Case Report of Cutaneous Rosai-Dorfman Disease with Bilateral Anterior Uveitis

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ABSTRACT:

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Rosai-Dorfman disease or sinus histiocytosis with massive lymphadenopathy is a rare, idiopathic, benign lympho-histiocytic proliferative disorder, which was first described by Rosai and Dorfman in 1969. It most commonly affects young people with predominance in the male population. Rosai-Dorfman disease was initially described with bilateral painless lymphadenopathy, fever, leukocytosis, and polyclonal gammopathy. Extranodal involvement has been reported in 25-40% of cases, the most common involving the skin, respiratory tract, soft tissue, visceral organs and central nervous system[3]. Ocular involvement is relatively rare, and mostly characterized as lymphoproliferation in the soft tissues of the orbit and the eyelids[2]. Cutaneous Rosai-Dorfman disease is present in about 3/100 case of Rosai-Dorfman disease with age distribution range from 15-68 years and clinically characterized by red-brown-yellow localized or disseminated papules, plaques, or nodules at any location[4]. Here we report an interesting case of extranodal Rosai-Dorfman disease with cutaneous lesions and ophthalmic manifestations of bilateral anterior uveitis.

Key words: Rosai-Dorfman disease, sinus histiocytosis with massive lymphadenopathy, uveitis, non-langerhan cell histiocytosis

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A 60-year-old Thai female presented with one month history of multiple papules on her back and upper chest with blurred vision in both eyes. The lesion grew slowly in size and number with occasional pruritus. She had underlying diseases including diabetes mellitus and hypertension. Her current medications were amlodipine 10 mg/day, pioglitazone 30 mg/day and aspirin 81 mg/day. She had no history of fever, malaise or weight loss. None of family members were affected by a similar skin lesion.

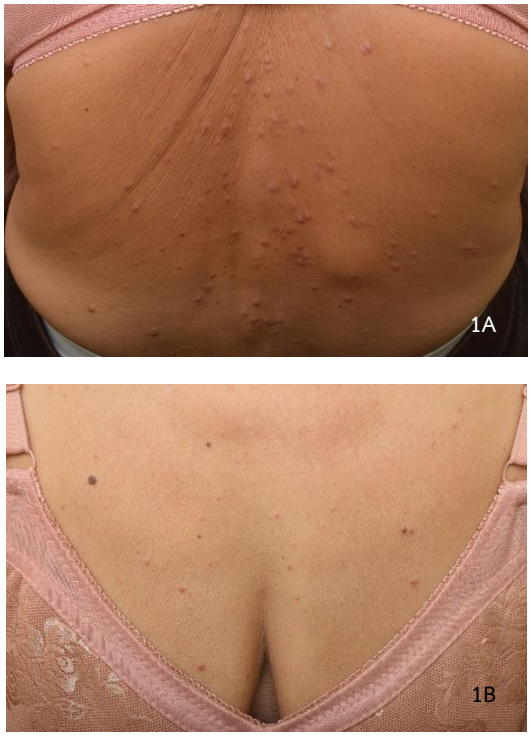

Figure 1 Multiple discrete well-defined borders indurated erythematous to brownish dome shape papules distributed on the back and upper chest

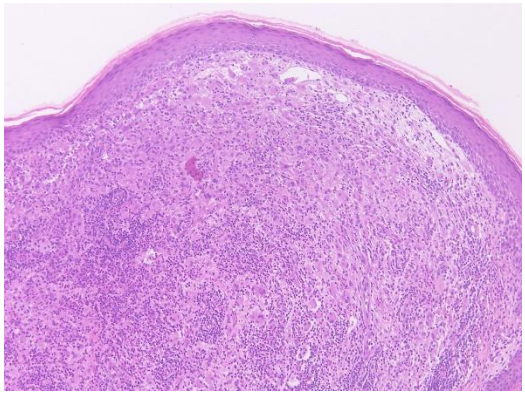

Figure 2 Well-circumscribed nodular infiltration in the dermis with sheets of histiocytes, lymphocytes, some eosinophils and plasma cells, H&E X100

