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Cutaneous Rosai-Dorfman Disease

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Abstract: Rosai-Dofman disease, also known as sinusoidal histiocytosis with giant lymphadenopathy, was first reported by Rosai and Dorfman in 1969. It is a rare histiocytic proliferative disease with typical .clinical features of enlarged cervical lymph nodes, fever, leukocytosis, increased sedimentation rate, anemia and hypogammaglobulinemia. Which occurs mainly in lymph nodes, and 43% of the patients have both Involvement of extranodal tissues, of which the skin is the most common site of involvement accounts for about 11%.other extranodal tissues include soft tissues, respiratory tract, genitourinary tract, oral cavity, gastrointestinal tract, orbits, testes, rarely involves the central nervous system, and only skin damage accounts for about 3%. When occurs in the skin alone and does not involve lymph nodes, it is known as cutaneous sinusoidal dyshidrotic dyshidrotic dysplasia (CRDD). CRDD usually affects middle-aged and older adults, with a female predominance, and is reported mainly in patients of Asian and Caucasian ethnicity.

1. Case information

(1) Lnitial Diagnosis: December 9, 2022
(2) Patient information: patient Fan, female, 68 years old
(3) Complaint: Hyperplastic nodule in the left mandible for 2 years.
(4) History: Erythema appeared on the left side of the jaw 2 years ago without any obvious cause, which was not taken seriously, and then the lesion gradually increased in size and raised on the surface of the skin, occasionally accompanied by itching, and was diagnosed as “granulomatous hyperplasia”. She was diagnosed as “granulomatous hyperplasia?” and was treated with a variety of ointments (details unknown), but did not see any significant improvement, and now the nodules are gradually increasing in size, so she came to our department to seek further diagnosis and treatment.
(5) Past history: Previously fit, no history of mosquito bites.
(6) 1Family history: There is no history of similar disease in the family.
(7) Specialized examination: superficial lymph nodes of the whole body were not palpable and enlarged, a grape-sized nodule was seen on the left side of the mandible, surrounded by scattered rice-grain-sized papules, red in color, soft in texture, with poorly defined borders.As shown in Figure 1.

(8) Laboratory tests: blood test showed: leukocytes 9.68x109/L, monocytes 0.92x109/L, neutrophils 6.89x109/L; coagulation, CRP did not show any significant abnormality.

(9) Consider the diagnosis: lymphoid granulomatosis?

(10) Treatment: patch therapy (extra-large); mandibular skin biopsy was performed and small pieces of skin tissue were sent for examination.

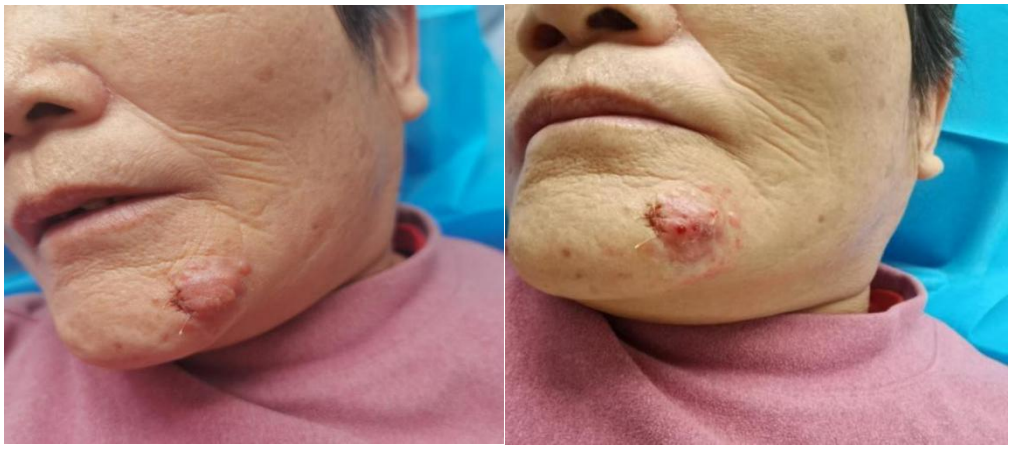

Figure 1: Photograph of the patient's lesions at the time of consultation

2. December 12, 2022 Follow-up

Pathological findings showed inflammatory cell infiltration throughout the epidermis and dermis with plasma cells and lymphocytes predominating, epidermal keratinization, incomplete keratinization and epidermal laxity, localized intra-epidermal fissure formation, and basophilic degeneration of the superficial dermis, as shown in Figure 2.

