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Cutaneous Rosai-Dorfmann Disease in Autistic Patient: Is there a Pathogenetic Correlation?

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Abstract

Rosai-Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a benign disorder of histiocyte proliferation that usually affects the lymph nodes. Purely Cutaneous Rosai-Dorfman Disease (CRDD) is a rare extranodal variant that is strictly limited to the skin. We report a patient with of cutaneous rosai-dorfman of the abdominal wall with a past medical history of autism spectrum disorders. Autism is surely a complex disease and the most prevailing opinion is that it is a neuro-immune disorder. Both the diseases are considered strictly correlated to the immune disorders and the immunodeficiency might play an important pathogenetic role. A brief review of the literature of CRDD is also provided.

Keywords: Cutaneous rosai-dorfman disease; Histiocytosis; Autism spectrum disorders

Introduction

Rosai–Dorfman disease or sinus histiocytosis with massive lymphadenopathy, is a very rare benign, idiopathic histiocytic proliferative disease. It was originally described by Destombes in 1965 [1] and was recognized as a unique histiolymphoproliferative disease of the lymph nodes with pathognomonic histological and immunohistochemical characteristics by Rosai and Dorfman in 1969 [2,3]. The disease is clinically characterized by massive cervical lymphadenopathy, fever, night sweats, weight loss and leukocytosis with neutrophilia, increased erythrocyte sedimentation rate and polyclonal gammopathy [4-6]. Pathologically the disease is characterized by dense inflammatory infiltrates composed of neutrophils, plasma cells, lymphocytes and histiocytes in the dermis. The histiocytes engulfed well-preserved inflammatory cells. This pathognomonic, histopathological cytoachitecture represent a phenomenon known as emperipolesis [7-9]. Immunohistochemical stains demonstrated that the histiocytes were positive for both S-100 protein and CD68. Little is known regarding the pathogenesis of Rosai-Dorfman disease. Some Autors consider it a neoplastic process, others as an immunological disturbance due to the high incidence of immunological disorders in patients with Rosai–Dorfman disease [7,10]. Currently, it is best considered a benign idiopathic histiocytosis. Rosai-Dorfman disease exists in two main forms. One form affects lymph nodes (sinus histiocytosis and massive lymphadenopathy), and the other form that is purely cutaneous without systemic or nodal disease. Although less common, compared to the cervical lymph node involvment, axillary, inguinal, paraaortic or mediastinal lymph node chains may be affected [4,11]. Lymph nodes are commonly affected, but any organs may be involved. Various affected sites have been described such as soft tissue, the respiratory and the genitourinary tract, the oral cavity, the gastrointestinal tract, the nasal and paranasal cavities, eyes and retro-orbital tissue, most commonly leading to uveitis, bones and skin [5,12-16]. Rosai–Dorfman disease involving the central nervous system is considered to be extremely rare [17-19]. Several authors have suggested that cutaneous Rosai–Dorfman disease is a distinct clinical entity because of its unique epidemiology and the lack of systemic involvement even with long-term follow-up [20-22]. Skin lesions can be found in any location, including the face, ears, trunk, extremities or genitalia [7-21]. The cutaneous form usually presents as one or several deep red papules, plaques, or deep nodules that enlarge, persist, or regress and disappear over time. Skin lesions may deeply infiltrate into tissue and cause functional or aesthetic problems to the patient. The cutaneous form of Rosai–Dorfman disease is generally self limited. However, the purely cutaneous form of the disease is extremely rare, accounting for approximately 3% of cases in one large study [23,24] and only a few such cases have been reported, thus justifying the present case report.

Case Report

A 28-year-old female with a past medical history of autism spectrum disorders presented with a 1-year history of an asymptomatic abdominal skin lesion localized in the epigastric region. Clinical examination showed an indurated erythematous plaque with clear borders and irregular contours measuring 10 cm, with reddish-yellow nodules around 0.5 cm in diameter (Figure 1).

The painless plaque grew progressively on the abdominal wall without any associated symptoms or lymphadenopathy. It had not changed in size over two months, despite treatment with antibiotics and oral glucocorticoids. She had no signs or symptoms of systemic

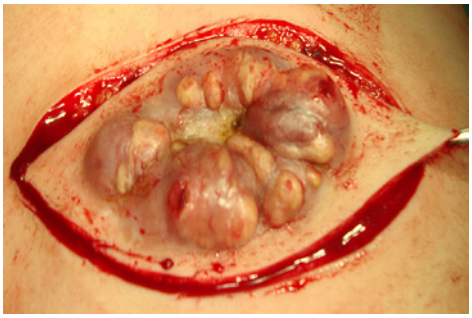

Figure 1: Abdominal skin lesion localized in the epigastric region.

