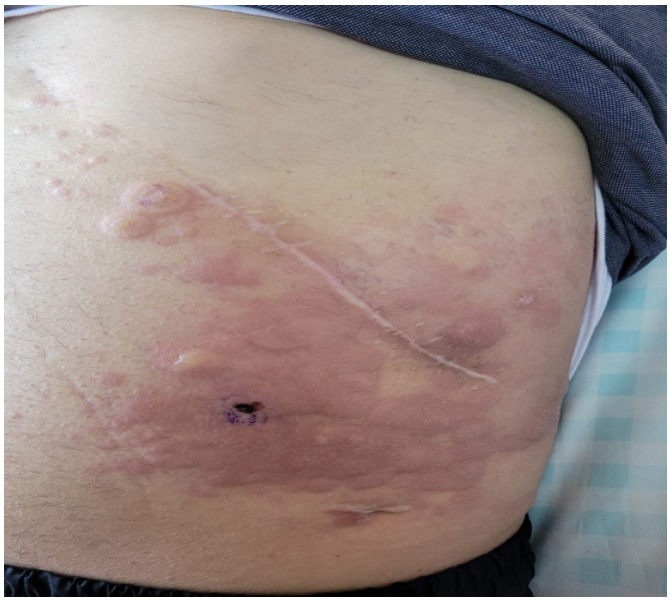

Figure. Erythematous, indurated, papular lesions spread over a large area on the left abdominal skin

head and neck, and skin/soft tissues. In a large cohort of 25.992 patients with DLBCL, primary skin/soft tissue involvement accounted for 3.3% of all cases.[5] Cutaneous involvement in DLBCL can be divided into two distinct subsets based on the primary site of involvement: primary cutaneous DLBCL, which initially presents in the skin, and DLBCL with secondary spread to the skin. While primary cutaneous DLBCL, leg type, has been extensively studied, there is limited data available regarding the clinical features or survival analysis of patients with secondary cutaneous DLBCL.[6]

A retrospective review identified that 44 out of 2.067 DLBCL cases (2.1%) had cutaneous involvement. Among these cases, 14 were diagnosed with pcDLBCL-LT and 30 with scDLBCL. Advanced stage, high (>2) IPI score, B symptoms, and elevated LDH levels were significantly more common in scDLBCL compared to pcDLBCL-LT. Patients with pcDLBCL-LT demonstrated significantly better survival outcomes than those with scDLBCL (5-year survival: pcDLBCL-LT: 65%, scDLBCL: 31%).[6]

In a study regarding the anatomical region of secondary cutaneous lymphoma involvement, it was found that extremities were more likely to be affected by T/NK SCL, while B-cell lineage SCL predominantly involved the trunk.[7] Another study has shown that pcDLBCL most commonly affects the legs (28.7%) and face (21.9%), while scDLBCL similarly affects the legs (32.3%), head (27.2%), and trunk (15.7%).[3] In our patient, trunk involvement was observed. The clinical presentation of SCL is highly heterogeneous, and the literature reports the presence of papules, plaques, tumors, and even erythroderma.[7-14] However, Lee and colleagues[7] observed that T/NK SCL is more likely to present as a maculopapular rash, while B-cell SCL is more likely to present with plaques or nodules. It has been described that some cases of angioimmunoblastic lymphoma (AIL) or otherwise unspecified peripheral T-cell lymphoma (PTNL) mimic reactive dermatoses or erythroderma.[14-16] HL is typically seen as reddish-brown papules, patches, or even nodules, sometimes accompanied by ulceration.[12,13,17]

In DLBCL, skin biopsies typically show infiltration by large and transformed B cells with prominent nucleoli and basophilic cytoplasm in the dermis and subcutaneous tissue; small lymphocytes (CD3+) may also be present in the samples. Immunohistochemistry reveals the general expression of all B-cell markers (CD19, CD20, CD22, CD79a), CD45, Bcl-2, Bcl-6, CD10, and MUM1, as well as possible variants such as the strongly expressed PAX-5 and CD30 in the polymorphic EBV+DLBCL variant, and weak CD20 and CD79a positivity in a background with mild inflammation.[13,18]

Cutaneous involvement associated with systemic DLBCL indicates disease progression and leads to worse outcomes compared to conventional DLBCL. The survival rates for secondary cutaneous DLBCL are lower than those for primary cases. The prognosis of secondary cutaneous DLBCL is related to the interval between the initial diagnosis and the development of skin lesions. The development of secondary cutaneous involvement shortly after the initial diagnosis of the primary disease predicts more aggressive clinical outcomes and is more likely to present with multiple skin lesions. In contrast, secondary cutaneous involvement that develops later after the initial diagnosis tends to have a less aggressive course.[19,20] It has been observed that other conventional prognostic factors such as stage, age, sex, and the IPI have a minimal effect on the prognosis of SCL.[7]

CONCLUSION

In conclusion, although secondary cutaneous involvement in DLBCL is rare, the presence of extensive skin lesions and skin involvement shortly after the initial diagnosis are associated with worse overall survival outcomes. There is no recommendation for treatment different from conventional DLBCL therapy. New therapeutic agents are needed to improve survival in the treatment of secondary cutaneous involvement.

ETHICAL DECLARATIONS

Informed Consent
The patient signed and free and informed consent form.

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

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The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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