3. December 15, 2022 Consultation was requested from the Department of Pathology, Baoji

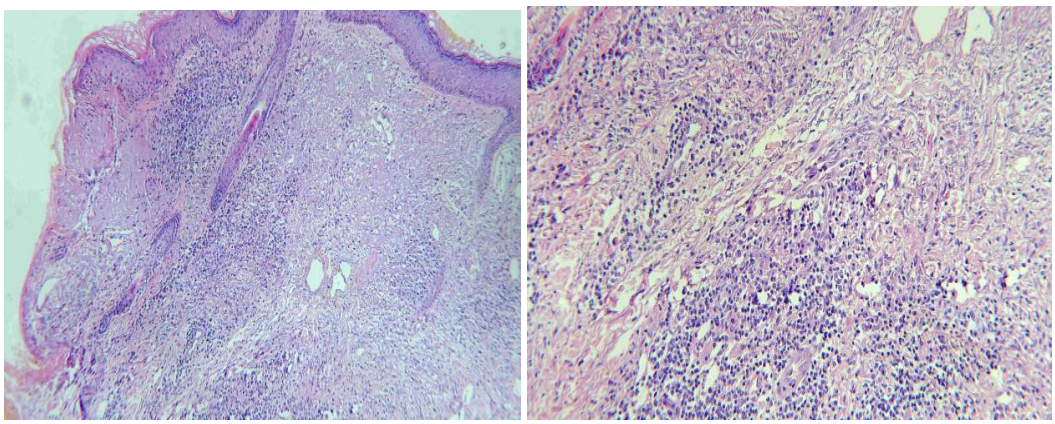

Figure 2: Pathology results show: left: 10x right: 20x

3.1. High-Tech Hospital

CONSULTATION OBSERVATIONS: Small piece of skin tissue in the left mandible with approximately normal epidermis, basophilic degeneration of some collagen in the superficial dermis, diffuse plasma cells in the reticular layer, and predominantly plasma-like cells proliferating.

Diagnostic findings: proliferative lesion of cutaneous lymphoid tissue, not excluded, possible B-cell lymphoma of the cutaneous marginal zone (not lymphogranuloma)

4. 2022 resumed on December 16, 2012

Consider the diagnosis: B-cell lymphoma?
Treatment: patch therapy (oversized); excision of superficial mass, sent for pathology.

5. December 20 pathology results

5.1. Pathologic Diagnosis

(Left mandibular skin biopsy) Combined with the rash and morphological changes consistent with Rosa1-Dorfiman disease, total excision of the mass was recommended for further diagnosis if necessary, as shown in Figure 3 and 4.

