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CASE REPORT

# Cutaneous Rosai-Dorfman disease in a 40-year-old female: A case report

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## ABSTRACT

**INTRODUCTION** Rosai-Dorfman disease is a rare disease that manifests with painless cervical lymphadenopathy, fever, anemia, an elevated erythrocyte sedimentation rate (ESR), and hypergammaglobulinemia. Extranodal lesions occur in 1/3 of patients, and the skin is involved in more than 10% of cases. Purely cutaneous disease is uncommon and only about more than 100 cases have been reported. Cutaneous Rosai-Dorfman Disease (CRDD) appears to be a distinct entity with different age and race predilection from cases with lymph node involvement.

**CASE REPORT** This is a case of a 40-year-old Filipino female who presented with multiple erythematous papules and plaques with pustules on the cheeks. Skin punch biopsy showed a dense dermal infiltrate of polygonal histiocytes with abundant cytoplasm and vesicular nuclei. Emperipolesis was also present. The histiocytes were highlighted by the immunohistochemical stains S-100 and CD68 and was CD1a negative. Complete blood count and ESR were normal. Cervical lymphadenopathy was absent. Findings were consistent with Cutaneous Rosai-Dorfman disease. The patient was started on methotrexate at 15mg/week with folic acid supplementation. Mild soap, benzoyl peroxide 5% gel and tretinoin 0.05% cream once daily were maintained during the treatment course. There was significant decrease in erythema and size of existing lesions after 2 months. The patient was referred to a hematologist for monitoring of possible future systemic involvement.

**CONCLUSION** Because of its rarity, clinicopathological correlation is always mandatory to establish a diagnosis of CRDD. Immunohistochemical stains are required to differentiate this entity form other forms of Langerhans cell histiocytosis. Multidisciplinary referral is required to rule out concomitant systemic involvement.

**KEYWORDS** Cutaneous Rosai-Dorfman Disease, Non-langerhans cell histiocytosis, lymphadenopathy

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## INTRODUCTION

Rosai-Dorfman Disease (RDD) is a rare disorder belonging to the group of non-langerhans cell histiocytosis (NLH). First described in 1969, RDD also known as sinus histiocytosis with massive lymphadenopathy, is a benign and self-limited disease characterized by fever, anemia, elevated erythrocyte sedimentation rate (ESR), hypergammaglobulinemia, and lymphadenopathy. The etiology of RDD is unknown; however, it was frequently observed after an infection with Epstein-Barr virus, human herpes-virus 6, or parvovirus.[1]

Cutaneous RDD is rare and has been increasingly recognized as a distinct entity. In contrast to systemic RDD, cutaneous RDD has a more benign clinical course with normal laboratory findings. Epidemiologically, cutaneous RDD has been identified to have a different age and racial predilection. It has a female preponderance, and is frequently seen in Caucasians, Asians, and older individuals.[2] This case report is focused on the clinical and histologic features of cutaneous RDD with management leading to a cosmetically acceptable result.

## CASE REPORT

We present a case of a 40-year-old female who sought consult at a tertiary hospital for a 3-month history of multiple erythematous papules on the cheeks. The patient sought prior consult with a dermatologist, and was prescribed unrecalled oral antibiotics and topical medications without improvement of lesions.

Upon consult with us, lesions were noted to increase in size and number, some coalescing to form multiple erythematous papules, and plaques with pustules on the cheeks. The patient did not present with systemic symptoms such as fever, and lymphadenopathy.

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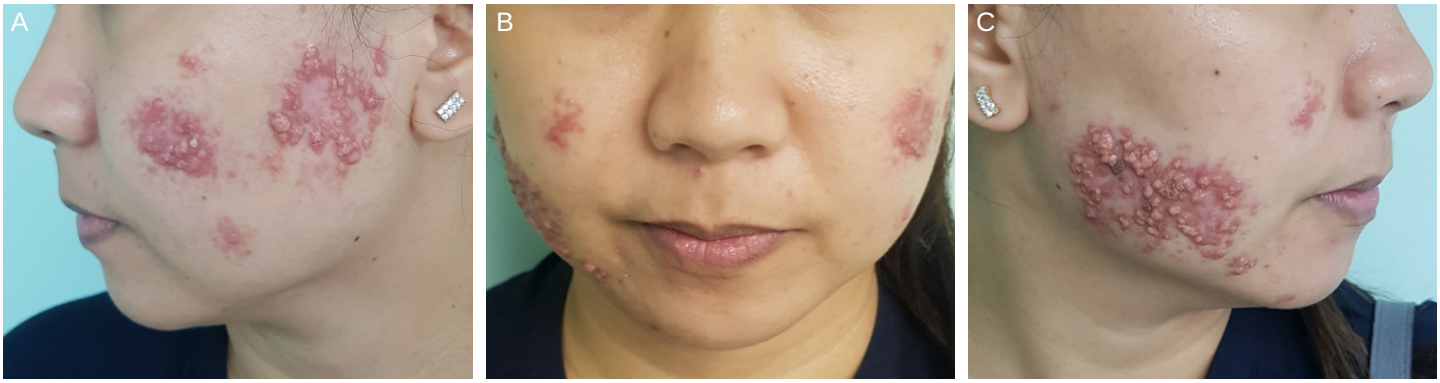


**Figure 1.** Multiple views of patient presenting with multiple, erythematous plaques with papules and pustules on the cheek.

