

Case Report

Rosai-Dorfman Disease and Juvenile Xanthogranuloma in a Thai Boy: Report of a Case

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A 3-year-old Thai boy suffered from two histiocytoses, Rosai-Dorfman disease (RDD) and juvenile xanthogranuloma (JXG). The patient first presented with massive cervical lymphadenopathy at the age of one year. Biopsy revealed typical RDD; abnormally large CD68- and S-100 protein-positive histiocytes with occasional emperipolesis filled up the sinuses. Two years later, he developed polyuria and polydipsia. Skull film demonstrated osteolytic lesions at the occiput and left parietal region. Enlargement of the pituitary stalk was found on the magnetic resonance imaging. Despite the clinical impression of Langerhans cell histiocytosis, biopsy of the occipital lesion disclosed numerous large histiocytes with foamy cytoplasm. Several Touton giant cells with wreath-like arrangement of the nuclei were also observed. The abnormal cells expressed CD68 and factor XIIIa, but were non-reactive with S-100 protein and CD1a. Biopsy of the pituitary stalk was not performed. According to the authors' literature search, this represents the first report of RDD and JXG affecting the same person.

Keywords: Rosai-Dorfman disease, Juvenile xanthogranuloma, Langerhans cell histiocytosis, Histiocytosis

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Rosai-Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy is an idiopathic histiocytic proliferative disorder, originally described by Rosai and Dorfman in 1969⁽¹⁾. Cardinal features of the disease include massive, painless cervical lymphadenopathy with fever, and in some cases, polyclonal hypergammaglobulinemia⁽²⁾. Although RDD was first documented in the lymph node, extranodal involvements are not uncommon⁽³⁾.

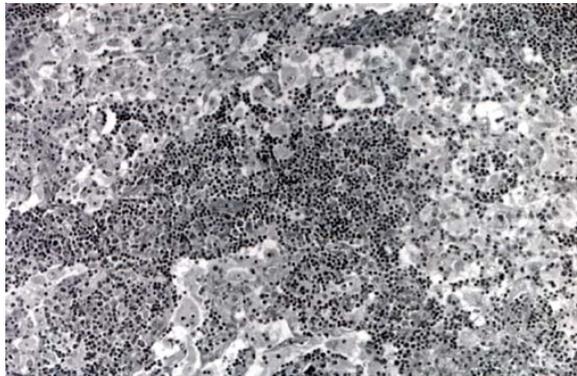
Juvenile xanthogranuloma (JXG) is a rather uncommon histiocytosis of infancy. Even though it is typically a localized prognostically favorable cutaneous lesion⁽⁴⁾, systemic involvement may occur⁽⁵⁾. JXG and Langerhans cell histiocytosis (LCH) may overlap clinically, and these two histiocytic disorders have been reported to affect the same patients⁽⁶⁾. The pur-

pose of this communication was to report a boy, who suffered both RDD and JXG. The combination of these histiocytoses has not previously been mentioned in literature.

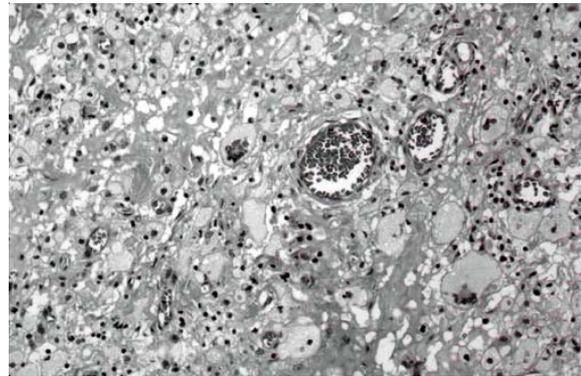
Case Report

At one year of age, a Thai boy presented with enlarged cervical lymph nodes. Biopsy revealed distended sinuses, filled with numerous abnormal histiocytes, with large vesicular nuclei and abundant pale eosinophilic cytoplasm. Some of the histiocytes contained intact lymphocytes and plasma cells in their cytoplasm, characteristic of the so-called "emperipolesis" (Fig. 1). A large number of mature plasma cells were also scattered in the intersinusoidal tissue. The histiocytes were strongly immunoreactive for S-100 protein and CD68, but were negative for CD1a and Factor XIIIa. Pathological diagnosis of Rosai-Dorfman disease was rendered. The patient remained well after excision, with no additional treatments.

