Rosai-Dorfman Disease Presenting with Solitary Liver Mass Without Lymphadenopathy: Case Report and Literature Review

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Abstract

This care report presents a 51-year-old woman patient with a cyst-like mass in the liver. The proliferated histiocytes, with the eosinophilic nucleolus, occasionally showing lymphophagocytosis (emperipolesis) positively for CD68 protein S-100 were reported in the pathological study, and the plasma cells were positive for CD138, consistent with Rosai-Dorfman disease.

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Abstract

This care report presents a 51-year-old woman patient with a cyst-like mass in thew liver. The proliferated histiocytes, with the eosinophilic nucleolus, occasionally showing lymphophagocytosis (emperipolesis) positively for CD68 protein S-100 were reported in the pathological study, and the plasma cells were positive for CD138, consistent with Rosai-Dorfman disease.

Keywords

Rosai-Dorfman Disease, Destombes–Rosai–Dorfman Disease, Histiocytosis, Liver Mass

Introduction

Rosai–Dorfman disease, or sinus histiocytosis with massive lymphadenopathy, is characterized by histiocytosis in different organs specially in lymph nodes [1, 2]. The exact etiology of the disease is unknown but most of the patients present with fever, leukocytosis, and nonpainful cervical lymphadenopathy. It can involve the skin, soft tissue or less commonly central nervous system. The gastrointestinal engagement is rare [3-7]. This article is a rare case report of solitary liver mass without lymphadenopathy with a review of previous literature.

Case Presentation

A 51-year-old lady was admitted to hospital with chronic abdominal pain, weight loss (5% of body weight), history of undulant fever and nocturnal sweating. In physical examination, orthostatic hypotension, conjunctival pallor and abdominal right upper quadrant tenderness were noticed. Laboratory tests showed elevated Erythroid Sedimentation Rate (ESR=87$^{mm/h}$) and normocytic normochromic anemia (hemoglobin=9.3 g/dl). Abdominal ultrasound revealed a 37mm×49mm cyst-like mass in the left lobe of liver (4A segment) without internal septation, and no other abnormality in abdominopelvic cavity was identified. Computed tomography showed a non-enhanced hypodense mass with regular margin (sized: 4×5^{cm}) in the left lobe of liver (Figure 1) without any further abnormal findings.

We re-reviewed patient's past medical history for any diagnostic clues for the solitary liver mass. Personal and family history was negative for chronic liver disease and viral hepatitis risk factors. No stigmata for cirrhosis were identified. Viral hepatitis panel, alpha fetoprotein and CA19-9 were undetectable. Screening colonoscopy for colorectal cancer was normal 6 months before symptoms start.

Finally, she was admitted to Ghazi Hospital, affiliated to Tabriz University of Medical Sciences, for diagnostic mass resection and underwent partial hepatectomy surgery. In pathological study, the liver tissue contained a cystic lesion composed of proliferated histiocytes, with eosinophilic nucleolus, some double or multinucleated, occasionally showing lymphophagocytosis (emperipolesis). The histiocytes were mixed with a polymorph infiltration composed of mononuclear and plasma cells. Histiocytes stained positively for CD68 and protein S-100, and plasma cells were positive for CD138, kappa and lambda. Hodgkin's lymphoma was ruled out by negative CD15 and CD30 staining. Peripheral blood smear and bone marrow aspiration were normal. Bone marrow biopsy showed lymphoplasmacytosis with slight megakaryocytosis. The liver histological pattern was consistent with Rosai-Dorfman disease (RDD). The patient was consequently referred to the hematology service and we decided to start prednisone, $30^{\mathrm{mg/day}}$. She was followed conservatively with repeat imaging after 3 months. The follow-up CT revealed no recurrence and she responded clinically to steroids. She continues to be followed with yearly imaging and $5^{\mathrm{mg/day}}$ prednisone and will likely remain on steroids for the long term.

Discussion

Rosai-Dorfman Disease (RDD) which is also referred to as sinus histiocytosis with massive lymphadenopathy, is an exceedingly rare non-Langerhans cell reactive histiocytic disorder that was initially described in 1969 [2, 8]. The prevalence of RDD is approximately 1:200,000 in the United States, and may present with fever, neutrophilia, increased serum erythrocyte sedimentation rate, leukocytosis, lymphopenia, polyclonal hyperglobulinemia, and anemia. In most cases, however, there is no apparent or specific symptom[9-13].