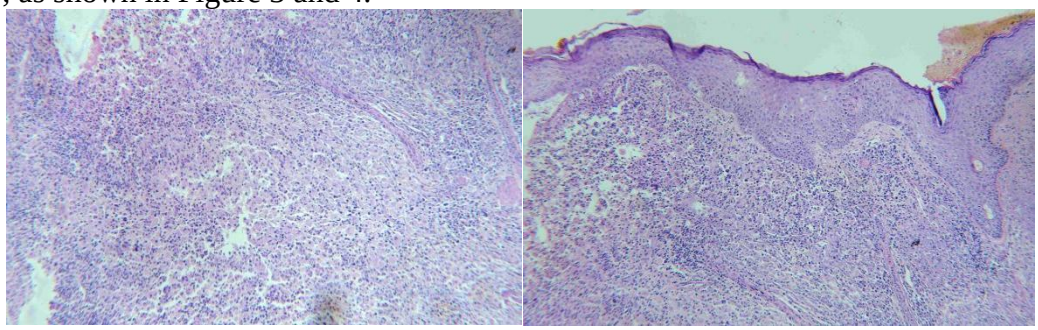

Figure 3: Pathology results show:10x

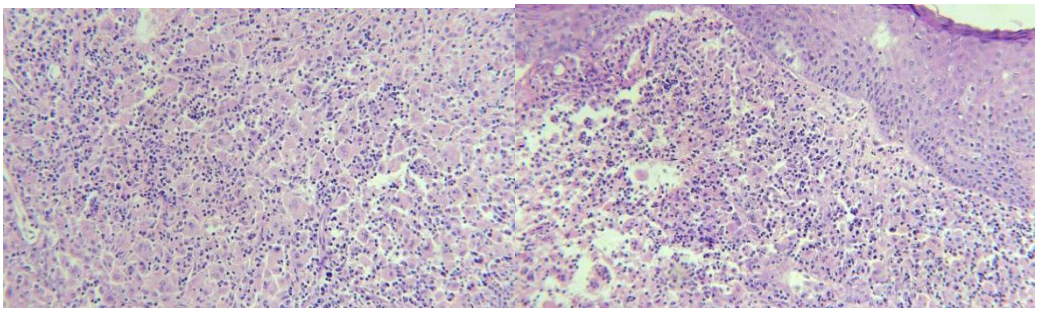

Figure 4: Pathology results show:20x

5.2. Immunohistochemistry

Results:CD3(foci+), CD20(partial+), CD138(partial+), CD68(+), CD43(partial+), CD10(foci+), CD1a(-), Ki67(5%+), P53(-), S100(+), CD5(partial+), Bc12(+), CD21(-), CD23), ...CD34 (vascular+), Vim(+).

As shown in figure 5 below.

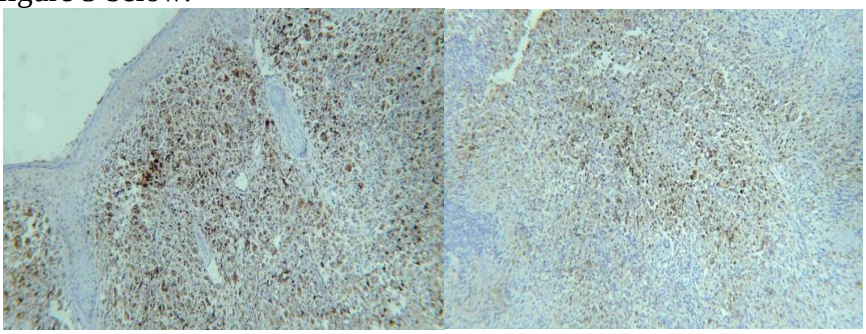

Figure 5: Pathology results show: left:CD68 right: S100

6. Resumed on January 7, 2023

(1) Diagnosis: cutaneous Rosa1-Dorfiman disease?
(2) Ancillary tests: no abnormalities were found in coagulation, blood counts, and CRP.
(3) Treatment: Perform excision of cutaneous malignant tumor and send for pathological examination.As shown in figure 6 below.