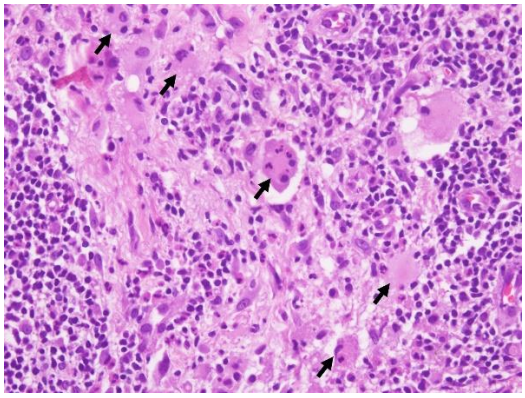

Figure 3 Scatter emperipolesis in the dermis (black arrow), H&E X400

General physical examinations were normal, without sign of lymph node enlargement. However, a dermatologic examination showed multiple discrete well-defined borders indurated erythematous to brownish dome shape papules distributed on the back and upper chest (Figure 1). No mucosal involved was observed.

Ophthalmologic examination revealed bilateral anterior uveitis with bilateral optic disc edema and nonproliferative diabetic retinopathy in both eyes. Other examinations were unremarkable. Lymphoma cutis, pseudolymphoma, infectious and noninfectious granuloma were considered as differential diagnosis.

The histopathologic findings from punch biopsy of the papule on her back revealed well-circumscribed nodular infiltration in the dermis with sheets of histiocytes, lymphocytes, some eosinophils and plasma cells (Figure 2). Scatter emperipolesis was observed in the dermis (Figure 3). Neither storiform fibrosis nor obliterative phlebitis was observed in this case. Immunohistochemistry showed diffuse staining for the S-100 protein and CD68. The tumor cells had negative staining for CD1a which confirmed a diagnosis of cutaneous Rosai-Dorfman disease (Figure 4 A-C).

Laboratory results showed negative for Epstein-Barr virus IgM/IgG, Anti-HIV and VDRL. QuantiFERON for TB was indeterminate. Serum protein electrophoresis showed evidence of a polyclonal gammopathy. Other laboratory results including complete blood count, liver function, renal function tests and antinuclear antibody were unremarkable. Computed tomography of chest and whole abdomen revealed normal findings without mass or lymphadenopathy. Magnetic resonance imaging of brain and orbits demonstrated scleritis and mild intra-orbital inflammation both eyes.

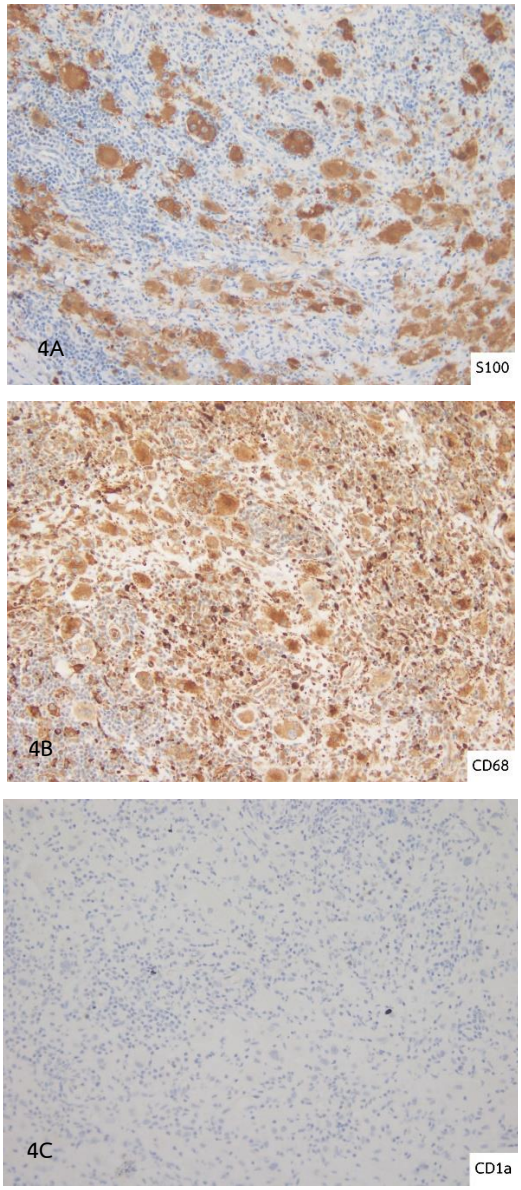

Figure 4 A-C Immunohistochemistry showed positive staining for the S-100 protein, CD68 in histiocytes and negative staining for CD1a.

