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Intravascular diffuse large B-cell lymphoma with acquired ichthyosis: A case report

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Abstract

Intravascular diffuse large B-cell lymphoma is an exceedingly rare subtype of B-cell lymphomas. This cancer is often associated with poor prognosis and can be lethal if left untreated. Intravascular diffuse large B-cell lymphoma is divided into three variants: the 'classical variant', the hemophagocytic syndrome-associated variant or 'Asian variant', and the 'cutaneous variant', according to the clinical presentation and affected organs. We present a unique case of 'classic variant' intravascular diffuse large B-cell lymphoma with cutaneous findings, peripheral nervous system involvement and acquired ichthyosis in a patient of Asian descent. This case highlights the importance of a prompt dermatology consultation in the diagnosis of intravascular diffuse large B-cell lymphoma. As bone marrow biopsy is often negative, clinicians must recognize the cutaneous findings and acknowledge that skin biopsy can be an essential tool to establish the diagnosis rapidly. Additional finding making this case unique is the concurrent presence of acquired ichthyosis, which has only been previously reported in one case of intravascular diffuse large B-cell lymphoma.

Keywords

Intravascular diffuse large B-cell lymphoma, R-CHOP, methotrexate

Introduction

Intravascular diffuse large B-cell lymphoma (IVDLBCL) is an exceedingly rare subtype of diffuse large B-cell lymphomas, accounting for less than 1% of all lymphomas. This cancer is often associated with a poor prognosis and can be lethal if left untreated.[1] However, early diagnosis and prompt treatment have significantly improved the outcomes.[1] IVDLBCL is divided into three different types of variants according to the clinical features and affected organs.[2] The 'classical variant' accounts for over 75% of cases, and skin lesions are reported in about 40% of them. The hemophagocytic syndrome-associated variant, also known as the 'Asian variant' because it has been described in Asian countries, has the worst prognosis and classically presents with fever, thrombocytopenia, splenomegaly, and bone marrow involvement.[3] The 'cutaneous variant', comprising about 20% of cases, presents with disease limited to the skin and negative workup for systemic involvement.[4] On histopathology, IVDLBCL is characterized by large neoplastic cells infiltrating the lumens of small- and medium-sized vessels without the involvement of lymph nodes or peripheral blood.[4] Hence, unlike other systemic lymphomas, the diagnosis is typically made through biopsies of affected organs (e.g. skin) or otherwise normal-appearing skin.[5] Importantly, bone marrow, flow, smear, and imaging are often normal, leading to difficulty in diagnosis and delay, hence this disease is often diagnosed post-mortem. We present an illustrative case of IVDLBCL where non-blanching infiltrative skin lesions and acquired ichthyosis led to a very rapid diagnosis and life-saving treatment initiation in less than 2 weeks. Additional finding making this case unique is the concurrent presence of acquired ichthyosis, which has only been previously reported in one case of IVDLBCL.[6]

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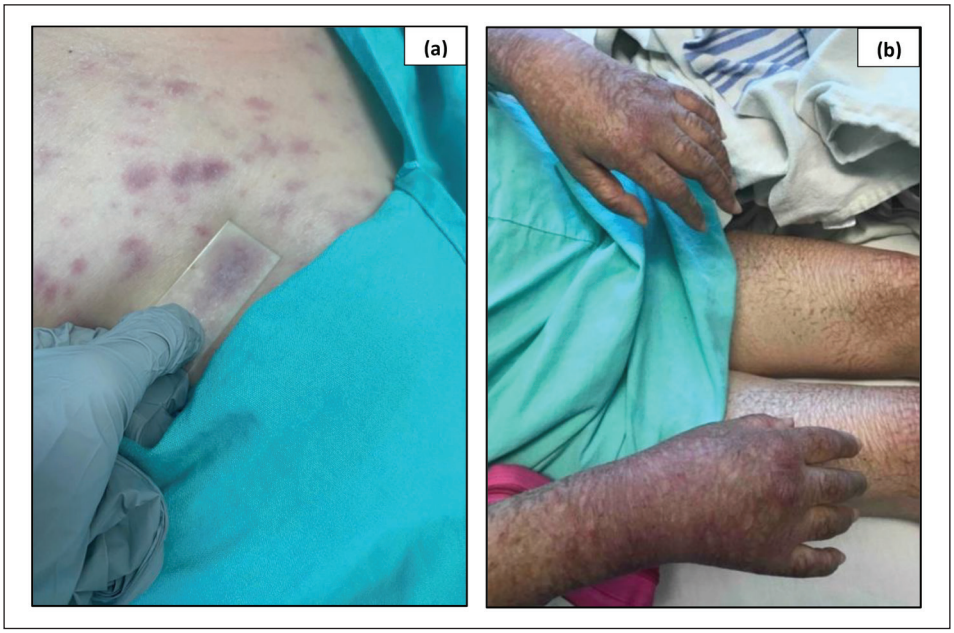

Figure 1. Intravascular diffuse large B-cell lymphoma: (a) multiple grey-violaceous macules and patches, non-blanching on diascopy and (b) extensive dry 'fish scale' like skin on extremities.