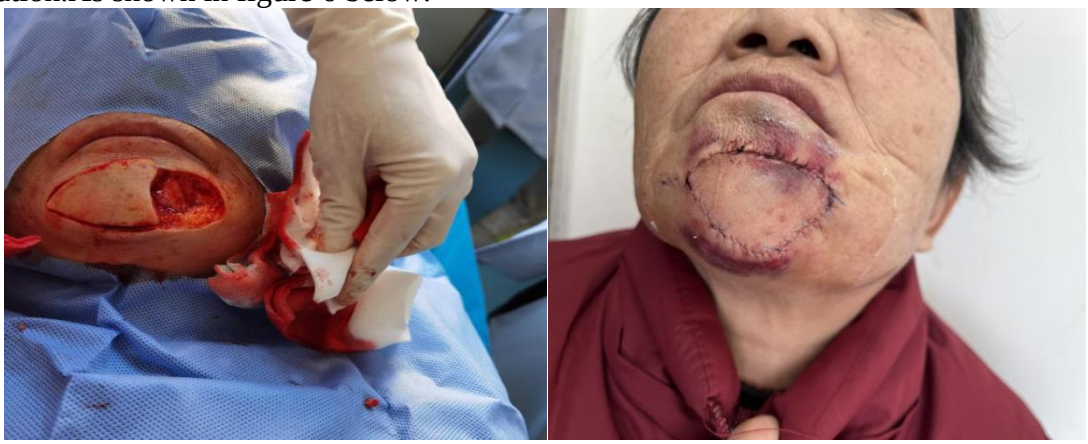

Figure 6: Surgical removal of skin lesions

7. January 11, 2023

Pathologic findings showed: cutaneous Rosai-Dorfman disease (left mandible) with negative specimen and basal margins.As shown in figure 7and 8below.
Diagnosis: cutaneous Rosai-Dorfman disease (cutaneous sinus histiocytosis)

