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A report of Rosai–Dorfman disease with systemic multiple lymphadenopathy and high IgG4 plasma cell infiltration

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Abstract

The Rosai-Dorfman disease (RDD) is a kind of sinus histiocytosis with massive lymphadenopathy and is remarkably rare. RDD is characterized by large histiocytes with emperipolesis. However, the cause of RDD is unknown, and most cases are relieved spontaneously. In rare cases, patients may have onset and remission of lymph nodes and extranodal involvement. This report showed an RDD case in a 67-year-old male patient with systemic superficial lymphadenopathy and high IgG4 plasma cell infiltration. We showed that a possible RDD diagnosis should be kept in mind when encountering a systemic multiple lymphadenopathy and high IgG4 plasma cell infiltration. Also, an overlap between RDD and IgG4-related disease might be present, which might help in clinical recognition of RDD.

Keywords

Rosai-Dorfman disease, sinus histiocytosis with massive lymphadenopathy, IgG4 plasma cell infiltration, IgG4 related disease

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Introduction

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with multiple lymphadenopathy, is a rare disease in clinical.[1] The most common presentation of RDD is bilateral painless massive cervical lymphadenopathy associated with fever, night sweats, fatigue, and weight loss. Mediastinal, inguinal, and retroperitoneal nodes might also be involved.[2,3] Herein, we reported the histological characteristics, clinical morphology and course of an RDD case with painless swelling of multiple superficial lymph nodes as the first clinical manifestation and high IgG4 plasma cell infiltration.

Case report

A 67-year-old male patient was hospitalized due to painless progressive enlargement of superficial lymph nodes for more than 3 months. The lesion gradually increases, and the swollen lymph nodes were about the size of soybeans to pigeon eggs. The skin temperature was not high, no tenderness was detected, and the pressure was active. During the disease course, there was a slight cough, a small amount of yellow pus sputum, slight frequent urination, urgency of urination, and pain of urination. The patient had no special past medical history and was healthy in other aspects,: without fever, fatigue, weight loss and other medical history. No skin or mucous membrane was involved. The physical examination showed that several swollen lymph nodes of different sizes were palpated on both sides of the back of the ear, neck, subclavian and groin, with sizes ranging from soybeans to eggs. There was no tenderness, the quality was medium, and the activity was acceptable. Color Doppler ultrasound of enlarged lymph nodes in groin and neck (Figure 1).

Complete lymph nodes of the right neck and right groin were excised for pathological biopsy. The pathological examination results were as follows: histiocyte-like cells significantly proliferated with multiple plasma cell infiltration and interstitial fibrosis (Figure 2). Immunohistochemistry: the structure of the right inguinal lymph node was destroyed, and a small number of follicles remained. Immunohistochemical

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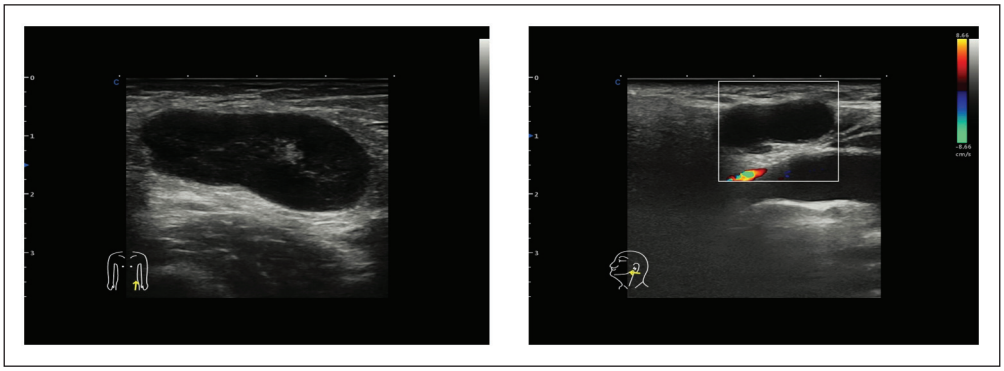

Figure 1. Color Doppler ultrasound of enlarged lymph nodes in groin and neck.

