Systemic Generalized Lymphangiomatosis: A Diagnostic Challenge

Dan Levy Faber MD[1], Ronen Galili MD[1], Orna Nitzan MD[2] and Erez Sharoni MD[1]

[1]Department of Cardiothoracic Surgery, Carmel Medical Center, affiliated with Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
[2]Infectious Disease Unit, Emek Medical Center, Afula, Israel

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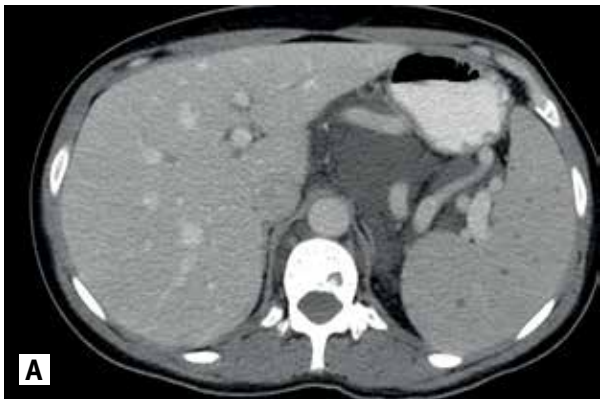
Systemic generalized lymphangiomatosis is a rare condition characterized by proliferation of normal mature lymphatic ducts. This disorder may involve an array of body organs and structures. This benign disease may mimic malignancy with severe and debilitating symptoms and aggressive behavior. The obscure nature of this condition carries a diagnostic challenge. We present here the case of a young patient with complex imaging findings who after extensive clinical evaluation was diagnosed with systemic generalized lymphangiomatosis.

PATIENT DESCRIPTION

A 39 year old female with a 4 month history of vomiting, diarrhea and weakness presented for consultation. Her previous medical history included thalassemia minor and hyperthyroidism related to Grave's disease.

There was no evidence of fever, night sweating, loss of weight, skeletal related pain or other gastrointestinal or urinary symptoms. Physical examination was unremarkable. Complete blood count was noted for microcytic anemia (hemoglobin 8.2 g/dl, mean corpuscular volume 55.3 fl) and normal platelets count. White blood cell count was 4.34 K/µl. C-reactive protein level was 0.28 mg/L and lactate dehydrogenase level 248 U/L, both within normal limits. Electrolyte levels, and liver and kidney functions were normal. Cancer markers including CEA, CA-125, CA-15-3, CA-19-9 and alpha-fetoprotein were within normal range.

Serology tests for present infection with Toxoplasma, cytomegalovirus, Epstein-Barr virus, Q fever, human immunodeficiency virus and Bartonella were negative. Blood immunoglobulin, protein electrophoresis and flow cytometry were normal and did not support the diagnosis of hematologic disorder. Abdominal ultrasound was performed, revealing retroperitoneal and mesenteric lymphadenopathy. Abdominal computed tomography (CT) study demonstrated mild splenomegaly, 13 cm, with multiple hypodense foci and large retroperitoneal and mesenteric lymphadenopathy of up to 6 cm. Lymphatic tissue was also found around the vascular abdominal vessels including the celiac artery, superior mesenteric artery and the splenic veins. Small lytic lesions were noticed in the pelvic and sacral bones. A chest CT revealed mediastinal lymphadenopathy, mediastinal fat infiltration and thoracic vertebrae lytic bone lesions.



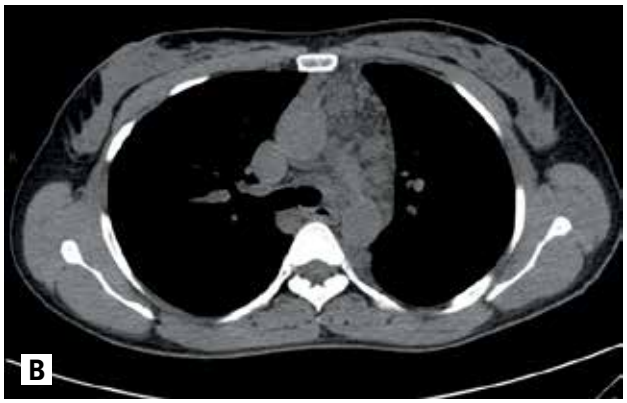


Figure 1. [A] Abdominal CT fragment showing multiple hypodense foci in the spleen and liver. Lymphatic tissue spreads around the vascular abdominal vessels

[B] Chest computed tomography fragment showing mediastinal lymphadenopathy in the aorto-pulmonary window, retrocaval space and lymphatic spread in anterior mediastinal fat

An initial attempt at ultrasound-guided core biopsy of mesenteric lymph node yielded only fluid. Fluid cytology showed many small lymphocytes and histiocytes with no sign of malignancy. After this failed attempt it seemed that the mediastinal nodes were the most reachable for biopsy through left thoracoscopy. Operative findings revealed numerous cystic lesions at the posterior mediastinum and pericardial fat granulation. Biopsies were obtained from both types of lesions. The operative and postoperative course was uneventful.

Pathology was consistent with lymphangioma with no evidence of malignancy. Immune staining for pankeratin, HMB-45, S100 and calretinin were negative, while staining for CD31 and desmin were positive.

After a multidisciplinary discussion a consensus was reached for the diagnosis of systemic generalized lymphangiomatosis. The patient's symptoms subsided with no specific treatment and at one year follow-up she remained asymptomatic.

COMMENT

Systemic generalized lymphangiomatosis is a rare condition commonly appearing in childhood. The disorder is characterized by proliferation of normal mature lymphatic ducts with formation of cysts in numerous body organs. Apart from the brain, which lacks lymphatic vessels, all other organs may be involved [1,2].

Although this condition is considered benign in nature, sometimes it may lead to a severe symptomatic and debilitating course. Imaging studies may reveal pleural effusion and ascites, mesenteric thickening, lytic bone lesions, pulmonary nodules, mediastinal masses and cystic lesions in solid organs such as spleen and liver [1,2]. Some systemic generalized lymphangiomatoses are asymptomatic. For symptomatic cases the treatment is still under debate. Surgery can be performed for localized disease, although the recurrence rates are high. In systemic cases various treatment modalities such as radiotherapy, chemotherapy, interferon-alfa and systemic corticosteroids have been used with varied success. Recent publications suggested an improvement with the use of angiogenesis inhibitors such as vascular endothelial growth factor (VEGF), mammalian target of rapamycin (mTOR) inhibitors, and the tyrosine kinase inhibitor pazopanib [2].

Most cases of systemic generalized lymphangiomatosis in adults have a very slow progression and tend to be an incidental finding. The majority of patients will remain asymptomatic [2,3]. As in the case presented here, the symptoms leading to diagnosis were non-specific and subsided spontaneously. Symptoms may vary, expressing local organ compression by a large lymphoid vessel malformation and overgrowth. Magnetic resonance imaging study may support the diagnosis but large tissue sampling is still required to establish it [3,4].

In general, the diagnosis of systemic generalized lymphangiomatosis is considered only after a wide range of infection and malignant conditions are excluded. The present case demonstrates the gradual clinical investigation of this rare condition.

Correspondence
Dr. D. Levy Faber
Dept. of Cardiothoracic Surgery, Carmel Medical Center, Haifa 34362, Israel
Phone: (972-4) 825-0256
Fax: (972-4) 825-0047
email: danfaber1@hotmail.com

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