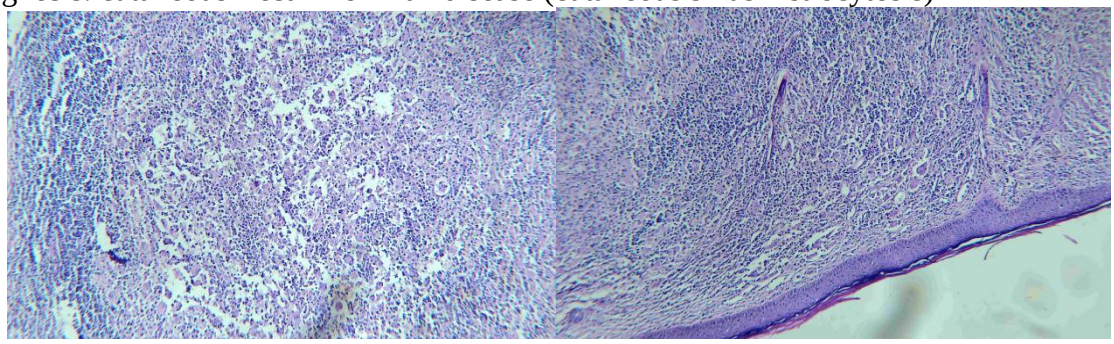

Figure 7: Pathology results show:10X

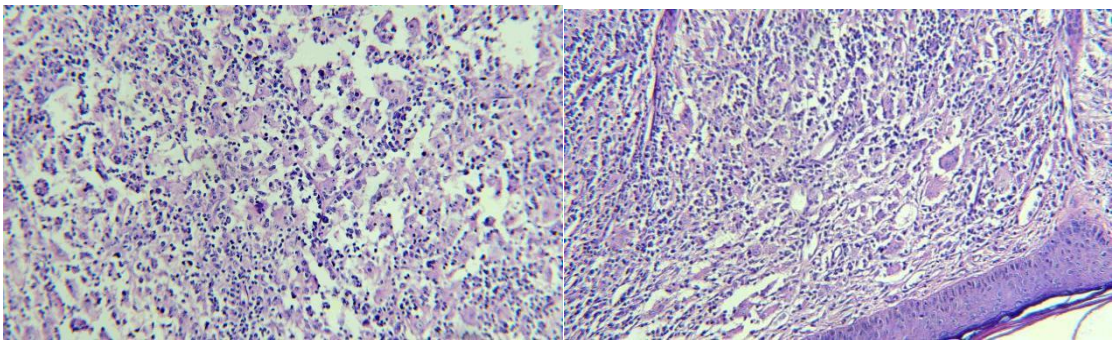

Figure 8: Pathology results show:20X

8. Resumed on January 20, 2023

8.1. Pulsed laser therapy

Rosai-Dofman disease, also known as sinusoidal histiocytosis with giant lymphadenopathy, was first reported by Rosai and Dorfman in 1969[1]. It is a rare histiocytic proliferative disease with typical clinical features of enlarged cervical lymph nodes, fever, leukocytosis, increased sedimentation rate, anemia and hypogammaglobulinemia, which occurs mainly in lymph nodes, and 43% of the patients have both Involvement of extranodal tissues, of which the skin is the most common site of involvement accounts for about 11%, other extranodal tissues include soft tissues, respiratory tract, genitourinary tract, oral cavity, gastrointestinal tract, orbits, testes, rarely involves the central nervous system, and only skin damage accounts for about 3%, when occurs in the skin alone and does not involve lymph nodes, it is known as cutaneous sinusoidal dyshidrotic dyshidrotic dysplasia (CRDD)[2]. CRDD usually affects middle-aged and older adults, with a female predominance, and is reported mainly in patients of Asian and Caucasian ethnicity[3].

According to previous literature, cutaneous RDD can be divided into three basic types: papulonodular-nodular, infiltrating plaque and tumor-like. Papulonodular-nodular type is the most common type, with papules and nodules of varying sizes (0.1~1.0 cm in diameter) and numbers, unevenly distributed, and with a variety of anatomical sites and combinations of involvement. The skin of all parts of the body can be involved, and the color is mostly dark red, brownish red, some of them are light red or bright red, most of the surface is smooth and rounded, and a few of them can be desquamated, and are arranged in scattered ring clusters. The infiltrated plaque type often evolves from the fusion of papular nodular lesions with the slow development of the disease. Firm infiltrating plaques are smooth, uneven, rounded and blunt nodules, often 2-5 cm in diameter, surrounded by a few scattered papules and nodules that have not yet fused. The color of this type of lesion often changes from bright red to dark red, and may be accompanied by hyperpigmentation. Tumor-like lesions are basically round or round-like exophytic masses, single or two or three, often >2 cm in diameter, and up to 4-6 cm in diameter, with a smooth skin surface that may be bright red or dark red. The epidermis of individual lesions may break down and form ulcers, which are often misdiagnosed as various benign or malignant tumors before biopsy[4].

Currently, there are relatively few studies on Rosai-Dorfman disease, and most of them are based on case reports The etiology of Rosai-Dorfman disease is still unclear, and the pathogenesis is complex, and it is currently hypothesized that it may be mainly related to infections and immune disorders, with the expression of cytokines (TNF-α, IL-1β, IL-6, and M-CSF), the immune status (Klebsiella, EBV, microvirus B19, HHV-6, HIV infection, lymphoma, IgG4-RD, AIHA, and LCH), and autogeny (gene mutation, activation of ERK pathway). The disease can be caused by a variety of factors, including Klebsiella, EBV, HPV-6, HIV infection, lymphoma, IgG4-RD, AIHA, LCH, etc., and autogenous factors (gene mutation, activation of ERK pathway).

The diagnosis mainly relies on histopathology and immunohistochemistry, and the pathology is characterized by the proliferation of histiocytes in the dermis, and the histiocytes can be phagocytosed with intact lymphocytes, plasma cells, or neutrophils, which is known as the reach-in movement [4]. Some scholars retrospectively analyzed the clinical and histopathological data of 15 patients with CRDD, and the results showed that the histopathological changes were diffuse or focal infiltration of lymphocytes, histiocytes, and plasma cells in the dermis and subcutaneous tissues, and the typical feature was the reaching movement (i.e., histiocytes phagocytosis of inflammatory cells such as lymphocytes and plasma cells, which is of great diagnostic significance)[5].

Pathologic diagnosis of CRDD special [6]①Low magnification showed light-stained and dark-stained areas, and foamy histiocytes with nodular or diffuse infiltration. ② High-magnification

microscopy showed phagocytosis of intact lymphocytes or plasma cells, also known as “movement into”. Immunohistochemistry: CD68 (+) is stained brown, S-100 (+) is stained brown, and CD1a (-) is stained brown. The diagnosis can be established if the above three conditions are met.