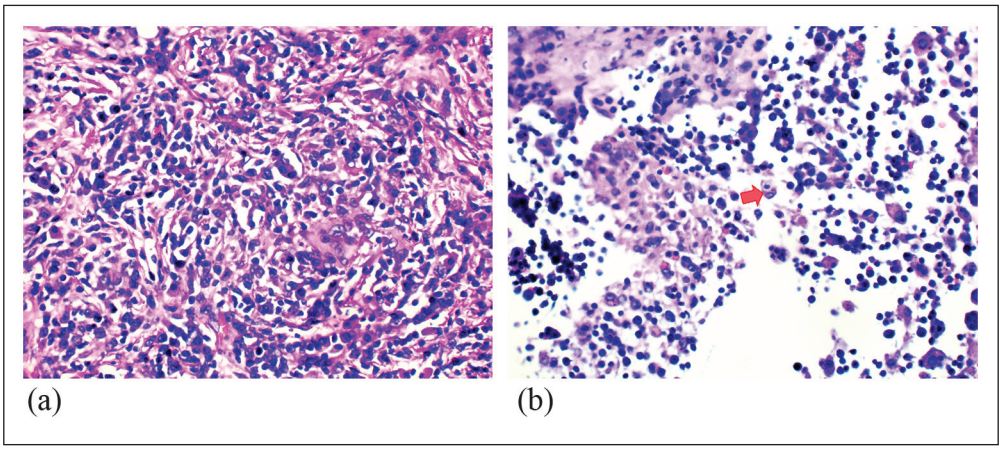

Figure 2. Hematoxylin and eosin(H&E x 200) straining shows the nodal architecture effacement by diffuse sheets of histiocytes with abundant eosinophilic cytoplasm and surrounding lympho-plasmacytic infiltrate (a). The areas where the histiocytes engulf intact chronic inflammatory cells are called emperipolesis (red arrows) (b).

staining: plasma cell IgG (+), IgG4 (partial +, < 100 /HPF), IgG4 < IgG < 40%, CD38 (+), CD138 (+), K (dominant +), λ (partial +), residual follicular CD20 (+), interstitial CD3 (+), histiocytic like cells CD1a (-), langerin (-), S-100 (+), CD163 (+) (Figure 3), and penetration phenomenon (Figure 2). PAS(-). Therefore, combined with morphological changes, RDD with increased IgG-positive cells was considered.

The laboratory examination results were as follows: HB 99 g/L; ALP 216 u/L, GGT 138 u/L, globulin 57.7 g/L, albumin 26.4 g/L; IgG 44.8 g/L, C3 208 mg/L, C4<16.7 mg/L, Kappa 31.6 g/L, Lambd 24.7 g/L, K/ λ 1.279; Bone marrow staging negative. The immune typing of lymphoma was normal. No obvious abnormality was found in chest plain scan CT, head plain scan CT, color Doppler ultrasound of heart, color Doppler ultrasound of deep abdominal lymph nodes, color Doppler ultrasound of abdominal organs and color Doppler ultrasound of thyroid gland.

Considering that the disease did not involve other organs, and the swollen lymph nodes of the patient's whole body did not significantly compress the organs, the patient was not given special treatment. However, during the follow-up of 3 months, the swollen lymph nodes of the patient consciously and gradually shrank.

Discussion

Azoury and Reed first reported the rare RDD in 1966, and Rosai and Dorfman studied it in detail and officially named it in 1969.[4] The etiology and pathogenesis of RDD are unclear, and most scholars believe that it might be related to infection and low autoimmune function.[5,6] Currently, hormones, radiotherapy, chemotherapy, anti-infection, surgery, and clinical observation are the main treatments for RDD, and there is no clear treatment plan.

Herein, the patient was a middle-aged man with painless enlargement of lymph nodes in the bilateral neck, supraclavicle, axillary and inguinal areas as primary clinical manifestations. The laboratory tests showed that the blood sedimentation rate rapidly increased, eosinophils significantly increased, hypoalbuminemia, hyperglobulinemia, hyperiggemia, high IgG4 plasma cell, low complement, the κappa rose, the lambd rose, and the κ/λ Decreased. The