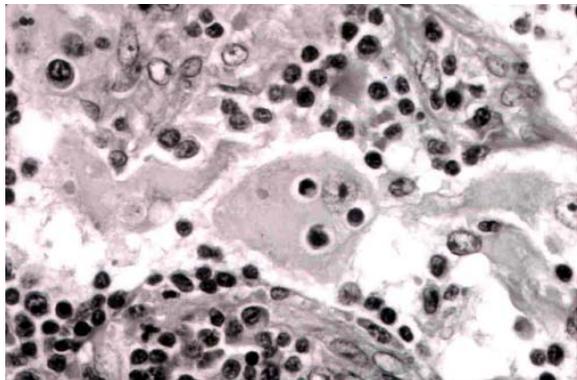
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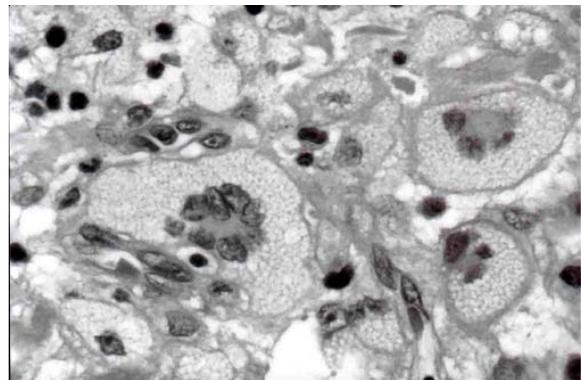
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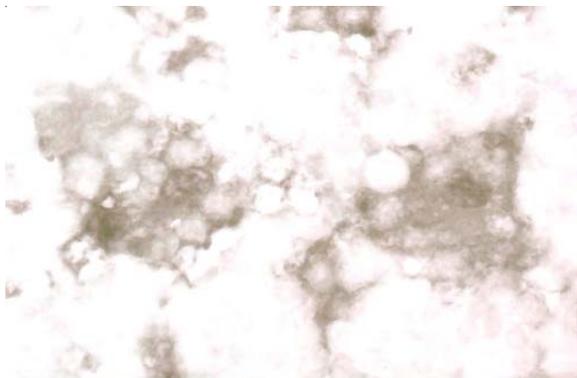
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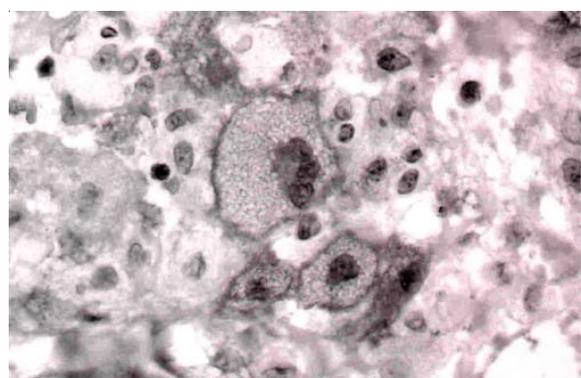
1B



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1C



2C

Fig. 1 Pathology of Rosai-Dorfman disease. Nodal sinuses are distended with numerous large histiocytes 1(A), some of which contain intact lymphoplasmacytes in the cytoplasm, characteristic of “emperipolesis” 1(B). The histiocytes express S-100 protein 1(C). (A and B, hematoxylin-eosin; C, S-100 immunostain)

Fig. 2 Pathology of juvenile xanthogranuloma. Sheet of large foamy histiocytes is depicted 2(A). Touton giant cells with wreath-like arrangement of the nuclei are highlighted 2(B). The histiocytes are immunoreactive with Factor XIIIa 2 (C). (A and B, hematoxylin-eosin; C, Factor XIIIa immunostain)

Two years later, the patient developed polyuria and polydipsia. Neurological examination was unremarkable. Skull film revealed osteolytic lesions at the occiput and left parietal area. The upper portion of

the pituitary stalk was enlarged on brain magnetic resonance imaging. Langerhans cell histiocytosis was clinically suspected. Biopsy of the occipital lesion, however, disclosed sheets and clusters of large histio-

Table 1. Immunohistochemical Profile of the patient's RDD and JXG

	RDD	JXG
CD68	+	+
S100	+	-
CD1a	-	-
Factor XIIIa	-	+

RDD = Rosai-Dorfman disease,
JXG = Juvenile xanthogranuloma

cytes, with voluminous foamy cytoplasm. Touton giant cells with wreath-like arrangement of the nuclei were occasionally identified (Fig. 2). These histiocytes expressed CD68 and Factor XIIIa, but failed to be reactive with S100-protein and CD1a. Pathological diagnosis of juvenile xanthogranuloma was then made. Diabetes insipidus was controlled by Minirin and DDAVP. The clinicians opted to follow the patient closely, with no additional management. No biopsy was taken from the pituitary stalk. Table 1 summarizes the immunohistochemical profile of the two histiocytic disorders of this patient.

Discussion

Disorders of the histiocytic and dendritic cell are broad, and have been difficult to classify. According to the World Health Organization, childhood histiocytosis syndromes are divided into 3 classes⁽⁷⁾. Langerhans cell histiocytosis (LCH) represents Class I histiocytosis, whereas Class II encompasses histiocytosis of mononuclear phagocytes other than Langerhans cells, hemophagocytic lymphohistiocytosis (familial and reactive), sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) (RDD), juvenile xanthogranuloma (JXG) and reticulohistiocytoma. Class III stands for malignant diseases of the histiocyte, including malignant histiocytic disorder, acute monocytic leukemia (FAB M5), malignant histiocytosis and true histiocytic lymphoma. In spite of the attempts, overlapping remains both clinical and pathological. Coexistence of LCH and RDD has been reported⁽⁸⁾. More recently, LCH and JXG has been put together under the "dendritic cell-related" histiocytoses⁽⁶⁾.