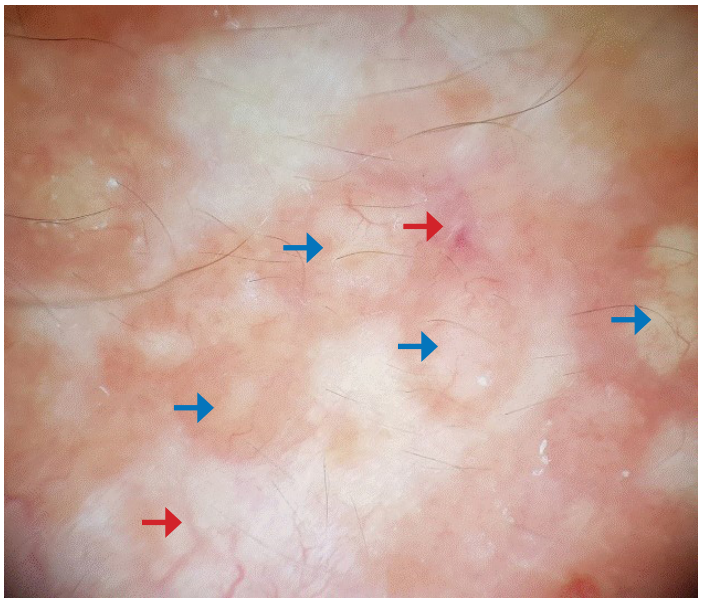

**Figure 2.** Dermoscopy of the lesions revealed milky white globules (blue arrows), and small curvilinear vessels on a red-orange background (red arrows).

Past medical and family history were unremarkable. Menstrual history was likewise unremarkable with no history of any gynecologic or hormonal disorders. Similar lesions were not described in the family and workplace. The patient is a non-smoker and an occasional alcoholic beverage drinker.

On cutaneous examination, we describe multiple, well-defined, irregularly shaped, erythematous plaques with papules and pustules on the cheeks (Figure 1). The lesions were limited to the face and were not seen on other areas of the body. There were no lymphadenopathies present. Dermoscopy of the lesions revealed milky white globules and small curvilinear vessels on a red-orange background (Figure 2).

Complete blood count and ESR were requested and results were within normal limits. A 3-mm skin punch biopsy was taken from a lesion on the right cheek. Histopathologic examination using Hematoxylin and Eosin stain revealed parakeratosis of the stratum corneum, spongiosis of the epidermis with focal areas of ulceration, dense dermal infiltrates of polygonal histiocytes with abundant cytoplasm, and vesicular nuclei. Emperipolesis was present. The S-100 and CD68 immunohistochemical stains highlighted histiocytes, and CD1a was negative (Figure 3).

Clinicopathologic findings confirmed the diagnosis of cutaneous RDD. The patient was started on methotrexate at 15mg/week, and folic acid supplementation at 5mg/day on days

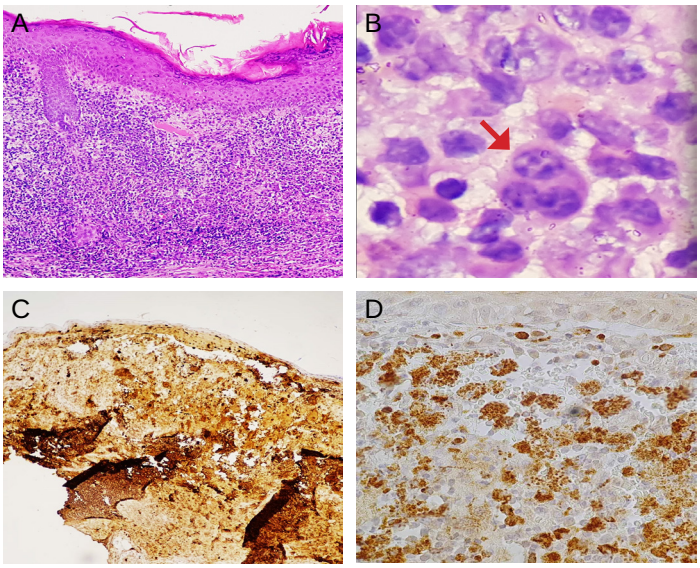


**Figure 3. A.** Section showing parakeratosis of the stratum corneum, spongiosis of the epidermis with focal areas of ulceration. Dermis reveals mild edema and a dense mixed inflammatory infiltrate consisting of plasma cells, lymphocytes, and histiocytes (Hematoxylin and Eosin Stain. Original Magnification, 100x). **B.** Emperipolesis (red arrow) (Hematoxylin and Eosin Stain. Original Magnification, 1000x). **C.** Histiocytes highlighted by S100, x100. **D.** Histiocytes highlighted by CD68, x400.