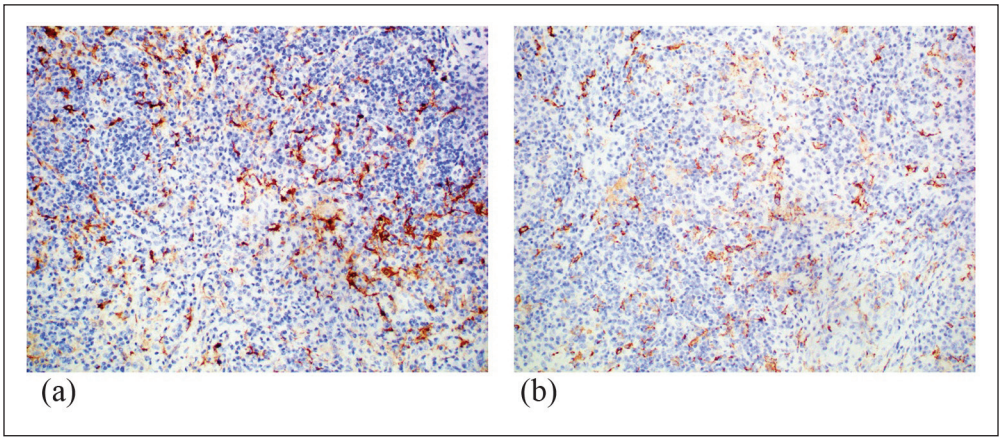

Figure 3. (immunohistochemistryX200) shows the characteristic histiocytes were strongly positive for S-100 protein (a) and CD163 (b).

pathology and immunohistochemistry of the right cervical and the right inguinal lymph node biopsy showed many typical pathological features such as plasma cell infiltration, interstitial fibrosis, extensive expansion and extension of lymph sinuses, S-100 positivity, and no clinical evidence such as infection or tumor. Hence, RDD diagnosis with IgG-positive cells was evident.

For this patient, the question was whether RDD was complicated by digestive system diseases, such as liver disease. Indeed, the patient had liver function damage. Nevertheless, after liver protection treatment, the liver enzymes were normal, bile enzymes significantly improved, and hypoproteinemia and hyperglobulinemia were improved. The patient had RDD and IgG4 of 93.7 g/L. Therefore, it is also necessary to consider a combination with the IgG4-related disease (IgG4-RD).

The IgG4-RD was first described in 2001 in sclerosing cholangitis patients with elevated serum IgG4 levels.[7] It can be seen from the current case that RDD can be accompanied by IgG4 infiltration, which was higher than in typical IgG4-RD patients. The current diagnostic criteria for IgG4-RD are as follows:[8] (1) clinical and radiological features: One or more organs show diffuse or localized swelling or a mass or nodule characteristic of IgG4-RD. In single organ involvement, lymph node swelling is omitted. (2) Serological diagnosis: Serum IgG4 levels greater than 135 mg/dl. (3) Pathological diagnosis: Positivity for two of the following three criteria: ① Dense lymphocyte and plasma cell infiltration with fibrosis. ② Ratio of IgG4-positive plasma cells /IgG-positive cells greater than 40% and the number of IgG4-positive plasma cells greater than 10 per high powered field. ③Typical tissue fibrosis, particularly storiform fibrosis, or obliterative phlebitis. Definited diagnosis: 1) + 2) + 3) .

For this patient, the ratio of IgG4-positive plasma cells/IgG-positive cells lower than 40% and have no typical tissue fibrosis, so the diagnosis of IgG4-RD is not considered. However, in 2014, a histopathology journal proposed the phenomenon of mutual simulation between RDD and IgG4-RD.[9] Unfortunately, the BRAF mutation in this case was not detected, so there were some limitations.

Conclusion

Herein, we highlighted that RDD and IgG4-RD are very rare cases, and the pathogenesis of this rare disease is still poorly understood. RDD and IgG4-RD have similar clinical manifestations, and almost all organs can be involved. When rheumatism immunologists find a large amount of IgG4 infiltration in the patient's serum and pathological examination in clinical work, they need to distinguish it from RDD. Although almost all organs can be involved in RDD, almost 90% of RDD patients have cervical lymph node involvement. Since the outcomes are usually favorable, it is essential to correctly identify RDD and IgG4-RD for formulating treatment plans.

RDD is a rare disease, most of which is characterized by lymph node enlargement. Nevertheless, further studies are required to interpret the major involvement of lymph nodes and the high incidence rate in Asian patients. At present, there is an increasing amount of literature on this disease process, but it is very necessary to review the case reports and similar presentations in this age group.

Author contributions

Pan Lv and Maoling Zhu participated in patient treatment and collection of relevant data, Pingdan Liu reviewed the literature and participated in the drafting of the manuscript; Jangping Liu was responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

Declaration of conflicting interests

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Ethical approval

According to national and local regulations, the approval by Ethics Committee is not required for a case report.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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