

Clinical & Histological Review of Cutaneous Rosai-Dorfman Disease



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ARTICLE INFO

Received: 📅 December 18, 2019

Published: 📅 January 06, 2020

ABSTRACT

Citation: Mohammed Al Abadie, Hamdi Hamad, Faris Oumeish, Mohammed Al-Rubaye, Nabeel Salmons. Clinical & Histological Review of Cutaneous Rosai-Dorfman Disease. Biomed J Sci & Tech Res 24(2)-2020. BJSTR. MS.ID.004028.

Introduction

Pathologists Juan Rosai and Ronald Dorfman initially described in 1969 “sinus histiocytosis with massive lymphadenopathy” after they observed symptomatic extensive lymph node enlargement; and subsequently came to be designated “Rosai –Dorfman” disease [1]. Rosai-Dorfman disease is a rare disorder characterized by increased production and accumulation of non-Langerhans sinus histiocytes within lymph nodes, most commonly affecting the cervical lymph node chain. Histiocytes may also accumulate in extranodal areas including the skin; central nervous system, kidney, and digestive tract. 43% of cases of Rosai Dorfman disease demonstrate extranodal involvement. With skin being the most commonly site [2]. Thawerni et al were the first to report a case of cutaneous Rosai-Dorfman disease in 1978 [3].

Clinical Review

The aetiology of cutaneous Rosai-Dorfman disease is still unknown, immune and viral causes have been hypothesized. The signs and symptoms of this disease depend on which parts of the body are affected. Skin lesions seen in cutaneous Rosai-Dorfman disease are indurated firm papules or nodules measuring between 1-10 cm [1]. Age groups affected include children, adolescents and young adults [4]. The disease presents more commonly in males and in African descent [5]. Cutaneous Rosai-Dorfman disease (without nodal involvement) typically occurs at a later

age of onset with a median age of 43.5 years and demonstrates female predominance with a ratio of (2:1), Asian and Caucasian individuals are mostly affected [6]. Laboratory findings are not specific and include: leucocytosis, elevated sedimentation rate and polyclonal gammopathy, elevated serum ferritin and normochromic/normocytic and autoimmune haemolytic anemia [7]. In our experience we recently encountered a patient who is sixty-eight-year-old gentleman of black Caribbean origin with clinical signs and histology suggestive of Cutaneous Rosai-Dorfman syndrome. His past medical history included: insulin dependent diabetic, Hypertension, chronic kidney disease stage 3, recurrent anterior uveitis, sickle cell trait and anaemia. There is no history of fever, night sweats, weight loss, fatigue and ECOG performance status of 0. On examination there is no evidence of any enlarged lymph node clinically, no evidence of organomegaly, chest, cardiovascular and neurological examination is grossly normal. Laboratory findings include low HB, Thrombocytosis, high ESR, high CRP, low albumin, normal Iron, raised globulins. He presented with skin hyperpigmentation on his arms and legs for 1-2 years which became more noticeable during the last couple of months. He then presented with asymptomatic lesion on the face, upper limbs and trunk (Figures 1-6). Examination revealed multiple popular nodular lesions on the face and abdomen and arms. Some are typical of molluscum contagiosum, but some are different.



Figure 1: A-Raised nodular hyperpigmented lesions on the face with post-inflammatory hyperpigmentation. B-Close up to one of the raised nodules.



Figure 2: Papular eruption with hyperpigmentation legs.

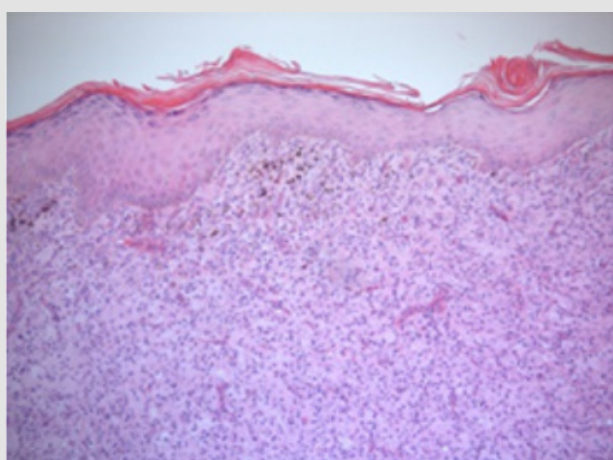


Figure 3: Low power (x4 magnification) H& E skin nodule in which the dermis shows diffuse sheets of histiocyte-like cells.

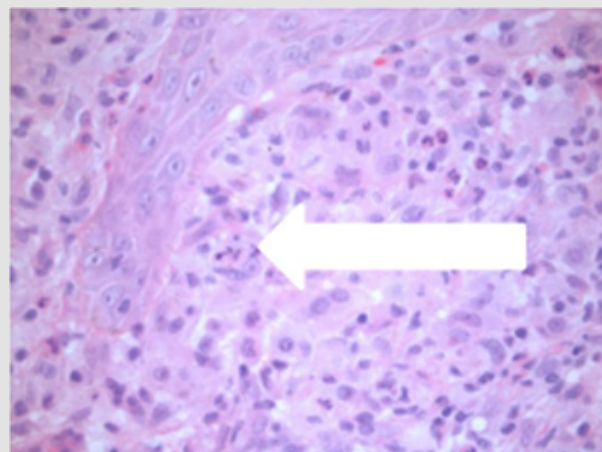


Figure 4: High power (x 40 magnification) demonstrating emperipolesis by histiocytes.

