

Cutaneous Rosai-Dorfman Disease

Maren Gaul, DO; Timothy Chang, MD

PRACTICE POINTS

- Rosai-Dorfman disease generally is characterized by painless cervical lymphadenopathy and systemic involvement.
- Cutaneous Rosai-Dorfman disease can clinically present with great variety, mimicking many other dermatologic conditions.
- Patients presenting with cutaneous lesions and lymphadenopathy warrant workup with systemic imaging.

Cutaneous Rosai-Dorfman disease (CRDD) is a rare form of Rosai-Dorfman disease (RDD) (also known as sinus histiocytosis with massive lymphadenopathy) that has a varied clinical presentation, an unknown etiology, and multiple treatment options that lack efficacy. We present a case of a 31-year-old woman who presented with grouped flesh-colored to light pink papules and plaques within a hyperpigmented patch on the thigh that were treated with topical, oral, and intralesional steroids with minimal improvement.

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Case Report

A 31-year-old black woman presented with a slow-spreading pruritic rash on the right thigh of 1 year's duration. She had previously seen a dermatologist and was prescribed triamcinolone acetonide cream 0.1% and mupirocin ointment 2% but declined a biopsy. Review of symptoms was negative for any constitutional symptoms. Family history included hypertension and eczema with a personal history of anxiety. Clinical examination revealed grouped flesh-colored to light pink papules and plaques within a hyperpigmented patch on the right medial thigh (Figure 1).

Histopathology—A punch biopsy was negative for fungal, bacterial, or acid-fast bacilli culture. Histopathologic evaluation demonstrated a dense dermal infiltrate of large histiocytes admixed with inflammatory cells composed predominantly of lymphocytes and plasma cells. The histiocytes within the inflammatory infiltrate had vesicular nuclei and abundant eosinophilic cytoplasm (Figure 2A). Areas of emperipolesis were noted (Figure 2B). The large histiocytes stained positive for S-100 protein (Figure 2C) and negative for CD1a.

Course and Treatment—Laboratory studies revealed leukopenia. Prior to histopathologic results, empiric treatment was started with doxycycline 100 mg twice daily for 2 weeks. Once pathology confirmed the diagnosis of Rosai-Dorfman disease (RDD), computed tomography of the chest, abdomen, and pelvis was performed and within normal limits. Due to the lack of systemic involvement, we diagnosed the rare form of purely cutaneous Rosai-Dorfman disease (CRDD). In subsequent visits, treatment with



FIGURE 1. Grouped flesh-colored to light pink papules and plaques within a hyperpigmented patch on the right medial thigh.

Dr. Gaul was from Western Reserve Hospital, Cuyahoga Falls, Ohio, and currently is from Tanana Valley Clinic, Fairbanks, Alaska. Dr. Chang is from Case Western Reserve University School of Medicine, Beachwood, Ohio.

The authors report no conflict of interest.

Correspondence: Maren Gaul, DO, 1001 Noble St, Ste 300, Fairbanks, AK 99701 (marenness@gmail.com).

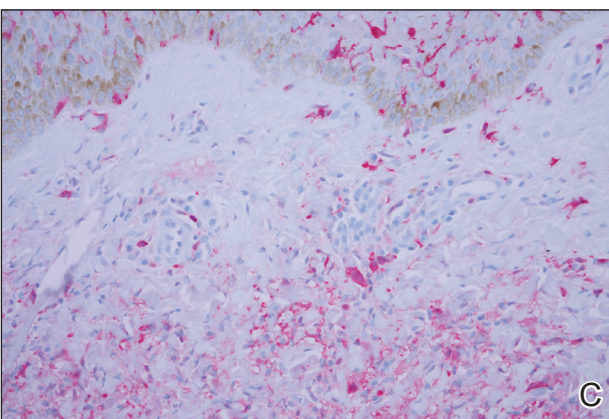
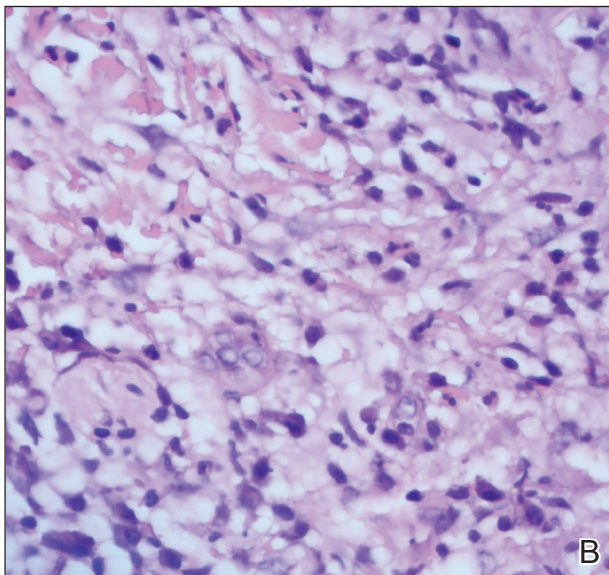
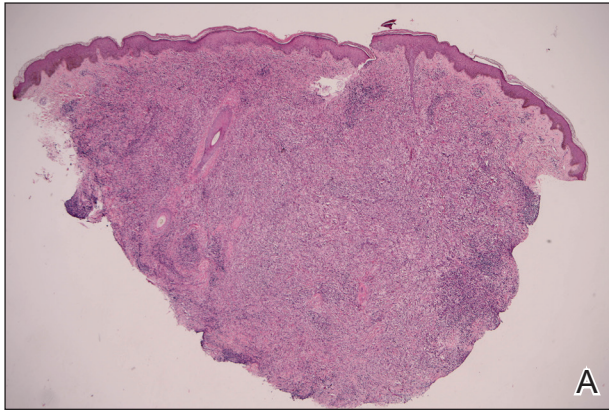