In its most recent revised classification in 2016, the writing group of the Histiocyte Society has classified RDD into the following subtypes: familial RDD, classical RDD, extranodal RDD, neoplasia-associated RDD, and immune disease-associated RDD [14]. Classic RDD presents with massive painless cervical lymphadenopathy in children and young adults, with a slight (58%) male predominance and a benign self-limiting course [8, 13, 15, 16]. Older age and underlying immunologic abnormalities (autoimmune hemolytic anemia, Wiskott-Aldrich syndrome, glomerulonephritis, rheumatoid arthritis) are associated with a more extensive disease and chronic relapsing course[17].

The pathologic features of nodal RDD include the sinus expansion of large histiocytes, described by Destombes as possessing "watery-clear" cytoplasm with a large foamy nucleus and prominent nucleolus. Consistent features, regardless of the site, include the cytomorphology of the large pale histiocytes and their immunophenotype. Emperipolesis, the trafficking of intact leukocytes through the cytoplasm, is a helpful finding but is not required for diagnosis, because it can be focal, especially at extranodal sites, and may be seen focally in other histiocytoses such as juvenile xanthogranuloma, and malignant histiocytoses. Extranodal lesions are usually associated with more fibrosis, fewer RDD histiocytes and less emperipolesis. In such cases, immunostains are needed to highlight the residual RDD histiocytes in a rich lymphoplasmacytic background with stromal fibrosis and a variable xanthomatous histiocytic reaction. The immunophenotype of the large RDD histiocytes is characterized by cytoplasmic and nuclear S100 and fascin positivity, with CD68 and variable CD163 and CD14 positivity. The cells are CD1a-/CD207- in contrast to Langerhans cell histiocytosis[18-22].

Extranodal involvement is common and may occur in more than 40% of patients, sometimes without associated lymphadenopathy, and only 23% of patients have exclusive extranodal disease [13, 23, 24]. Virtually every organ can be affected by RDD (respiratory, bone, CNS, genitourinary, orbit, soft tissue, visceral organs, nasal cavity, etc.) and in contrast to isolated lymphadenopathy, the mortality of extranodal RDD is higher in patients with lower respiratory tract, hepatic, or renal involvement (30%, 33%, and 40%, respectively)[13].

Intraabdominal extranodal disease is uncommon, with an incidence of 4% [25]. The gastrointestinal (GI) system is one of the least commonly affected sites (<1%); we are aware of only 41 examples reported in the English literature[7, 13, 25-40]. The GI disease mostly affects middle-aged females. Most digestive system cases arise in the tubular GI tract with most cases being located beyond the pylorus[40]. Pancreatic or hepatic involvement is reported but extremely rare [13, 34, 41]. Hepatic lesions tend to present in younger patients; all but the 1 reported patient has had systemic disease [25, 29, 33]. To our knowledge, our case is the first adult patient reported with solitary liver RDD, without lymphadenopathy.

No uniform approach has been delineated for RDD, and treatment is best tailored to the individual clinical circumstances. Therapeutic strategies in literature include: observation, steroids (prednisone 40-70^{mg} per day, followed by taper), surgical resection/debulking, radiotherapy, chemotherapy, Sirolimus, Thalidomide, Rituximab and Imatinib [42-49]. In our case, the patient had a partial response to steroids and her symptoms have been improving. The authors do not expect a complete resolution of the disease, however in cases such as these we recommend beginning with steroids and escalating to other treatments only if the disease is non-responsive to steroids and difficult to manage or life threatening. We encourage serial imaging and follow-up for any changes.

Declarations

Ethics approval and consent to participate

The patient's identity is secret and preserved unknown in the article and the patient received an oral and written permission form that was approved by the ethics committee of Tabriz University of medical sciences and Urmia university of medical sciences. The consent was obtained from the study participant prior to study commencement and the study participants gave consent to publish.

Consent to publish

Signed consent for publication have been obtained from the patient and legal guardian.

Availability of data and material

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests

All of authors report no kind of conflict of interests in this study.

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Authors' Contributions

All of the authors in this study have contributed equally in design, performance, data collection, and writing and review of the manuscript.

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Figure Legends

Figure 1: Computed tomography showed a non-enhanced hypodense mass.

Figure2: Histiocytes, with the eosinophilic nucleolus, some double or multinucleated, occasionally showing lymphophagocytosis (emperipolesis).

Figure3: Histiocytes stained positively for CD68 and protein S-100.