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Intravascular Large B-Cell Lymphoma Diagnosed by Skin Biopsy and Immunohistochemical Study: A Case Report

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Abstract

Intravascular Large B-Cell Lymphoma (IVLBCL) is a rare extranodal diffuse lymphoma type that can involve central nervous system, skin, and bone marrow. Here we present a case of a 64-year-old female patient found to have an intravascular large B-cell lymphoma diagnosed two years after the start of the cutaneous symptoms, with a 1-year delay on the diagnosis. We aim to report this rare case due to a diagnosis defined only with skin biopsy and immunohistochemical and add more data concerning the disease.

Introduction

Intravascular large B-cell lymphoma is a rare extranodal diffuse lymphoma type characterized by abnormal cells in the lumen of small blood vessels, involving dermatological, neurological and hematological findings.[1-3] This article describes a two year evolution case of Intravascular large B-cell lymphoma diagnosed on a 64-year-old woman with typical cutaneous and hematological manifestations. We aim to report the case considering it's a rare lymphoma that can be aggressive and rapidly fatal, with challenging diagnosis, seeing that it is nonspecific and has no pathognomonic symptoms or signs.

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Case Report

We present a case of a 64-year-old female patient, from São Paulo - Brazil, who attended a dermatological clinic with a 1-year history of hematomas and disseminated telangiectasis in trunk, hands and feet. She had no comorbidities and a history of breast implant 18 years before the symptoms. At the time she presented laboratorial exams with a positive FAN 1/60 nuclear homogeneous and mild anemia. She was referred to a rheumatologist who diagnosed scleroderma and started chloroquine and deflazacort for a year, with progressive worsening of the cutaneous manifestations. One year after the first appointment, dermatological examination showed hemangiomatous infiltrated plaques, symmetric and disseminated in the trunk, as well as generalized telangiectasias. She also presented palpable nodules on lower limbs with hemangiomatous surface and no systemic symptoms or adenopathy. Laboratorial exams revealed severe anemia, leukopenia, high ferritin levels and polyclonal gammopathy on protein electrophoresis. There were no collagen diseases serologies positive. The patient had also a history of infection by SARS-COV 2 one year before. The hypotheses at this time were: systemic amyloidosis, multiple myeloma and leukemic infiltration. She was urgently referred to a hematologist for the investigation of anemia and also underwent a skin biopsy. The anatomopathological study revealed the vast majority of blood vessels in the dermis and the hypodermis, filled by anaplastic cells with hyperchromatic nuclei and scarce cytoplasm suggesting neoplastic embolization, confirmed later with immunohistochemical expressing Ki-67, CD45 and CD20, and CD34 on the vessels. The bone marrow biopsy showed reactional hypercellularity and PET-CT only increased lymph nodes in the inguinal region. The findings - anatomopathological and immunohistochemical study - conclude the diagnosis of an intravascular large B-cell lymphoma (Figure 1-4).

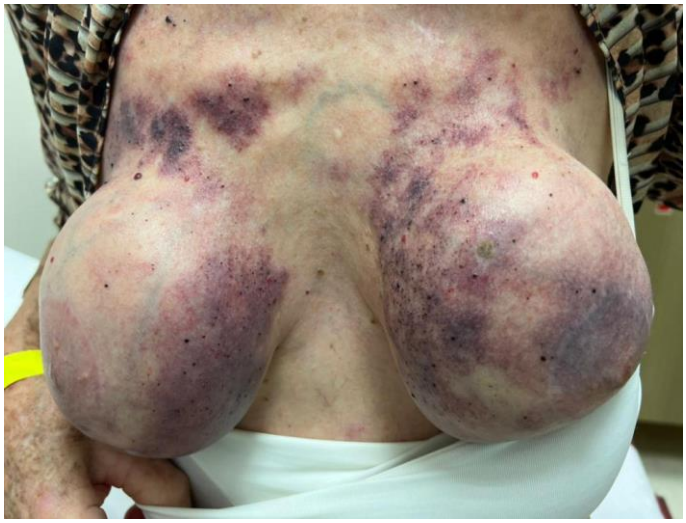

Figure 1: Clinical manifestation showing symmetric hemangiomatous infiltrated plaques.