FIGURE 2. A, A punch biopsy showed histiocytes within the inflammatory infiltrate had vesicular nuclei and abundant eosinophilic cytoplasm (H&E, original magnification $\times 4$). B, Emperipolesis was noted (H&E, original magnification $\times 60$). C, Histiocytes stained positive for S-100 protein (original magnification $\times 10$).

oral prednisone (40 mg daily for 1 week followed by 20 mg daily for 1 week) and intralesional triamcinolone acetonide (5 areas on the right medial thigh were injected with 1.0 mL of 10 mg/mL) was attempted with mild improvement, though the patient declined surgical excision.

Comment

Rosai-Dorfman disease (also known as sinus histiocytosis with massive lymphadenopathy) is a non-Langerhans cell histiocytosis.¹ There are 2 main forms of RDD: one form that affects the lymph nodes and in certain cases the extranodal organs, and the other is purely CRDD. Cutaneous RDD is extremely rare and the etiology is unknown, though a number of viral and immune causes have been postulated. Cutaneous RDD presents as solitary or numerous papules, nodules, and/or plaques. Treatment options include steroids, methotrexate, dapsone, thalidomide, and isotretinoin, with varying efficacy reported.¹

Extranodal forms occur in 43% of RDD cases, with the skin being the most common site.¹ Other extranodal sites include the soft tissue, upper and lower respiratory tract, bones, genitourinary tract, oral cavity, gastrointestinal tract, orbits, testes, and rarely central nervous system involvement.²

Approximately 10% of RDD patients exhibit skin lesions, and in 3% it is contained solely in the skin.³ Pure CRDD was first documented in 1978 by Thawarani et al⁴ who presented the case of a 48-year-old man with a solitary nodule on the shoulder.

Cutaneous RDD and RDD may be distinct clinical entities. Cutaneous RDD has a later age of onset than RDD (median age, 43.5 years vs 20.6 years) and a female predominance (2:1 vs 1.4:1). It most commonly affects Asian and white individuals while the majority of patients with RDD are of African descent with rare reports in Asians.¹

The etiology of CRDD remains unknown with hypotheses of viral and immune causes such as human herpesvirus 6, Epstein-Barr virus, and parvovirus B19. The polyclonal nature of the cell infiltrate and the clinical progression of RDD suggest a reactive process rather than a neoplastic disorder.¹ Rosai-Dorfman disease has been hypothesized to be closely related to autoimmune lymphoproliferative syndrome, an inherited disorder associated with defects in Fas-mediated apoptosis.⁵

Histologic findings in CRDD are similar to those in RDD, with a superficial and deep perivascular infiltrate of lymphocytes and plasma cells. A diffuse and nodular dermal infiltrate of foamy histiocytes exists in a background infiltrate of lymphocytes and plasma cells. Foamy histiocytes may be seen in dermal lymphatics, and lymphoid follicles with reactive germinal centers also may be present. Emperipolesis, the presence of intact inflammatory cells within histiocytes, is common in CRDD. Less often, histiocytes may contain plasma

cells, neutrophils, and red blood cells. Mitoses and nuclear atypia are rare. Cutaneous RDD histiocytes stain positive for S-100 protein, CD4, factor XIIIa, and CD68, and negative for CD1a. Birbeck granules are absent on electronic microscopy of CRDD tissue, eliminating Langerhans cell histiocytosis.^{1,3,5}

The clinical diagnosis of CRDD is hard to confirm in the absence of lymphadenopathy. The lesions in CRDD may be solitary or numerous, usually presenting as papules, nodules, and/or plaques. More rarely, the lesions may present as pustules, acneform lesions, mimickers of vasculitis and panniculitis, macular erythema, large annular lesions resembling granuloma annulare, or even a breast mass.^{1,3} One case report with involvement of deep subcutaneous fat presented with flank swelling beneath papules and nodules.⁶

The most common site of lesions in CRDD is the face, with the eyelids and malar regions frequently involved, followed by the back, chest, thighs, flanks, and shoulders.^{1,5} Rarely, CRDD may be associated with other disorders, including bilateral uveitis, antinuclear antibody-positive lupus erythematosus, rheumatoid arthritis, hypothyroidism, lymphoma, and human immunodeficiency virus.¹

Numerous treatments have been attempted, yet the response often is poor. Because RDD is a benign and self-limiting disease, less aggressive therapeutic approaches should be used, if possible. Surgical excision of the lesions has been helpful in certain cases.⁶ Cryotherapy and local radiation, topical steroids, or laser treatment also have been found to improve the condition.^{1,7} For refractory cases, dapsone and thalidomide have been effective. Mixed results have been observed with isotretinoin and imatinib; some patients improved whereas others did not. Utikal et al⁸ described a patient with complete remission of CRDD after receiving imatinib therapy; however, a different study reported a patient with

CRDD who was completely resistant to this treatment.⁹ One case presenting on the breast did not respond to topical steroids, acitretin, and thalidomide but later responded to methotrexate.¹⁰

Conclusion

Cutaneous RDD is an unusual clinical entity with varied lesions. Generally, CRDD follows a benign clinical course, with a possibility of spontaneous remission. Further studies are required to confidently classify the etiology and variance between both RDD and CRDD.

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