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Autoimmune Diseases and Rosai-Dorfman Disease Coexist More Commonly than Expected: Two Case Reports

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Data Collection B
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Case series
Patient: Male, 56 • Male, 52
Final Diagnosis: Rosai-Dorfman disease
Symptoms: Incidental finding
Medication: —
Clinical Procedure: Biopsy
Specialty: Hematology

Objective: Rare co-existance of disease or pathology

Background: The educational objective of this study was to describe 2 case reports in which patients were found to have an autoimmune disease concomitantly with a rare, benign histiocytic disorder known as Rosai-Dorfman disease (RDD). It is unclear if there is an underlying association between autoimmune disease and RDD. Lymphadenopathy, although most frequently seen bilaterally in the cervical region in RDD, may be present anywhere. A biopsy with histologic confirmation is required to not only evaluate for malignancy in these cases, but also necessary to diagnose RDD.

Case Report: We describe 2 cases in which RDD was found incidentally in 2 patients who concomitantly had known autoimmune diseases. The first patient's history included Factor II deficiency, antiphospholipid syndrome, and autoimmune hemolytic anemia; whereas the second patient had a positive antinuclear antibody test, elevated rheumatoid factor, positive lupus anticoagulant, and positive beta-2 glycoprotein 1 antibodies, as well as positive anticardiolipin antibody panel, immune mediated thrombocytopenia, and pernicious anemia. Lymphadenopathy and an enlarged mass were seen in these cases respectively, which were histologically proven to be RDD. Steroid therapy was the mainstay of treatment.

Conclusions: Autoimmune diseases are relatively common in the general population and it appears that RDD coexists more often than suspected. When lymphadenopathy or a mass is seen, especially in those with other autoimmune diseases, RDD should remain within the differential diagnosis. Further research is required to determine characteristics and optimal management of RDD. We have observed in the cases presented, that if the autoimmune disease is well controlled, RDD can be an indolent disease.

MeSH Keywords: Autoimmune Diseases • Histiocytosis, Sinus • Immunoblastic Lymphadenopathy

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/915627

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Background

Rosai Dorfman disease is a sinus histiocytosis which classically presents with massive lymphadenopathy and a variety of constitutional symptoms. It is characterized by a non-clonal proliferation of distinctive cells of macrophage or histiocyte lineage, that primarily accumulate in lymph nodes [1]. We present 2 case reports in which patients were found to have an autoimmune disease as well as a rare, benign histiocytic disorder known as Rosai-Dorfman disease.

Case Reports

Case 1

A 56-year-old male with a history of Factor II deficiency and antiphospholipid syndrome, diagnosed at age 35, presented to the hospital with back pain. Laboratory studies documented autoimmune hemolytic anemia. A computed tomography (CT) scan was performed which revealed nephrolithiasis and enlarged lymph nodes in the celiac, perigastric, and peripancreatic areas. A subsequent 18-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT scan confirmed the presence of many abnormal lymph nodes in the periesophageal, mediastinum, and celiac area as well as in the perigastric and peripancreatic regions. Excisional biopsy of one of the perigastric lymph nodes confirmed Rosai-Dorfman disease: sinus histiocytosis with massive lymphadenopathy. Despite the fact that the role of steroids is not known in the treatment of RDD, this patient responded well to steroid therapy, which also ameliorated his autoimmune hemolytic anemia. A repeat CT scan several years later showed enlargement of a mediastinal lymph node. At that time, he also had a reactivation of hemolytic anemia. A bone marrow biopsy was performed in the setting of worsening anemia which revealed erythroid hyperplasia but no neoplastic process. A brief course of methylprednisolone was resumed in addition to treating using rituximab. He completed 4 doses of weekly rituximab with no improvement of his anemia. The patient was eventually transitioned to danazol with no response either. The patient has required chronic low-dose steroid treatment, with no plan to taper, as the patient has had stable hemoglobin and hematocrit and has worsening of autoimmune hemolytic anemia with even slow steroid taper.

