JAMA Dermatology Clinicopathological Challenge

Leonine Facies and Madarosis in a Man With Shortness of Breath

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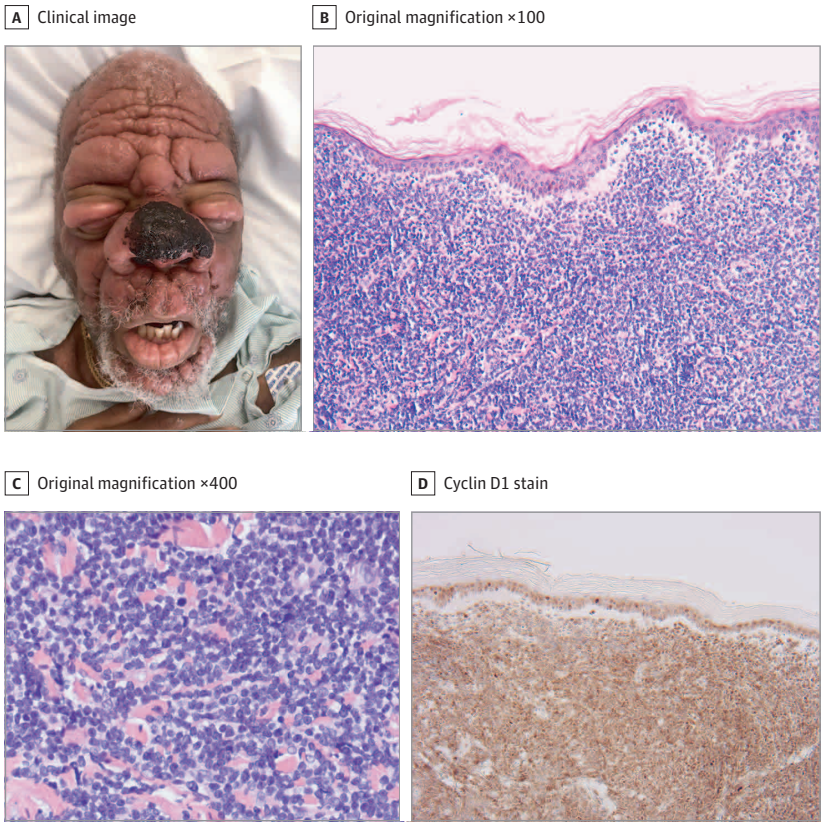

Figure. A, Infiltrative plaques and nodules obscuring normal facial architecture. B and C, Histopathologic images show normal epidermis with dense diffuse dermal lymphoid infiltrate composed of small to medium cells with irregular nuclear contours (hematoxylin-eosin stain). D, Immunohistochemistry shows diffusely positive cyclin D1 staining.

A man in his 60s presented as a transfer from an outside hospital. The division of dermatology was consulted for evaluation of lesions on the face, chest, back, and arms that were gradually increasing in size and number over the past year. Physical examination revealed leonine facies with madarosis and an eschar on the nasal dorsum (**Figure**, A). Red-to-brown dome-shaped papules coalescing into plaques were present on the upper extremities. The lesions were nontender and nonpruritic. Cervical and axillary lymph nodes were palpable. The patient had a muffled voice and reported shortness of breath with exertion. Results of laboratory investigation demonstrated marked leukocytosis with a white blood cell count of 77.5 × 10^3/uL with 76.5% lymphocytes. No blasts were present on peripheral smear. Computed tomography of the chest, abdomen, and pelvis demonstrated multiple enlarged mediastinal, axillary, subpectoral, abdominopelvic, and inguinal lymph nodes. Small pulmonary nodules were also detected. A punch biopsy was obtained from the right arm (Figure, B, C, and D).

WHAT IS YOUR DIAGNOSIS?

A. Mantle cell lymphoma

B. Folliculotropic mycosis fungoides

C. Diffuse large B-cell lymphoma

D. Marginal zone lymphoma

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Diagnosis

A. Mantle cell lymphoma

Clinical and Histopathologic Course

Histopathological findings revealed normal epidermis with a dense diffuse dermal infiltrate of small to medium lymphocytes with irregular nuclear contours. Results of CD20 and cyclin D1 stains were diffusely positive.