The presented patient first came with RDD involving the cervical lymph nodes, followed by JXG of the skull 2 years afterwards. To the authors' best knowledge, no such combination of histiocytic disorders has previously been recorded. Although the

cutaneous lesion in a patient with RDD reported by Thawerani et al (Case 2) has raised the possibility of coexistent JXG, the authors noted lymphophagocytosis in the lesion and concluded that it was a cutaneous manifestation of RDD⁽⁹⁾. A lesion in the pituitary stalk associated with diabetic insipidus (DI) was of interest. It would represent a histiocytic disease, particularly the LCH, RDD or xanthoma disseminatum; the latter is a form of JXG which has been reported to cause DI when arising in the pituitary region^(10,11). Unfortunately, no tissue diagnosis of the neurohypophysial lesion was available in the presented patient.

From the pathological standpoint, the common histiocytoses can be diagnosed or highly suspicious on routine stains. Immunohistochemistry is often used to confirm the diagnosis or to identify small amounts of abnormal histiocytes in small biopsy specimens. Sinus pattern of RDD is very distinctive, and the lesion typically contains numerous non-neoplastic plasma cells. The histiocytes in RDD possess large vesicular nuclei and voluminous pale eosinophilic cytoplasm. "Emperipolesis" is the diagnostic hallmark. JXG consists of large histiocytes with foamy cytoplasm. They are often multinucleated and the Touton giant cells with wreath-like arrangement of the nuclei are characteristic. Nuclear irregularity and grooving are features of Langerhans cells in LCH, and the lesion usually contains eosinophils. Immunohistochemically, RDD is CD68+, S-100 protein+, CD1a-, Factor XIIIa^(1,2), whereas JXG CD68+, S-100 protein-, CD1a-, Factor XIIIa⁽⁶⁾ and LCH CD68+, S-100 protein+, CD1a+, and Factor XIIIa⁽⁸⁾. It should be noted that the JXG are somewhat histologically and immunohistochemically similar to another histiocytosis, Erdheim-Chester disease (ECD) (CD68+, S-100 protein-/+, CD1a-, and Factor XIIIa^(12,13)). The latter, however, commonly affects middle-aged adults, and has typical changes in the long bones. Clonal study using chromosome X-inactivation analysis has favored the clonal proliferation of LCH⁽¹⁴⁾ and ECD⁽¹⁵⁾, and the polyclonal nature of RDD⁽¹⁶⁾. Information regarding the clonality of JXG is currently unavailable.

The majority of RDD and cutaneous JXG carry an excellent prognosis, with a high rate of spontaneous regression. Nevertheless, RDD requiring radiation or chemotherapy, and multiple extracutaneous involvements in JXG have been observed^(2,6).

To summarize, the combination of Rosai-Dorfman disease and juvenile xanthogranuloma has been described, for the first time, to affect the same patient. Whether the lesions are related or coincidental

remains unknown.

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Rosai-Dorfman disease และ juvenile xanthogranuloma ในผู้ป่วยเด็กชายไทย: รายงานผู้ป่วยหนึ่งราย

วัชรวิ โปธิ์กลาง, สมฤทัย ช่างโชติ, มุกดา ชัยพิพัฒน์, อิศรางค์ นุชประยูร, ชนพ ช่างโชติ

ได้รายงานผู้ป่วยเด็กชายไทยอายุ 3 ปี ซึ่งเป็น *Rosai-Dorfman disease (RDD)* ร่วมกับ *Juvenile xanthogranuloma (JXG)* ผู้ป่วยรายนี้มาพบแพทย์ด้วยเรื่องต่อมเหงื่อที่คอโต เมื่ออายุ 1 ปี ผลการตรวจชิ้นเนื้อเป็น RDD ที่ให้ผลบวกต่อ CD68 และโปรตีน S-100 สองปีต่อมาผู้ป่วยมีอาการกระหายน้ำบ่อยและปัสสาวะบ่อย เอกซเรย์กะโหลกศีรษะพบรอยโรคที่บริเวณท้ายทอยและ parietal ด้านซ้าย จากการตรวจเอกซเรย์ magnetic resonance พบว่าแกนของต่อมใต้สมองมีขนาดใหญ่ขึ้น ผลการตรวจชิ้นเนื้อที่บริเวณท้ายทอยพบเป็น JXG ซึ่งให้ผลบวกต่อ CD68 และ Factor XIIIa ในขณะที่ให้ผลลบต่อโปรตีน S-100 และ CD1a ไม่ได้ทำการตัดรอยโรคที่แกนของต่อมใต้สมองเพื่อตรวจทางพยาธิวิทยา จากการทบทวนวรรณกรรมทางการแพทย์ ผู้ป่วยรายนี้เป็นรายแรกที่เป็นทั้ง *Rosai-Dorfman disease* และ *juvenile xanthogranuloma*
