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.3 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.

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 (emperipolysis). 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 computed 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

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

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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
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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Table I. Cases of RDD and malignant lymphoma

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