The patient had been diagnosed with stage IV mantle cell lymphoma 2 years prior to presentation on the basis of a lymph node biopsy in the setting of unexplained weight loss and night sweats. Further investigation including fluorescence in situ hybridization testing and flow cytometry was confirmatory. The patient was previously treated at an outside institution, and multiple courses of chemotherapy had failed. On admission, the patient was started on treatment with high-dose steroids intravenously. Despite this, he developed upper airway obstruction and was intubated. He then became febrile, encephalopathic, and nonresponsive. He subsequently died in hospice.

Discussion

Mantle cell lymphoma is a rare type of non-Hodgkin B-cell lymphoma. It is characterized by a cytogenetic translocation resulting in overexpression of the cyclin D1 protein, which is required for progression from G1 to S phase of the cell cycle.[1] Mantle cell lymphoma often involves extranodal sites, including the bone marrow, gastrointestinal tract, and Waldeyer ring. In this patient, involvement of the Waldeyer ring led to upper airway obstruction that necessitated intubation. Men older than 60 years are the most commonly affected demographic. Mantle cell lymphoma is often aggressive and portends a poor prognosis. The median survival time after diagnosis is 4 to 5 years.[1]

Histologic features include diffuse monomorphous infiltrates of intermediate-sized lymphocytes with irregular nuclei and nucleoli. The immunophenotype of malignant B-cells involves coexpression of CD20, CD5, and cyclin D1, which is positive in more than 95% of cases. In rare cyclin D1–negative cases, SOX11 can be a useful diagnostic marker.[2,3] In addition, CD23 expression is often absent and is useful in distinguishing mantle cell lymphoma from chronic lymphocytic leukemia.

Cutaneous involvement by mantle cell lymphoma is rare and occurs as secondary dissemination in stage IV disease. Approximately 17% of stage IV cases will exhibit skin involvement.[4] Typically, cutaneous mantle cell lymphoma presents with solitary or multiple nodules. Leonine facies is an exceedingly rare presentation, with only 1 prior case reported to our knowledge.[5] The differential diagnosis for leonine facies is broad and includes entities such as lepromatous leprosy, scleromyxedema, lipoid proteinosis, nonlangerhans cell histiocytosis, and pachydermoperiostosis, in addition to cutaneous lymphoma.

Subtypes of cutaneous T-cell lymphoma have been reported to present in this manner, including folliculotropic mycosis fungoides, classic mycosis fungoides, and Sézary syndrome. Folliculotropic mycosis fungoides can be distinguished histopathologically by the presence of atypical lymphocytes invading the follicular epithelium. In addition, immunohistochemistry demonstrates CD3 and CD4 positivity with loss of CD7.[6]

Less commonly, B-cell lymphomas may present with leonine facies. In such cases, histopathology and immunohistochemistry can be used to differentiate between subtypes. Diffuse large B-cell lymphoma often displays a dense dermal infiltrate of large, atypical lymphocytes that variably express BCL2, MUM1, FOXP1, and MYC. Marginal zone lymphoma is typically characterized by nodular dermal infiltrates surrounded by pale small to medium lymphocytes with indented nuclei. Cells typically stain positively for BCL2 and negatively for BCL6 and CD10. Cases of mantle cell lymphoma are uniquely distinguished by expression of cyclin D1, a highly sensitive and specific marker.

In summary, skin involvement by mantle cell lymphoma is rare yet important to recognize because it signifies disseminated disease and an aggressive clinical course. It is crucial to differentiate this entity from primary cutaneous B-cell lymphomas, such as marginal zone lymphoma and follicle center lymphoma, which may be localized to the skin and often exhibit indolent behavior. Careful analysis of histopathologic features, immunohistochemical studies, and correlation with systemic diagnostic examination are necessary to establish the diagnosis.

ARTICLE INFORMATION

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