Rosai-Dorfman disease with a concurrent mantle cell lymphoma

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Rosai-Dorfman disease (RDD), also known as *sinus histiocytosis with massive lymphadenopathy* (SHML), is a rare, benign histiocytic disorder characterized by generalized lymphadenopathy and constitutional symptoms.[1] The classic presentation of RDD is painless cervical lymphadenopathy with associated fever, night sweats, and weight loss.[2] Extranodal involvement is present in up to 40% of cases of RDD, with the skin being the most common site.[1] Although considered benign, 10% of patients with RDD have coexisting immunologic abnormalities, such as postinfectious conditions and hematologic malignancies.[1,2] There have been only 25 reported cases of RDD in association with Hodgkin or non-Hodgkin lymphomas.[3-5] We present a case of RDD in association with mantle cell lymphoma with a primary presentation of extranodal skin involvement without constitutional symptoms.

Abbreviations used:

RDD: Rosai-Dorfman disease
SHML: sinus histiocytosis with massive lymphadenopathy

CASE REPORT

In August of 2014, a 54-year-old man presented with a several-month history of nontender, nonpruritic well-circumscribed erythematous plaques on his temples. The patient was otherwise feeling well without constitutional symptoms. A biopsy at that time found a benign lymphocytic infiltrate consistent with pseudolymphoma. Additional evaluation with blood work and imaging was advised but not completed by the patient as he stated the lesions self-resolved. In June 2017, the patient returned to the clinic with similar lesions on the temples with additional widespread, asymptomatic erythematous papules on the trunk and lower extremities (Fig 1, *A*). The patient was otherwise feeling well and denied any constitutional symptoms.

Three skin biopsy specimens were taken from the left central temple, the left lower back, and right medial distal pretibial region (Fig 2). Histopathologic examination found intact lymphocytes and plasma cells within the cytoplasm of histiocytes (emperipolesis). Immunohistochemically, the histiocytes were positive for CD68 and CD163 with coexpression of S100. Based on the clinical and histopathologic findings, a diagnosis of Rosai-Dorfman was made.

Laboratory evaluation found a normocytic anemia (hemoglobin, 12.4 g/dL), eosinophilia (11%), and peripheral blood flow cytometry showing excess polyclonal IgG and IgA. A total-body competed tomography scan found extensive lymphadenopathy within the chest, abdomen, retroperitoneum, and pelvis; moderately severe splenomegaly; a mural mass in the sigmoid colon; and mild pulmonary nodularity in the left lower lobe. Bone marrow and lymph node biopsies were performed and were consistent with mantle cell non-Hodgkin lymphoma stage IVa.

The patient was enrolled in a clinical trial at MD Anderson Hospital for further treatment, which involved ibrutinib/rituximab and hyperCVAD for consolidation (fractionated cyclophosphamide, vincristine, Adriamycin, and dexamethasone). Two cycles of therapy resulted in a marked decrease in his number of skin lesions (Fig 1, *B*) and resolution of his

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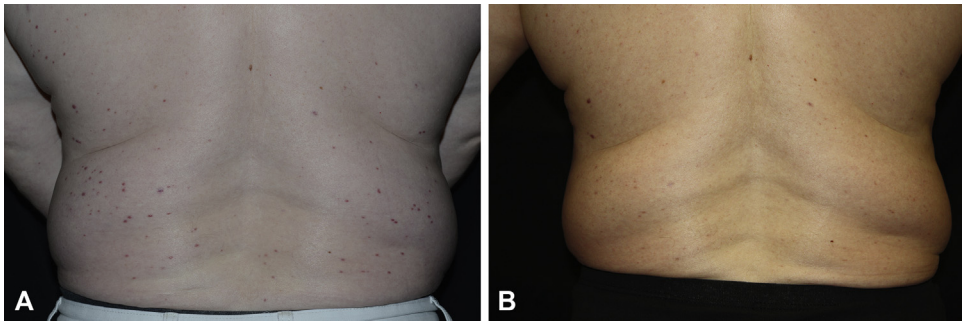

Fig 1. Patient observed initially (**A**) and 5 months after consolidation therapy (**B**).

