Primary cutaneous marginal zone lymphoma with leptomeningeal involvement and a durable response to rituximab

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BACKGROUND

Primary cutaneous marginal zone lymphoma (PCMZL) is an indolent B-cell lymphoma, typically characterized by frequent cutaneous recurrences and rare systemic involvement. Lymph nodes, bone, and bone marrow are commonly affected sites in rare cases of extracutaneous disease. Secondary involvement of central nervous system (CNS) in confirmed PCMZL is unreported.

CASE PRESENTATION

A 47-year-old man presented with a slowly expanding, asymptomatic lesion on the right arm of 1-year duration (Fig 1, *A* and *B*). Skin biopsy as reviewed by the Department of Pathology at Memorial Sloan Kettering Cancer Center was consistent with low-grade cutaneous B-cell lymphoma of marginal zone type (Fig 2, *A* and *B*). The immunohistochemical stains showed mixed population of cells positive for CD3 and CD20 and negative for CD10 and BCL-2. Sheets of $CD20^{+}$ cells showed λ light chain restriction (Fig 2, *C* and *D*). Findings from staging workup, including complete blood count, comprehensive metabolic profile, protein electrophoresis, serum immunoglobulin levels, and computed tomography scans of the chest, abdomen, and pelvis were within normal limits.

Abbreviations used:

CNS:	central nervous system
CSF:	cerebrospinal fluid
PCMZL:	primary cutaneous marginal zone lymphoma
WBC:	white blood cells

New lesions subsequently developed on the patient's arms and lower back, which showed identical histology and clonal immunoglobulin heavy chain (IgH) gene rearrangement. Rapid progression of disease prompted us to perform restaging workup including repeat computed tomography scans and bone marrow biopsy, results of which were again within normal limits. The patient was treated with topical and intralesional steroids with resolution of most lesions. Follow-up every 3 to 6 months found minimal cutaneous disease for nearly 3.5 years, when a transient left facial droop developed that resolved spontaneously. He later reported persistent headaches with diplopia associated with right fourth cranial nerve palsy. The diplopia gradually resolved but then recurred with new right sixth cranial nerve palsy. Electroencephalogram and gadolinium-enhanced magnetic resonance imaging of spine and orbits were unremarkable. Cerebrospinal fluid (CSF)

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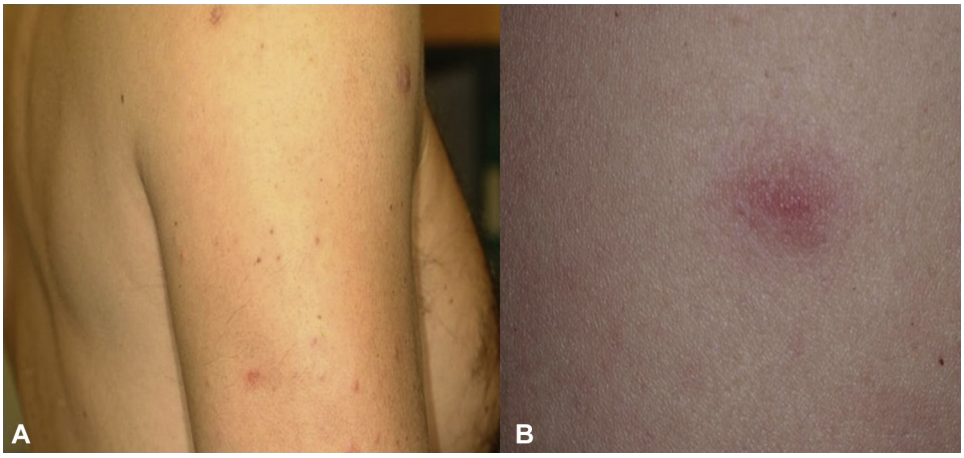

Fig 1. Clinical overview images. **A**, Multiple red papules on upper arm. **B**, Close-up view of the erythematous papule.

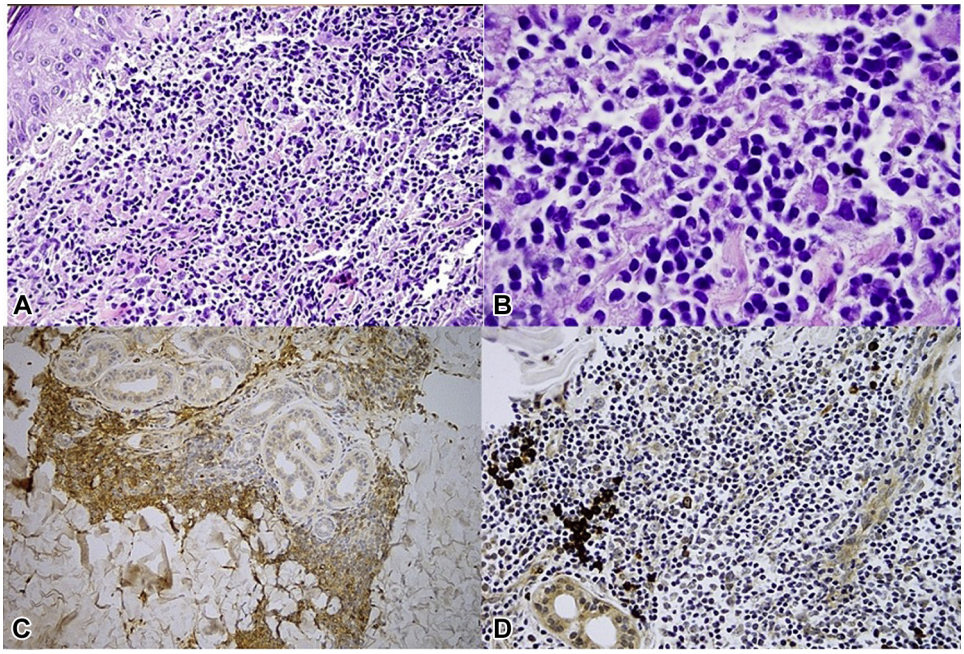

Fig 2. Representative photomicrographs of skin biopsies. **A**, Striking infiltrate of atypical lymphoplasmacytoid cells involving superficial and deep dermis. **B**, interstitial and perivascular infiltrate of atypical small-to-intermediate lymphocytes, some with abundant cytoplasm and plasmacytic differentiation. **C**, The B lymphocytes show a dominance of λ light chain. **D**, Kappa is essentially negative. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×200; **B**, ×1000.)

analysis found elevated WBCs (27 cells/μL, 99% lymphocytes), 71 mg/dL protein, and 62 mg/dL glucose. Cytology (Fig 3) and flow cytometric results were consistent with B-cell lymphoma, with λ to κ ratio of 41:1. Polymerase chain reaction of CSF found clonal rearrangement of IgH chain identical to the clone in skin. Positron emission tomography scan and bone marrow biopsy were unremarkable. Fluorescence in situ hybridization performed to rule out t (11; 18) (q21; q21) translocation was negative.

The patient received high-dose rituximab (750 mg/m^2 weekly × 4 weeks), without initial symptomatic improvement. CSF testing at 2 months found significant reduction in WBCs (5 cells/μL, 97% lymphocytes) and light chain–restricted B cells (λ to κ ratio of 5:1) but persistent IgH clone. A second course of high-dose rituximab led to marked improvement in headaches. CSF testing at 1 month found a WBC count of 7 cells/μL and 95% lymphocytes, absence of light chain restriction