

Intravascular B-cell lymphoma with generalized telangiectasias

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Dear Editors,

Intravascular large B-cell lymphoma (IVLBCL) is a rare, clinically aggressive lymphoma entity characterized by an almost exclusive growth of large cells within the lumen of all-sized blood vessels. Cases that show disease limited to the skin, following extensive staging workup, are called cutaneous variants and show a better prognosis.^{1,2} Generalized telangiectasias is a type of cutaneous manifestation of this rare entity.

An 86-year-old female patient was first admitted to the outpatient clinic of infectious diseases with a complaint of fever that did not respond to oral antibiotics, with night sweats and weight loss of 10 weeks duration. Generalized telangiectasias were noted in the physical examination and were more pronounced in her face, chest and back with a severe edema resembling anasarca (Figure 1). She had a normocytic normochromic anemia with a hemoglobin level of 8 g/dl (normal range: 11.5–16 g/dl) with a normal leukocyte and platelet count. Creatinine level was mildly elevated at the time of presentation, 1.18 mg/dl (0.6–1.1 mg/dl) and she had an elevated lactate dehydrogenase (LDH; 579 U/l [135–214 U/l]) and uric acid level (11.6 mg/dl [3.5–7 mg/dl]).

A skin biopsy from the chest revealed large atypical lymphoid cells filling the lumen of the vessels throughout the dermis, some extravasated to the adjacent tissues. These atypical lymphoid cells were positive for CD20 and MUM-1, and Ki-67 proliferation index was calculated as 90% (Figure 2). A hematopathologist confirmed the diagnosis of IVLBCL according to the aforementioned findings. Positron emission tomography/ computed tomography (PET/CT)

showed no other involvement and bone marrow biopsy was also negative for any involvement of IVLBCL. There was no lymphoma infiltration in the pathological and flow cytometric examination of the cerebrospinal fluid. There was also no sign of hemophagocytosis.

Regarding the age and the performance status of the patient we decided to initiate a less aggressive chemo-immunotherapy with a combination of rituximab, cyclophosphamide, vincristine, and methylprednisolone (R-CVP) every 21 days. She did well with this combination, with all the telangiectatic lesions disappearing and the edema also resolving within the first two cycles of therapy. She received a total of six cycles of R-CVP with no dose-limiting toxicity.

During the follow-up period she had no recurrence of the skin lesions until the 14th month of the last chemo-immunotherapy. Thereafter, she suffered from a new onset edema, re-appearance of the telangiectasias and oliguria. She had a severe spontaneous tumor lysis syndrome which required a temporary hemodialysis and administration of rasburicase. Laboratory results were as follows: Hemoglobin: 6.2 g/dl (11.5–16 g/dl), creatinine: 4.6 mg/dl (0.6–1.1 mg/dl), uric acid: 16.2 mg/dl (3.5–7 mg/dl), calcium: 5.8 mg/dl (8.5–10 mg/dl), potassium: 6.6 mmol/l (3.5–5 mmol/l) and LDH: 912 U/l (135–214 U/l). She was not a candidate for high-dose therapy, and we opted for salvage therapy with a combination of rituximab and bendamustine. She was discharged on the 10th day of R-bendamustine therapy, but unfortunately she was readmitted to the emergency room with renal failure, hypotension, and severe