Therapeutically, current reviews indicate that many approaches have been attempted for the treatment of facial CRDD, including surgical excision, methotrexate, vincristine, corticosteroids, retinoids, thalidomide, cytotoxic chemotherapy, radiotherapy, laser and cryotherapy. Although surgical excision has been reported to be the most effective approach for single, smaller lesions, steroids have been shown to be the least effective[7].CRDD is mostly self-limiting and usually does not require active intervention. Currently, surgery is considered the most effective treatment for small skin lesions [8].

Kong [9]et al. gave surgical resection to 9 patients and 7 patients recovered and had no recurrence during the follow-up period.

9. Differential diagnosis [10]

1) Infectious granulomas: The most common pathogens are Mycobacterium leprae, Mycobacterium tuberculosis, and fungi, all of which have granuloma formation. Histopathologically, Mycobacterium leprae infections tend to show epithelioid granulomas with infiltration of Langerhans cells, foreign body giant cells, or histiocytotic granulomas, and the diagnosis is easy because of the negative staining of antacids and the strong positivity of Mycobacterium leprae.

2) Yellow granuloma: most common in infants and young children, histopathological changes in the dermis and mucosa can be seen fibroblasts, mononuclear histiocytes, multinucleated histiocytes and eosinophils infiltration; ③ Langerhans' cell histiocytosis: the histopathological manifestations of this disease is infiltrated histiocytes smaller size, with characteristic kidney-shaped nuclei, and infiltrated cells contain a large number of eosinophils, with the phenomenon of pro-epidermal; Birbeck's vesicles were seen on electron microscopy. Immunohistochemistry: positive CD1a monoclonal antibody staining is an important basis for diagnosis, immunohistochemistry S-100 neuroprotein is positive, α-D-mannosidase is positive, and it can bind to peanut agglutinin. Birbeck's granules were found in the lesion cells by electron microscopy[11].

3) Fibrous histiocytoma: when CRDD has a longer course of fibrous tissue proliferation is more obvious and shows a matted structure, it needs to be distinguished from fibrous histiocytoma, which also shows a large area of histiocytes and is easily confused with this disease, but the histiocyte volume of fibrous histiocytoma is usually smaller and foamy cells, cells, and other morphologies are seen, with negative protein labeling for S-100 protein, and no characteristic dark-stained and light-stained areas of structure at low power microscopy. There is no characteristic dark-stained and light-stained structures at low magnification.

4) IgG4-related disease: characterized by fibrosis of the involved tissues, infiltration of IgG4-positive plasma cells, and elevated serum IgG4. Some studies have confirmed an increase in IgG4-positive plasma cells and elevated IgG4/IgG ratios in some cases of RDD, suggesting a link between RDD and IgG4-related diseases. RDD is currently listed as one of the diseases that may be clinically or histologically similar to IgG4-related diseases[12].

5) Cutaneous plasmacytosis (CP): is a chronic disease characterized by the proliferation of idiopathic polyclonal mature plasma cells, a rare type of cutaneous B-cell lymphoma. It is a rare type of cutaneous B-cell lymphoma. It is commonly found on the trunk and limbs, and manifests as multiple purplish-red or reddish-brown infiltrative plaques, plaques, and nodules, with varying shapes and sizes, and mild itching. The histopathology of the lesions is dominated by polyclonal mature plasma cell infiltration, which may be accompanied by lymphocyte and histiocyte

infiltration and accompanied by hypergammaglobulinemia. Based on the above characteristics, the diagnosis can be established[13].

6) B-cell lymphoma: a solid tumor of B-cell origin, includes Hodgkin's lymphoma and non-Hodgkin's lymphoma. Immunoglobulin tests show Smlg (+), κ light chain and/or free chain (+), and λ light chain and/or free chain (+). Primary cutaneous B-cell lymphomas have similar clinical symptoms, such as asymptomatic papules, nodules, plaques, and sometimes erythema with infiltratio[14].

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