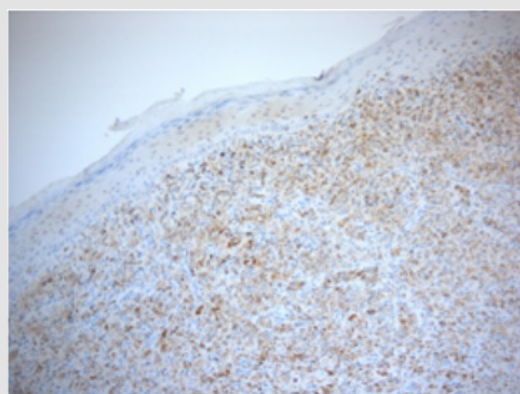


Figure 5: CD68 stain showing scattered positive cells within the dermis.

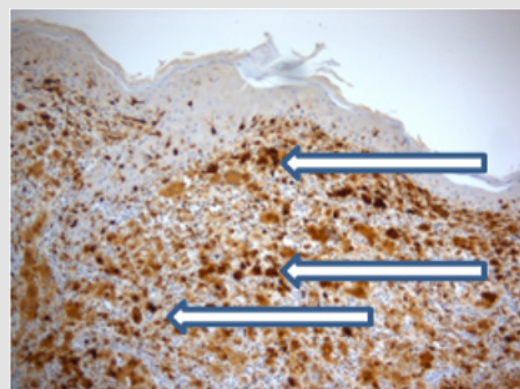


Figure 6: S100 (x 10 magnification) is strongly nuclear positive in the dermal histiocytic population

Treatment

Cutaneous Rosai Dorfman syndrome is a self-limiting disease. Treatment options reported in literature include surgical excision is recommended when lesion are localized, cryotherapy was successfully used for cutaneous Rosai-Dorfman syndrome that was refractory to topical and intralesional steroids [8]. Dapsone was found to be effective in the treatment of cutaneous Rosai-Dorfman

syndrome [9], 100mg daily of dapsone was used to treat a patient with resistant to isotretinoin and oral, intralesional steroid with complete regression after 3 months of treatment with dapsone and patient remained in remission on his 1 year follow up [10]. Acitretin treatment for 4 months was found to be effective in a 12 year old patient [11,12]. High doses of Thalidomide (300 mg/d) can be effective in cases of extensive disease if patients can tolerate its side effects [13]. Other forms of treatment include isotretinoin, radiotherapy, Intralesional steroids.

Histology Review

The findings in Rosai-Dorfman disease and Cutaneous Rosai-Dorfman Disease are similar. Dermal infiltrates include large histiocytes, lymphocytes, and plasma cells. The histiocyte known as Rosai-Dorfman cell is considered diagnostic of Rosai-Dorfman disease, this cell is having an amorphous cytoplasm, large vesicular nucleus with prominent nucleoli and indistinct border [13]. Presence of lymphocytes and plasma cells engulfed within the cytoplasm of histiocytes is referred to as emperipolesis. This population express S-100 and are considered diagnostic although not pathognomonic of Rosai-Dorfman disease. This histiocytes population also may stain positive for CD68, and negative for CD1a [14,15], helping to exclude other differential diagnoses. In our patients shave excisions from right maxilla, left upper and left lower cheek, on separate occasions showed normal epidermis with a dermal based histiocytic lesion admixed with lymphocytes and plasma cells. This consisted of florid numbers of large epithelioid histiocytes with abundant eosinophilic cytoplasm with round nuclei, wrinkled nuclear membranes and small inconspicuous nucleoli. Emperipolesis of small lymphocytes was identified within occasional large histiocytic cells which helped narrow the differential diagnosis. Interspersed single and clusters of small lymphocytes with scattered plasma cells also seen. Scattered mitoses were noted including a single quadripolar form, but there was no necrosis. Whilst the diffuse histiocytic population, and admixed inflammatory cells raised the possibility of cutaneous Rosai-Dorfman, in the initial assessment cells showing emperipolesis were difficult to identify and so other differential diagnoses for an histiocytic infiltrate were also considered such as xanthoma and langerhans cell histiocytosis. Immunohistochemistry demonstrated cells to be positive for S100, and variable CD68 positivity, but this population were negative with melanocytic markers including Melan A and HMB45; other markers undertaken (CD1a, CD56, Factor 13a) were also negative as were special stains to exclude infective aetiology. S100 assisted in identifying emperipolesis as described by Brenn et al. [6] In conclusion the histological and immunohistochemical findings were all supportive of a pathological diagnosis of cutaneous Rosai-Dorfman disease.

Conclusion

Cutaneous Rosai-Dorfman disease is considered a distinct clinical entity of Rosai-Dorfman syndrome [14]. Extranodal Rosai-

Dorfman disease without nodal involvement is extremely rare [6]; skin is considered the commonest extranodal site. Histologically both Rosai-Dorfman disease and Cutaneous Rosai-Dorfman disease have similar findings. However, demographically the disease differs in age, gender and ethnic backgrounds. The median age of presentation of cutaneous Rosai-Dorfman disease is 43.5 years while in Rosai-Dorfman disease is 20.6 years. The Cutaneous Rosai-Dorfman disease shows female predominance in contrast the Rosai-Dorfman disease showed male predominance. Population affected with Cutaneous Rosai-Dorfman disease is mostly white and Asian while in Rosai-Dorfman disease it was mostly black and rare in Asians [16]. The diagnosis is made by histopathological examination looking for the presence of histiocytes that stain positive for S-100 and identification of emperipolesis [17]. Cutaneous Rosai-Dorfman syndrome is a benign condition which is self-limiting but may require treatment or surgical excision [18,19].

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2020.24.004028

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