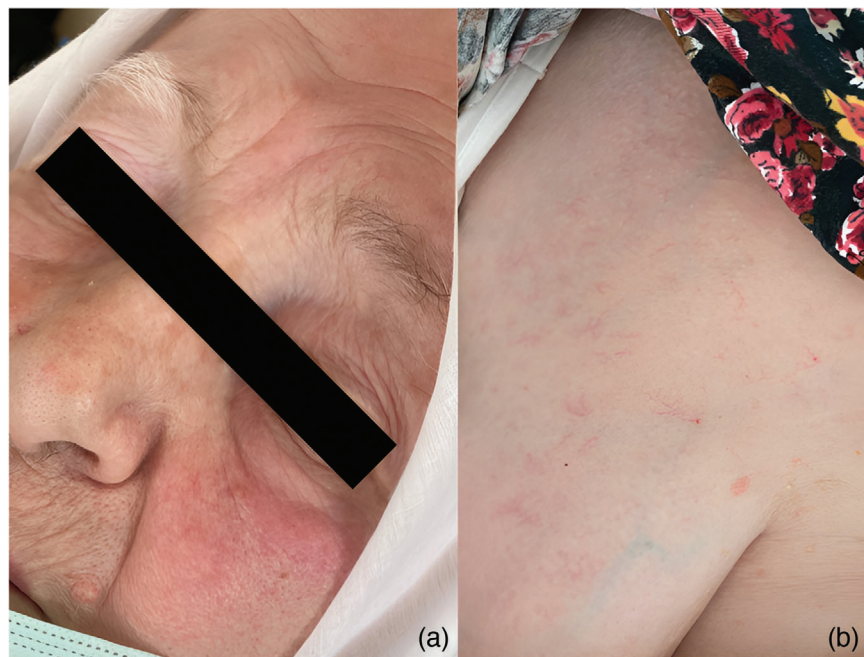


FIGURE 1 (a) Telangiectasias of the face. (b) Telangiectasias of the chest.