The methotrexate 7.5 mg/weekly was started, then she received ongoing follow up on her skin lesion. For bilateral anterior uveitis and optic disc edema, ophthalmic corticosteroid was started and response after 2 weeks of treatment was observed.

Discussion

Rosai-Dorfman disease (RDD), a rare benign type of non-Langerhans cell histiocytosis, first described by pathologists Juan Rosai and Ronald Dorfman in 1969, most commonly affects young people predominantly in male populations[1]. It initially presents as bilateral painless lymphadenopathy with cervical lymph nodes being most commonly affected. Patients may present systemic symptoms such as a fever, night sweats and weight loss[1,2]. Extranodal involvement had been reported in 25 to 40% of cases in which the skin is the most common site[3]. Cutaneous Rosai-Dorfman disease (CRDD) used to describe the forms of RDD that only involve the skin. The onset of CRDD has median age at 43.5 years. In contrast to RDD, CRDD shows a female predominance of 2:1, most commonly affects Asian and Caucasian populations[4] and is clinically characterized by red-brown-yellow localized or disseminated papules, plaques, or nodules at any location. The prognosis of CRDD varies, including spontaneous remission and recurrence or resolution after treatment[4,5]. No associated factor could predict the course of the disease.

The pathogenesis of CRDD is not fully understood. The association of various infections, e.g., human herpes virus (HHV)-6, Epstein-Barr virus or human Immunodeficiency virus, hematologic malignancies, lymphoproliferative diseases and autoimmune diseases have been reported[2,5].

Cell origin, both dendritic cell and monocyte-macrophage lineage has been considered to be involved in the pathogenesis of RDD[2]. An increased number of IgG4-positive plasma cells has a reported association of extranodal RDD involving the liver, lungs and colon[2].

Ophthalmic manifestations are involved in 11% of patients with RDD commonly presented as orbital mass and ocular involvement including optic neuropathy, anterior uveitis, scleritis, retinal detachment and optic disc edema[2,6]. The cases with ocular involvement demonstrated more aggressive and systemic involvement including cardiovascular, pulmonary, renal and intracranial lesions[6]. Nevertheless, uveal involvement in CRDD did not influence the prognosis but could increase morbidity[5].

Related literature suggested the clue in diagnosing RDD associated with uveitis is that patients often develop skin lesions and ophthalmic symptom around the same time without other causes of uveitis[7].

Histopathological findings in CRDD usually show normal epidermis. In the dermis, diffuse infiltration of histiocytes was accompanied by a background infiltrate of lymphocytes and plasma cells. Emperipolesis, the phenomenon which presents intact lymphocytes in histiocytes, has been commonly observed in this disease. Although RDD and IgG4-releated disease can mimic by clinical and pathological features. Previous literature indicated specific pathological features of IgG4-related disease by observed storiform fibrosis and obliterative phlebitis in the dermis which is not be seen in RDD[8]. Immunohistochemistry usually showed positive for S100 protein and CD68 but negative in CD1a staining[2].

Our patient, developed skin lesions of CRDD accompanied with bilateral anterior uveitis and optic disc edema. Further work-up found no other causes of uveitis and revealed no systemic involvement. Although we had no tissue pathologic confirmation from the eye, we proposed these findings were the same entity of extranodal RDD. She received systemic and topical immunosuppressive agents showing clinical improvement after 2 weeks of treatments.

RDD is characterized as a benign and self-limiting disease. It has been suggested that less aggressive therapeutic approaches should be considered. Surgical excision and cryotherapy for small localized lesions have been usually helpful. Systemic corticosteroids are usually helpful in reducing nodal size and symptoms result in complete or partial responses in cases of orbital, central nervous system and bone associated disease[2]. Many related studies have also demonstrated successful treatment of RDD and CRDD using methotrexate alone or combined with other agent including systemic corticosteroid or azathioprine[9,10].

In conclusion, we report the case of extranodal RDD associated with cutaneous lesions and bilateral anterior uveitis. Further work-up showed no systemic involvement. The patient responded well to methotrexate and topical corticosteroid eye drops.

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