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To the Editor:

Rosai-Dorfman disease (RDD) is a rare disorder in childhood. The association of RDD and systemic lupus erythematosus (SLE) is very rare, with only 2 previously reported cases, and neither of these in a child1,2. We describe a child who presented with histopathology-confirmed RDD, and developed SLE 3 years later.

A 7-year-old boy of Canadian First Nations background presented at age 4 years to the pediatric hematology/oncology clinic with a 3-month history of asymptomatic, bilateral massive lymphadenopathy involving the cervical, supravacular, mediastinal, hilar, and axillary lymph nodes. He has a healthy fraternal twin, and there is no family history of connective tissue diseases. The lymphadenopathy failed to respond to a course of antibiotics. Laboratory tests showed mild microcytic hypochromic anemia with lymphopenia (white blood cells 6.29 x 10^9/l, hemoglobin 103 g/l, mean corpuscular volume 74.3 fl, mean corpuscular hemoglobin 23.5 pg/cell, platelets 262 x 10^9/l, lymphocytes 0.63 x 10^9/l, absolute neutrophil count 4.98 x 10^9/l) and high erythrocyte sedimentation rate, 63 mm/h. Serial chest radiographs showed persistent nonprogressive large bilateral mediastinal, hilar, right infrahilar, and paratracheal lymphadenopathy (Figure 1). Computed tomography scan showed adenopathy, airway narrowing, and atelectasis as well as superior vena cava displacement (Figure 2). These lymph nodes were gallium avid. Investigations for infectious causes including tuberculosis, toxoplasmosis, mycoplasma, Epstein-Barr virus, cytomegalovirus, human immunodeficiency virus, and hepatitis viruses were negative. Lymph node specimens for bacterial, viral, and fungal cultures were negative. Immune investigation confirmed lymphopenia with reversed CD4/CD8 ratio. Flow cytometry for double-negative T cells was negative for autoimmune lymphoproliferative syndrome. Immunoglobulin G was 21.9 g/l (normal 5.04–14.65), immunoglobulin A 1.87 g/l (0.27–1.95), and immunoglobulin M 1.85 g/l (0.31–2.08). The patient developed protective antibodies against tetanus and diphtheria, and lymphocyte stimulation test was normal. A biopsy of the largest cervical lymph node showed sinus histocytosis with lymphophagocytosis (emperipolesis). Immunohistochemical staining for S100 protein was positive in lesional histiocytes and diagnostic of RDD (Figures 3 and 4).

Initially, the patient was followed without specific treatment, and 4 months later he presented with progressive cough and orthopnea. A radiograph showed progression of the mediastinal and perihilar lymphadenopathy.
pathy. He was started on oral prednisone 40 mg/m², with resolution of orthopnea, and a decrease in hiliar and mediastinal lymphadenopathy. However, with every attempt to taper the steroid, he had worsening respiratory symptoms, and therefore he was started on 6-mercaptopurine 60 mg/m²/day and methotrexate 12 mg/m²/week orally. There was partial clinical response to this treatment, but he had persistent respiratory symptoms. A repeat lymph node and bone marrow biopsy showed findings similar to the first sample (consistent with RDD).

He presented to hospital again in July 2008 with shortness of breath and tachycardia. On examination he was found to have pulsus paradoxus, and he moved to 4.1 x 10⁹/l and 233 x 10⁹/l, respectively. WBC and platelet counts required several months to be corrected to 4.1 x 10⁹/l and 233 x 10⁹/l, respectively. His hematologic findings were present for 3 years, and his hemoglobin and C3 had improved to 10.0 g/l and 0.73 g/l, respectively. The atypical infiltrates in lymph nodes, including lymphocytes, prominent plasma cells and cellular debris are characteristic of RDD. The atypical infiltrates in lymph nodes, including lymphocytes, prominent plasma cells and cellular debris are characteristic of RDD. The histology of lymph nodes resected from our patient had the hallmark of Rosai-Dorfman disease.

The causative agent for RDD is unknown. Its diverse clinical manifestations and frequent association with subtle or severe immunologic abnormalities suggest an immune-mediated etiology or at least that immune-mediated mechanisms play a major role in the pathogenesis. RDD and SLE are very rare association. Rituximab, an anti-CD20 monoclonal antibody, was effective and well tolerated in our case.

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