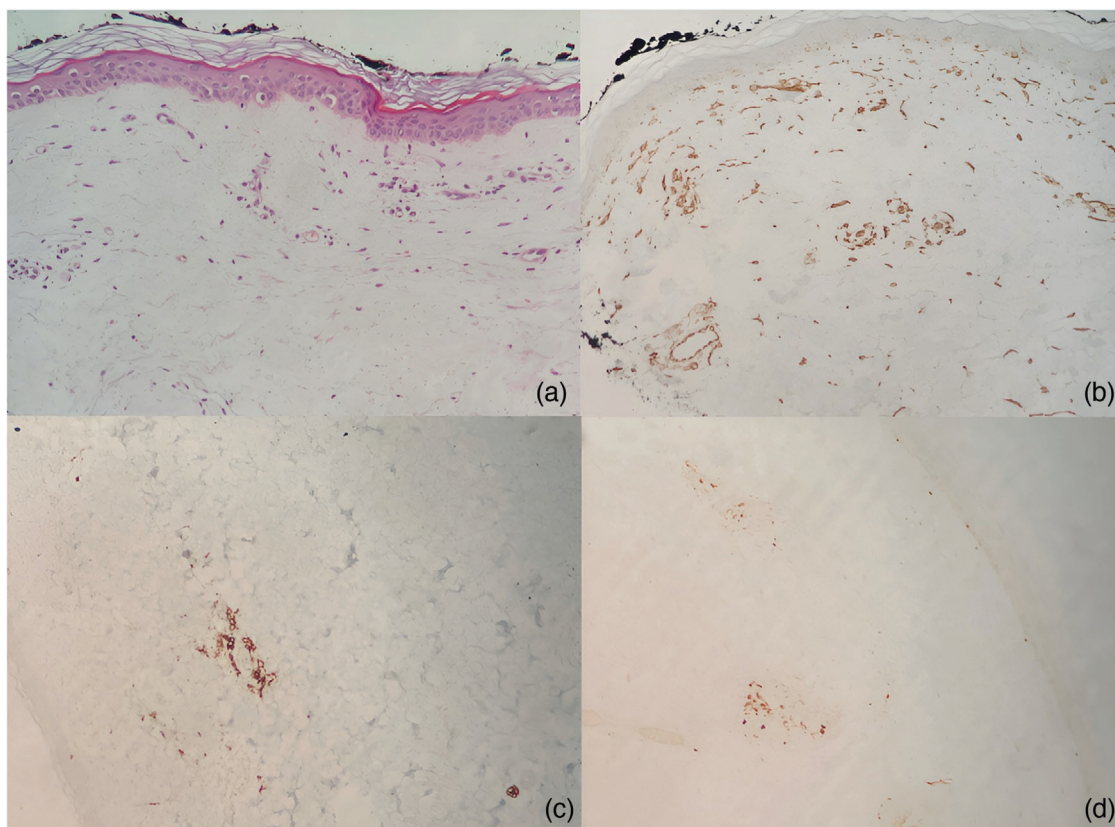


FIGURE 2 Skin biopsy sections: (a) Vessel proliferation in upper dermis and few atypical lymphoid cells in vessel lumens (hematoxylin-eosin stain, original magnification x 100). (b) Atypical cells are positive with PAX-5 (PAX-5, x 200). (c) CD20 expression in these cells (x 100). (d) MUM-1 expression in these cells (x 100).

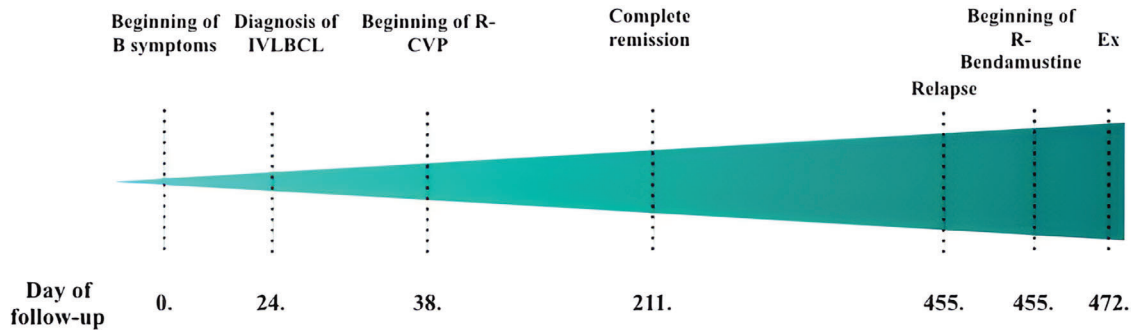


FIGURE 3 Patient follow-up chart: From initial symptoms to exitus.

tumor lysis syndrome with atrial fibrillation. Despite hospitalization in the intensive care unit, she was lost due to disease progression (Figure 3).

Prognosis of a patient with IVLBCL is unfavorable although retrospective studies suggest more promising outcome with the use of rituximab in conjunction with anthracycline-based chemotherapy.³ The use of high-dose chemotherapy followed by autologous stem cell transplantation is an important strategy in high-risk non-Hodgkin lymphomas. Successful treatment of IVLBCL with upfront stem cell transplantation has been reported; however, overall experience with this treatment modality in IVLBCL is extremely limited.^{4,5} Rituximab-based regimens are preferred in the treatment of IVLBCL and systemic treatment is necessary.^{6,7}

The most important difference in our case was the presentation. Intravascular large B-cell lymphoma cases, as defined in the literature, present with severe B symptoms and initial symptoms related to tumor burden.^{8–10} While our case shares common features with the literature counterparts in terms of being older, having a poor performance status, and having severe B symptoms, the most important difference is the absence of organ involvement and the absence of symptoms related to organ involvement.^{8–10} There was also no spread to the central nervous system, bone marrow and hepatosplenic region, which are defined as the most common sites of involvement in IVBCL. The only notable skin findings were telangiectasias. While a case with widespread skin findings was reported in 2009,¹¹ the presence of scattered and sparsely distributed telangiectasias, the absence of organ involvement, and the predominance of B symptoms are the points to keep in mind regarding IVBCL.

Although skin findings in IVLBCL are quite unusual, edema, pain, and vascular skin lesions such as venous stasis or telangiectasia may be suggestive. The most appropriate site for biopsy is the area of most intense involvement and largest lesion. PET/CT involvement may also indicate the most appropriate biopsy site.

Given the poor prognosis of conventional chemotherapy, there is a need to further investigate the

pathogenesis of the disease and to develop more accurate and effective treatment options.

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CONFLICT OF INTEREST

None.

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