when methotrexate was not given. Mild soap, benzoyl peroxide 5% gel once daily in the morning, and tretinoin 0.05% cream once daily in the evening were maintained during the treatment course. There was flattening of the lesions with significant decrease in erythema, resolution of pustules, residual post-inflammatory hyperpigmentation and minimal scarring after two months of treatment (Figure 4). Clinical improvement was accompanied by a marked positive impact on the patient's quality of life and self-image. The patient was referred to a hematologist for monitoring of possible future systemic involvement.

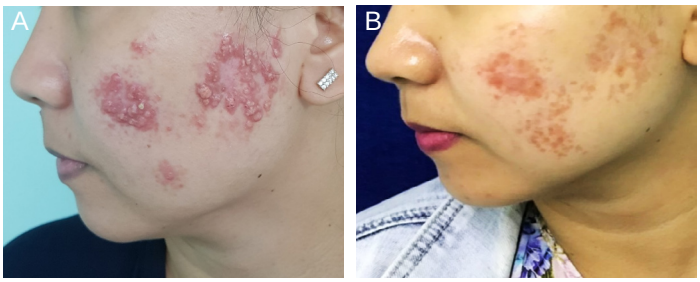


**Figure 4.** Side-by-side comparison of the patient's lesions before **(A)** and after **(B)** treatment showing decrease in erythema, number, and size of lesions.

## DISCUSSION

Cutaneous RDD is increasingly being recognized as a distinct disease from systemic RDD with different clinical presentation, age of onset, gender and racial predilection.[1,2] In 1990, a comprehensive review of case reports has been done. Among the 423 patients diagnosed with RDD, 13 patients presented with cutaneous lesions without lymph node involvement.[3] Subsequently, a comprehensive review of case reports has been done in 2006 where 72 cases of cutaneous RDD were identified. Cutaneous RDD appears to favor older patients with mean age of 43.5 – 45 years old, Caucasians, Asians, and females with a 2:1 female to male ratio.[2,4] Cutaneous lesions vary from <1cm to 30cm, some appear singly or as multiple papules, pustules, plaques, and nodules located on the trunk (40%), head and neck (31%), and extremities (29%).[2] The clinical variability of cutaneous RDD limits its clinical diagnosis in which several presentations may mimic different diseases including histiocytosis, sarcoidosis and cutaneous infectious diseases.[5]

Clinicopathological correlation is always mandatory to establish a diagnosis of cutaneous RDD. Histopathology typically reveals dermal polygonal histiocytic infiltrates with emperipolesis which is the hallmark of cutaneous RDD. Immunohistochemical staining demonstrates S100 positive, CD68 positive and CD1a negative.[1,2,5,6]

As it is self-limited, close observation of the lesions remains to be the cornerstone of management of cutaneous RDD. However, in cases wherein lesions result to substantial physical deformity and compression of vital structures, surgical excision is warranted. Topical and systemic corticosteroids, thalidomide, radiotherapy, and alkylating antineoplastic agents including cyclosporine and methotrexate have been used although have limited studies in terms of efficacy.[5,7] Improvement with methotrexate as monotherapy in the management of cutaneous RDD is inconsistent, resulting to non-response, partial, or complete response.[8] Methotrexate in combination with other agents, including prednisone, 6-thioguanine, 6-mercaptopurine and leucovorin have been utilized in both systemic and cutaneous RDD resulting to either partial or complete response.[8,9] Anti-inflammatory, bactericidal, and keratolytic effect of benzoyl peroxide have been demonstrated, and its use on inflammatory type of rosacea, folliculitis, decubitus ulcer, progressive macular hypomelanosis, and pitted keratolysis have been reported.[10] Systemic retinoids have also been used in the treatment of RDD; however, there are no published reports on the use of topical retinoids or benzoyl peroxide 5% gel in combination with methotrexate in the management of cutaneous RDD.[5,7] Due to cutaneous RDD's rarity, standard treatment has yet to be established.

## CONCLUSION

Clinicopathological correlation and immunohistochemical stains are required to establish the diagnosis of cutaneous RDD, and differentiate it from other forms of Langerhans cell histiocytosis. Treatment with immunomodulating agents such as methotrexate in combination with benzoyl peroxide 5% gel and tretinoin 0.05% cream shows promising results. It brought about a cosmetically acceptable outcome leading to marked improvement in the patient's quality of life. Multidisciplinary referral is required in order to rule out concomitant systemic involvement.

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