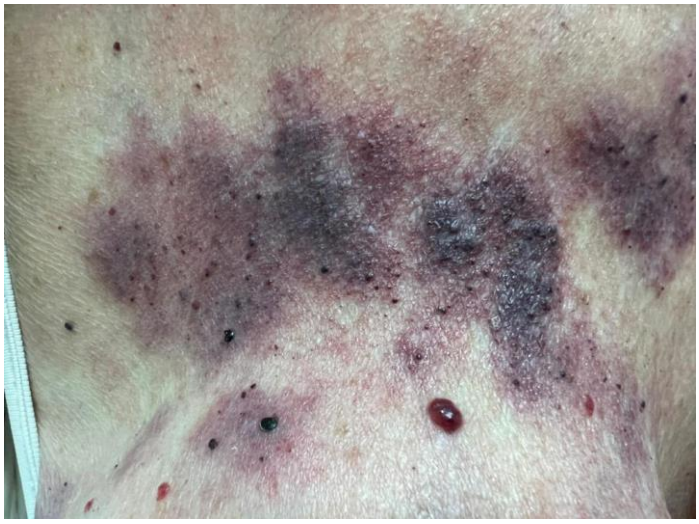

Figure 2: Clinical manifestation showing hemangiomatous infiltrated plaques.

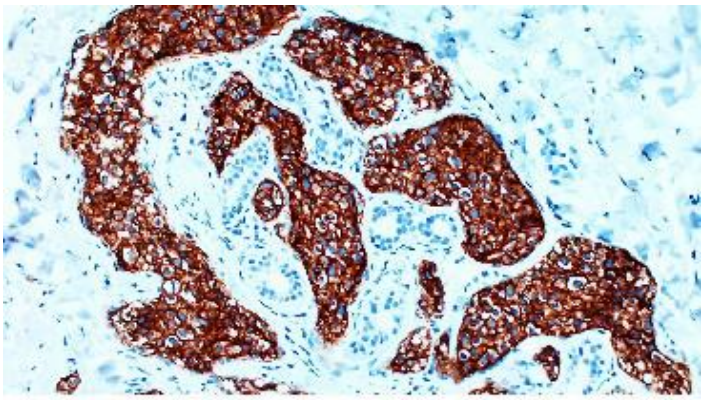

Figure 3: Immunohistochemical study showing atypical lymphoid cells expressing CD20.

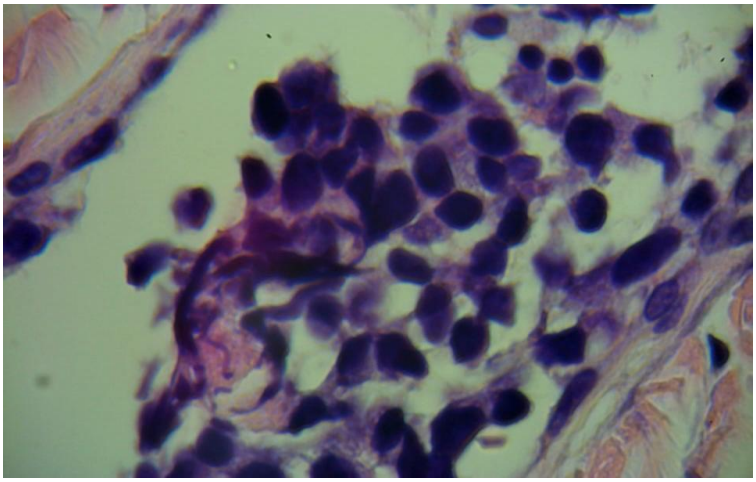

Figure 4: Skin biopsy showing a blood vessel filled by anaplastic cells with hyperchromatic nuclei and scarce cytoplasm.