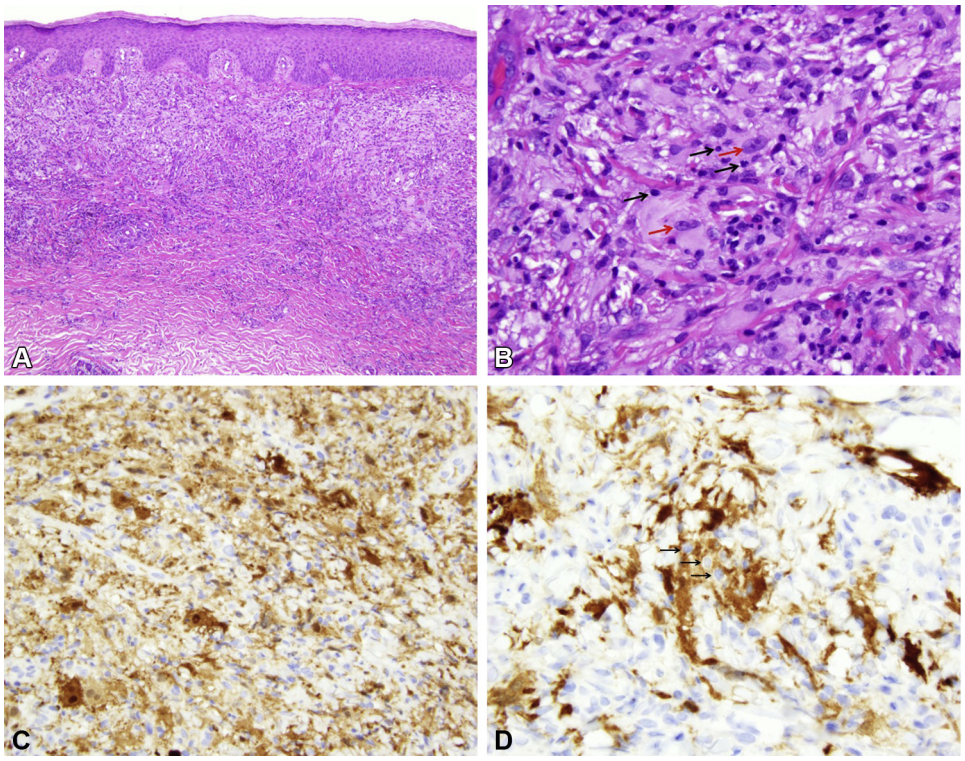

Fig 2. **A**, Biopsy findings show a diffuse infiltrate of mononuclear cells with abundant pale cytoplasm in the papillary dermis. **B**, On higher power, histiocytes with abundant cytoplasm and conspicuous nucleoli (*red arrows*) and emperiopolesis of lymphocytes and neutrophils (*black arrows*) are seen. **C**, $S100^{+}$ staining of histiocytes. **D**, Higher-power view of $S100^{+}$ histiocytes with negative staining of intracytoplasmic hematolymphoid cells (*arrows*).

widespread lymphadenopathy. The patient has remained free of constitutional symptoms.

DISCUSSION

RDD or SHML was first described in 1969, since then more than 400 cases have been reported in the RDD registry.[1,6] This disease is usually seen in children and young adults with a predilection for white males and those of African descent.[6] RDD is a rare entity; even rarer are reports of concomitant lymphoma. This report is the first, to our knowledge, to demonstrate RDD with concomitant mantle cell lymphoma. After reviewing the relevant literature, we found 25 cases of RDD in association with Hodgkin and non-Hodgkin lymphoma; of these, most of these cases (70%) had simultaneous diagnosis of RDD and lymphoma (Table I).[3-5] The pathogenesis of RDD is unclear. Suggested possibilities include a macrophage colony stimulating factor resulting in immune-suppressive abnormal histiocytes (an immune-related phenomenon), an exaggerated infectious response to an agent (both viral and bacterial), and/or a genetic predisposition.[2,21] Our patient's

Table I. Cases of RDD and malignant lymphoma

Case no.	Reference	Age/sex	Lymphoma type	Time interval
1	Foucar et al,[7] 1983	6/M	Large cell immunoblastic	NHL 8 mo after RDD
2	Rangwala et al,[8] 1990	62/M	Small noncleaved	NHL 4 y after RDD
3	Falk et al,[9] 1991	49/M	HD, MC	Concurrent
4		24/M	HD, NOS	Concurrent
5	Maia et al,[10] 1995	39/M	HD, LP	Concurrent
6		11/M	HD, LP	Concurrent
7	Koduru et al,[11] 1995	52/M	T cell	NHL 8 y after RDD
8	Alliot et al,[12] 1996	Unknown	HD, NOS	HD before RDD
9	Krzemieniecki et al,[13] 1996	17/F	High grade, NOS	NHL 5 y after RDD
10	Lossos et al,[14] 1997	67/M	Small lymphocytic	NHL 12 y before RDD
11	Lu et al,[15] 2000	62/F	FL grade II	Concurrent
12		30/F	HD, LP	Concurrent
13		28/M	HD, LP	Concurrent
14		63/F	FL grade I	Concurrent
15	Menzel et al,[16] 2003	?/F	NHL, NOS	NHL 6 y before RDD
16	Garel et al,[17] 2004	8/F	Anaplastic large cell	Concurrent
17	Shoda et al,[18] 2004	64/M	Diffuse large B cell	Concurrent
18	Moore et al,[2] 2008	33/F	Diffuse large B cell	Concurrent
19	Luca Di Tommaso et al,[19] 2010	65/F	Relapsed FL	Concurrent
20	Cvetkovic et al,[20] 2010	39/F	HD, NS	HD 2 y after RDD
21	Pang et al,[21] 2011	80/F	Nodal MZL	Concurrent
22	Wu et al,[22] 2012	42/M	Diffuse large B cell	Concurrent
23	Akria et al,[3] 2013	50/M	Nodal MZL	Concurrent
24	Fernandez-Vega et al,[4] 2014	51/F	HD, NS	Concurrent
25	Garg et al,[5] 2017	16/M	Anaplastic large cell	Concurrent
26	Present case	54/M	NHL, mantle cell	Concurrent

FL, Follicular lymphoma; *HD*, Hodgkin disease; *LP*, lymphocyte predominant; *MC*, mixed cellularity; *MZL*, marginal zone lymphoma; *NHL*, non-Hodgkin lymphoma; *NOS*, not otherwise specified; *NS*, nodular sclerosis.
Note. Table was created/adapted by Akria et al[3] with additional cases added since their publication in 2013.

concurrent diagnosis of mantle cell lymphoma after his diagnosis of RDD, and the observation that consolidation therapy of his lymphoma resulted in improvement of his RDD, lends support for the possible immune-mediated etiology of RDD.

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