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disease and her complete blood count was within normal limits. An Ultrasonography examination showed edema in the subcutaneous fat and skin overlying the abdominal muscles.

The skin lesion was removed under local anesthesia. The microscopic examination revealed numerous histiocytes with abundant cytoplasm invading the lymph sinuses and a pronounced mixed chronic inflammatory cell infiltrate. Immunological staining showed that the histiocytes were positive for CD68 and S-100 protein. These findings were consistent with the characteristics of Rosai-Dorfman disease. A computed tomography (CT) examination and Enhanced Magnetic Resonance Imaging (MRI) confirmed the non involvement of the central nervous system.

Discussion

We report a review of the literature with the addition of our clinical experience, in one case of cutaneous Rosai-Dorfman disease occurring in a patient with autism spectrum disorders.

The term cutaneous Rosai-Dorfman disease is used exclusively for the forms of the disease in which involvement is restricted to the skin in order to differentiate it from sinus histiocytosis with massive lymphadenopathy in which there is systemic involvement of multiple sites including the skin [5,15,25,26].

Histologically, the disease is characterized by large, proliferating histiocytes containing inflammatory cells within their cytoplasm, referred to as emperipolesis. Contrary to the systemic form, which affects principally children and young adults and which shows no preference for gender or ethnic group, the purely cutaneous form of the disease is slightly more common in older age-groups, in women and in nonblack ethnic groups [11,12,15,27,28]. Purely cutaneous Rosai–Dorfman disease without systemic involvement is rare (only 3% of reported cases), and has been recognized as a distinct clinical entity [23,29,30]. Extranodal involvment occur in 43% of cases and in 3% the disease is limited exclusively to the skin [31,32]. Clinically, it presents with papules, nodules, plaques, masses or tumors of a brownish- or yellowish- erythematous color, varying in size from less than 1 cm to 30 cm, either localized or disseminated. When the skin is affected the most common sites are, in order of decreasing frequency, the trunk, head, neck, lower and upper extremities. The lesions may occasionally resemble psoriasis or acne [11,25]. The etiology of the disease remains unknown despite some reports that the systemic form of the disease coexists with herpesvirus hominis-6 and 8 and Epstein-Barr virus infection [33]. Some researchers have suggested that either infection or immunodeficiency might play a role and recently, cases of Rosai-Dorfman disease associated with the autoimmune lymphoproliferative syndrome have been described [34,35]. In the present case there was a clinical association with autism spectrum disorders. Autism is a severe neurodevelopmental disorder which does not constitute a specific disease, but a syndrome of characteristic behavior problems. It is a disorder whose etiology and pathogenesis are largely unknown. Many factors have been implicated, but no one can claim the exclusive etiopathogenetic role in the disorder [36-38]. Autism is surely a complex disease and the most prevailing opinion is that it is a neuro-immune disorder [39,40] and there is considerable interest in determining factors that may be etiopathogenetically associated with the disease. The correlations between autism disorders and the two primary systems of the body, immune and nervous, is demonstrated. Particularly, studies have shown that autistic children have statistically significant fewer fever, tend to have more gastrointestinal problems or are at higher risk for the infections of the genitourinary system, compared with normal [41-45]. This might suggest that many autistic children have total or partial loss of the body's ability to develop defense mechanisms.

Conclusions

There is a recent surge in the documentation of Rosai–Dorfman disease in the literature, with a significant increase in the number of cases. When the disease is limited to the skin often fail to present any laboratory abnormalities. The cutaneous lesions typically follow a benign clinical course and conservative excision is the treatment of choice. As a consequence of the progressive growth and the absence of any systemic involvement, our patient was submitted to surgical excision and is currently being followed-up to monitor any possible recurrence or progression to systemic disease. The diagnosis of Rosai–Dorfman disease should be considered in any atypical chronic inflammatory lesion with a histiocytic component involving the skin. Immunohistochemical stains for the S-100 protein should be performed in these cases. In the reported case the inflammatory lesion was localized to the skin of the abdominal wall and the patient has a past medical history of autism spectrum disorders. Both the diseases are considered strictly correlated to the immune disorders and the immunodeficiency might play an important pathogenetic role. To our knowledge, this is the first case reported with such characteristics.

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