Case presentation

We present the case of a 57-year-old female of Asian origin known for type 2 diabetes, Graves' disease, and breast cancer. She presented with a 3-week history of rapidly progressive peripheral neuropathy, fever, fatigue, and weight loss. Skin examination revealed multiple asymptomatic non-blanching, bruise-like grey-violaceous patches on her trunk, abdomen, and back (Figure 1(a)). No green hue was seen on diascopy to suggest chloroma. No mucosal involvement or lymphadenopathy were noted. Acquired ichthyosis was noticed on extremities, sparing palms, and soles (Figure 1(b)). Skin features with a serum lactate dehydrogenase (LDH) of 3883 U/L and microcytic anaemia were suggestive of lymphoproliferative disease. Magnetic resonance imaging of the brain and spine and lumbar puncture excluded central nervous system (CNS) involvement. A positron emission tomography (PET) scan revealed no other fluorodeoxyglucose (FDG)-avid areas. Electromyography confirmed severe lower extremity axonal sensory-motor polyneuropathy. Peripheral smear and bone marrow biopsy were normal. In situ hybridization for Epstein–Barr virus was negative. Cutaneous biopsy revealed an intravascular proliferation of large, atypical B-cells with thrombi, with positive staining for BCL2, MUM1, and Myc by neoplastic cells and partial BCL6 staining (Figure 2). There was a high proliferation index of lymphoid cells highlighted by Ki67. These findings led to a prompt diagnosis of IVDLBCL. Treatment with R-CHOP chemotherapy and high-dose methotrexate was initiated within a week of presentation. One year later, there was no residual lymphoma on the PET scan. However, a post-treatment sural nerve biopsy revealed severe neurogenic atrophy.

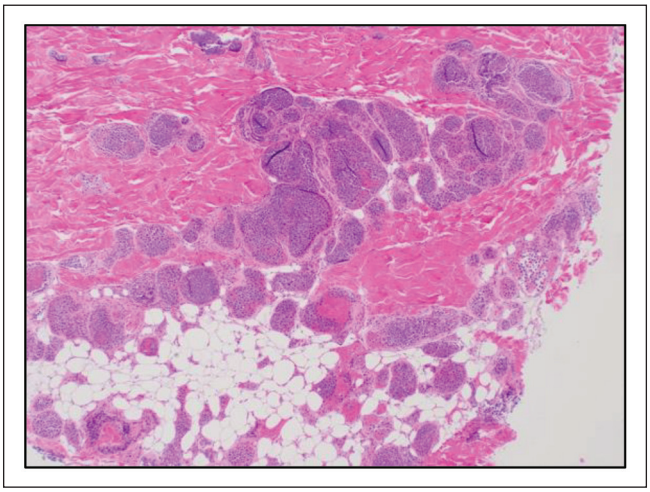

Figure 2. Cutaneous biopsy revealing intravascular proliferation of large atypical B-cells associated with thrombi.

Discussion

In IVDLBCL, neoplastic cells infiltrate vessels' lumen without readily observable neoplastic cells in blood or hematopoietic organs, making the diagnosis challenging.[1] Demonstration of positive expression of CD79a (100%), CD20 (96%), MUM1-IRF4 (95%), CD5 (38%), CD10 (12%), and Myc-positive lymphoma cells within the lumen

of blood vessels is diagnostic.[7,8] The main clinicopathologic differential diagnosis is that of intravascular natural killer T (T/NK) cell lymphoma, hence search for latent Epstein–Barr virus and immunostaining is important. Considering that skin is commonly involved in the classic or Western variant and cutaneous-only variant, a rapid skin biopsy is key for early diagnosis. In the absence of skin lesions in suspicious cases, random skin biopsy of healthy appearing skin may yield a diagnosis of IVDLBCL in 69% of patients.[9] Hence, the role of dermatology in establishing IVDLBCL diagnosis is important as the skin is much more accessible compared to other commonly affected organs such as CNS. In this case, cutaneous features of non-blanchable grey-violaceous infiltrative plaques in conjunction with acquired ichthyosis were highly suggestive of a hematologic origin. Of note, while the appearance of acquired ichthyosis in the context of lymphoproliferative malignancy is well described, co-occurrence with IVDLBCL has only been described once.[6]

IVDLBCL is a rare and aggressive cancer that should be suspected in patients presenting with infiltrative violaceous skin lesions, neurologic symptoms, possible B symptoms, and elevated LDH even in the absence of bone marrow or peripheral blood involvement.

Author contributions

All authors contributed to writing and reviewing this manuscript. E.N. reviewed the manuscript and supervised the research activities. All authors contributed to the article and approved the submitted version for publication.

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Informed consent

The patient gave informed consent for the collection and publishing of the non-identifiable images presented in this manuscript. Upon request, the informed consent form can be provided.

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