Case 2

A 52-year-old male with a history of hypertension, hyperlipidemia, type 2 diabetes mellitus, obstructive sleep apnea, and prior transient ischemic attack, presented to the hospital with a 2-week history of altered mental status, confusion, disorientation, and memory loss. This had progressed to the point that he had word-finding difficulty, and was unable to perform simple tasks such as dressing himself, keyboarding, and entering his password into a computer system. He was found to have impaired higher cortical function involving both dominant and non-dominant cortex. Head CT showed a left frontal hypodensity. A magnetic resonance imaging (MRI) showed acute infarct of the left frontal lobe, multiple additional punctate infarcts within the bilateral cerebellar hemispheres and within the right cerebellum. A magnetic resonance angiogram (MRA) demonstrated no focal flow-limiting stenosis, proximal large artery occlusion, or discrete aneurysm. Venous duplex of the bilateral legs showed no evidence of deep vein thrombosis (DVT) and an echocardiogram, while technically limited, showed no evidence of a cardiac source of emboli. He had electrocardiogram (ECG) changes showing sinus tachycardia and a possible age undetermined inferior infarct. His complete blood count (CBC) on admission showed white blood count (WBC) of 7800 per microliter, platelet count of 69 000 per microliter, hemoglobin 10.4 gram/dL, hematocrit 30.8%, mean corpuscular volume (MCV) 87 fL and red blood cell distribution width (RDW) was 14.9. Additional evaluation revealed antinuclear antibody screen positive at a titer of 1–80 with a nucleolar pattern. He had elevated rheumatoid factor, positive lupus anticoagulant, negative rapid plasma reagin (RPR) and positive beta-2 glycoprotein 1 antibodies, and positive anticardiolipin antibody panel with IgA >65, IgG >112 and IgM 48. He was started on intravenous (IV) heparin and later transitioned to warfarin. In addition, he was noted to have immune mediated thrombocytopenia for which he was started on prednisone, and cyanocobalamin for pernicious anemia, with confirmed intrinsic factor blocking antibody. Given suspicion for a hypercoagulable state, diagnostic evaluation for an occult malignancy was performed. CT scan of the chest and abdomen showed an exophytic, irregular mass extending from the sigmoid colon in the left lower quadrant, and infarcts in the spleen. No mediastinal or hilar adenopathy was noted. Colonoscopy showed no findings within the sigmoid colon. CT guided biopsy from the mesenteric mass near the sigmoid colon revealed RDD. It is noteworthy that extranodal presentation of RDD is seen in a substantial minority of cases. The patient was continued on prednisone for a total of 3 additional months. Since then, patient's RDD has been monitored with imaging studies. 2.5 years later, CT abdomen and pelvis showed a slight interval increase in mass-like lesion adjacent to the sigmoid colon, but no further treatment was deemed necessary. He did however develop worsening proteinuria over the last several months. A kidney biopsy confirmed lupus nephritis, for which patient has been prescribed mycophenolate.

Discussion

It was in 1969 that the pathologists Rosai and Dorfman first reported a non-neoplastic, lymphohistiocytic, idiopathic

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proliferative disorder of histiocytes of reactive nature, which is predominately nodal-based, now known as RDD [2,3]. Based on the cases described, the vast majority of RDD cases present with massive, painless cervical lymphadenopathy, which is usually bilateral [4]. While the precise etiology and pathogenesis of RDD is unclear, it has been shown that in 10% of cases, RDD coexists with other immunologic diseases [1]. Associated immunologic diseases include: autoimmune hemolytic anemia (as described in one of our cases), idiopathic juvenile arthritis, and systemic lupus erythematous [5]. On laboratory findings, an elevated erythrocyte sedimentation rate (ESR) and polyclonal hypergammaglobulinemia are seen in 90% of the cases, followed by fairly commonly seen leukocytosis with neutrophil predominance, normochromic normocytic anemia, and positive rheumatoid factor. It is rare however, to see hemolytic anemia and eosinophilia [6].

Our cases present 2 middle-aged Caucasian males who had incidental findings on CT scan of lymphadenopathy or a suspicious mass. In the setting of concern for malignancy, lymph node biopsy or fine needle aspiration (FNA) was performed, which revealed characteristic histology consistent with RDD.

Despite its diagnostic challenges, most cases of RDD have an indolent and relatively good prognosis. The natural history of the disease follows a gradual resolution of lymphadenopathy in about half of the cases [7]. If treatment is warranted, corticosteroids have been the first-line with fairly good response [8]. In selected cases, chemotherapy and radiotherapy, or even surgical resection have been used. The optimal duration of treatment with steroids or other systemic therapies, has not been established. However, experts believe that a 6-month to 12-month course of systemic therapy followed by close observation, assuming tolerance and a favorable response to treatment, is thought to be a reasonable approach [9].

Further research is required to fully understand the characteristics and management of RDD disease. It is important to emphasize however, that autoimmune diseases are fairly common in the general population and RDD should also be considered when lymphadenopathy is encountered. Similarly, in patients with histologically proven RDD, careful attention should be paid to autoimmune disease, as they coexist in a non-negligible percent of this population.

Conclusions

Autoimmune diseases are relatively common in the general population and it appears that RDD coexists more often than suspected. When lymphadenopathy or a mass is seen, especially in patients with known autoimmune diseases, RDD should remain within the differential diagnosis. If RDD is confirmed, it typically responds to steroid or systemic therapy such as rituximab, but it appears that it is most important to ensure adequate treatment of the autoimmune diseases. If autoimmune diseases are well controlled, RDD can be an indolent disease.

Conflict of interest

None.

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