Discussion

Intravascular large B-cell lymphoma is a rare extranodal diffuse lymphoma type, accounting for less than 1% of all lymphomas, characterized by abnormal cells in the lumen of small blood vessels.[1] The disease is known by its dermatological, neurological and hematological findings.[2,3] The pathogenesis is still unclear, although some hypotheses include the unbalance of molecules and metalloproteinases, expressing the ones involved in cell migration and endothelium adhesion, and lacking those involved in regulation of lymphocyte trafficking, extravasation and migration, integrin activation, and parenchymal invasion.[4-7] There are also case reports relating with infectious agents such as herpes virus 8, HIV, human T-lymphotropic virus type I and EBV.[8-11]

The diagnosis is made ranging 13-90 years, primarily afflicting the elderly, just like reported in our case. Some reviews describe a prevalence higher in males.[12,13] The disease can be manifested by nonspecific symptoms such as the B-symptoms: fever, weight loss and night sweats; neurological disorders in over 60% of the patients; and dermatological involvements, which are the most common.[14]

Cutaneous involvements include maculopapular eruption, nodules, violaceous plaques, purpura, ulcers, orange-peel-like chances and cellulite-like infiltration.[3] The lesions are usually located in the submammary region and breast, extremities and lower abdomen. It can be painful and desquamates.13,15] The prognosis is better in patients with exclusive skin involvement.[13]

Neurological symptoms are characterized by encephalopathy, seizure, myelopathy, radiculopathy, or neuropathy.[16,17] The imaging exams alteration is nonspecific but essential helping with differential diagnosis, such as isquemia and vasculitis. It can be presented with matter changes, scattered microinfarcts and widespread enhancement. Neurological symptoms were not found in our case.[18]

The hemophagocytic syndrome is also described in some forms, with bone marrow involvement, hepatosplenomegaly and thrombocytopenia[19]. Although our patient had bone marrow involvement with anemia, there were no other symptoms, physical exam or laboratorial alterations. The localization and characteristics of the skin manifestation described in literature were similar to the one we found in this case.

The diagnosis is made by cutaneous biopsy, which is preferred on hypervascular lesions, and bone marrow biopsy.[20] A recent report defends random skin biopsy from normal-appearing skin for the early diagnosis for patients with laboratory and clinical features.[1]

The histopathological findings presented in our case were consistent with those described in reports which are large neoplastic cells with high nuclear cytoplasmic ratio and scant cytoplasm, as well as a nuclear outline smooth and less often with irregular contour.[1] A few cases with smaller cells have been reported, although this is not the usual finding.[21] Mitotic figures and high proliferative index marked by Ki-67 immunostaining are indicative of the active replication of the cells inside the blood vessels. On immunophenotype CD20 expression is a marker of the disease, although some cases of CD20 negative have been reported.[22] In those cases, alternative B cell markers such as CD79a and Pax-5 can help with the diagnosis. Also, CD5 markers have been reported, which represented, in some reports, more neurological cases and CD10 positivity.[1]

Some laboratory alterations such as anemia, thrombocytopenia and leukopenia, abnormal hepatic and renal function tests are reported.[2] Elevation of lactate dehydrogenase and soluble interleukin 2 receptor can also be found.[1]

There is no therapeutic approach considered to be most appropriate. The main chemotherapy regimen involves the association of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone, which has been

described with good results, decreasing the mortality rate. A recent phase 2 trial showed the association of the R-CHOP treatment with high-dose methotrexate and intrathecal chemotherapy in patients with no apparent Central Nervous System involvement with a progression-free survival of 76%, showing promising clinical outcomes.[23]

The clinical, histopathology, immunohistochemical analysis and laboratorial findings presented in our case were consistent with the ones described in literature. We aim to report this case since it is a rare disease with challenging diagnosis and no pathognomonic symptoms or signs. In this case the diagnosis could be defined only with skin biopsy and immunohistochemical, with no other altered exams. Also, the relation with the breast implant 18 years before the symptoms is also relevant considering the association between lymphoma and silicon implant. Although there are several organ involvements, it is important to keep in mind there are cases with isolated organ involvement such as our patient on the first appointment.

Conclusion

IVLBCL is a rare type of lymphoma with nonspecific symptoms and difficult diagnosis. Although many systems can be involved, there are cases with skin manifestations only, and keeping this in mind can help to a precocious diagnosis and treatment.

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