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CASES FOR DIAGNOSIS

Nodules on the Legs

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Patient History

An 88-year-old woman consulted for rapidly growing, asymptomatic cutaneous lesions on the distal third of the left leg from 3 months previously. The patient reported no local or systemic symptoms.

Physical Examination

Examination revealed 4 erythematous nodular tumors, of firm consistency and with a smooth surface. The tumors showed no ulceration and varied in size from 2 to 6 cm (Figure 1). No enlarged lymph nodes were palpated and there was no apparent visceromegaly.

Additional Tests

The routine laboratory workup, lymphocytes in peripheral blood, imaging studies (computed tomography), and bone marrow study showed no signs of extracutaneous disease.

Histopathology

Histology revealed an atypical, densely cellular lymphoid infiltrate with a follicular growth pattern in the dermis and subcutaneous tissue (Figure 2). The infiltrate was composed of large cells resembling centroblasts or immunoblasts. Mitotic figures were common and the mitotic index was high. The immunohistochemical study was strongly positive for CD20, BCL-2 (Figure 3), and MUM-1/IRF4; weakly positive for BCL-6; and negative for T, CD30, and CD10 markers. Monoclonal rearrangement of immunoglobulin heavy chains was not detected by polymerase chain reaction. The t(14;18) translocation was also not found by polymerase chain reaction or fluorescence in situ hybridization.

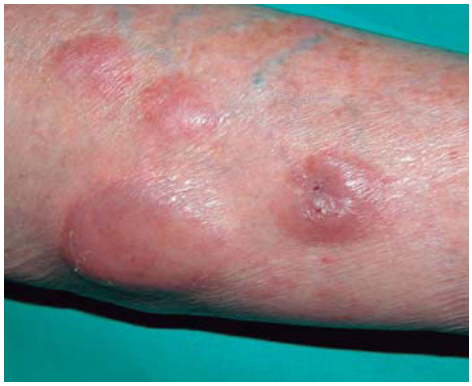

Figure 1.

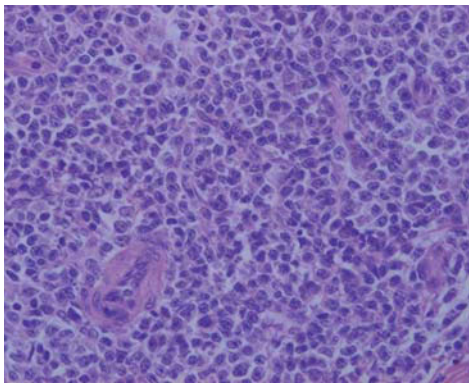

Figure 2. Hematoxylin-eosin, ×200.

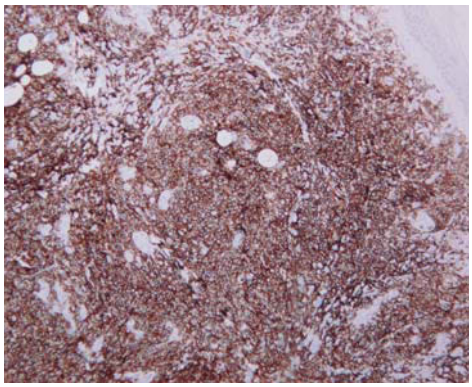

Figure 3. Positive immuno-staining for BCL-2, ×200.

What is your diagnosis?

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Diagnosis

Primary cutaneous diffuse large B-cell lymphoma (PCLBCL), leg type

Course and Treatment

Intravenous treatment with rituximab was started at a dose of 375 mg/m^2/wk. The infusions were well tolerated by the patient, but treatment was discontinued after the second infusion due to lack of response.

Comments

Primary cutaneous B-cell lymphomas include several independent clinical and pathologic entities, such as primary cutaneous marginal zone lymphomas, primary cutaneous follicular center lymphomas (PCFCL), PCLBCL, leg type, and PCLBCL, other.[1] This new consensus classification for B-cell lymphomas attempts to clarify and separate the various diseases, stressing the clinical, histologic, immunohistochemical, molecular, prognostic, and therapeutic differences between PCFCL and PCLBCL.[1]

PCLBCL, leg type, affects mainly older women, usually on the distal third of the lower limb.[1-4] Histologically, the infiltrate is diffuse and composed of large cells similar to centroblasts or immunoblasts, with frequent mitotic figures and a high mitotic index.[1-4] The cells express CD20, CD79a, BCL-6, BCL-2, and MUM-1/IRF4.[1-4] CD10 is usually negative and the t(14;18) translocation is not usually found in this type of lymphoma.[5] PCLBCL, leg type, is a more aggressive lymphoma than PCFCL, with a risk of extracutaneous involvement and a need for more aggressive therapies, such as chemotherapy or rituximab.[1-4]

The main differential diagnosis in our case was performed with follicular center lymphomas, which express BCL-2. Systemic follicular center lymphomas with secondary involvement of the skin are BCL-2 positive; however, they also present the t(14;18) translocation and, by definition, exhibit extracutaneous involvement at the time of diagnosis.[1] PCFCL are negative for BCL-2, although isolated cases that express this protein have been described. Some authors have suggested that the presence of BCL-2 in more than 50% of cells, associated with a diffuse growth pattern and the predominance of large cells, is indicative of poor prognosis and aggressive behavior of PCFCL.[6]

The World Health Organization-European Organization for Research and Treatment of Cancer classification of cutaneous lymphomas includes PCLBCL, leg type, within the diffuse large B-cell lymphomas.[1] Although the follicular growth pattern of the infiltrates in the case we describe makes it debatable whether the lymphoma should be classified as PCLBCL, leg type, the clinical characteristics (older woman, distal area of the leg, aggressive course), histologic characteristics (large cells similar to centroblasts/immunoblasts and high mitotic index), and immunohistochemical characteristics (CD20, BCL-6, BCL-2, and MUM-1/IRF4) are consistent with this type of lymphoma.

Another diagnostic possibility, in view of the nodular pattern of the infiltrate, would be to include this case within the follicular lymphomas that strongly express BCL-2 and, as mentioned by some authors, may have a worse prognosis.[6] However, all other clinical, histologic, and immunophenotypic data indicate that this diagnosis is less likely.

Conflicts of Interest
The authors declare no conflicts of interest.

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