OLGU SUNUMU / CASE REPORT

Kocaeli Med J 2024; 13 (3): 219-222, doi: 10.5505/ktd.2024.87533

Nadir Bir Pansitopeni Nedeni: Splenik Kistik Lenfanjiyomatozis, Vaka Sunumu ve Literatür Taraması

A Rare Cause of Pancytopenia: Splenic Cystic Lymphangiomatosis, Case Report and Literature Review

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ÖZ

Splenik lenfanjiyomatozis vakaları literatürde çok az sayıda bildirilmiştir. Daha önce bildirilmemiş bir prezantasyonu ile splenik lenfanjiyomatozis vakası sunuyoruz. 70'li yaşlarında kadın hasta mevcut olan pansitopenisinin kötüleşmesi nedeniyle bize yönlendirildi. Batın tomografisinde splenomegali (17 cm) ve dalak parankiminde öncelikle benign olduğu düşünülen kistik hipodens lezyonlar görüldü. Hastaya splenektomi yapıldı. Lezyonlar lenfanjiyomatozis olarak tanımlandı. Trombositopenisi, nötrofpenisi ve lenfopenisi ameliyat sonrası düzeldi. Anemisi geriledi ancak muhtemelen mevcut kronik hastalıkları sebebiyle devam etti. Lenfanjiyomatozis, hipersplenizm ve pansitopeni ayırıcı tanısında nadir bir neden olarak göz önünde bulundurulmalıdır. Ayırıcı tanı için hipersplenizm ve pansitopeninin diğer potansiyel nedenleri de detaylı bir şekilde araştırılmalıdır.

Anahtar Kelimeler: splenik lenfanjiyomatozis, splenik kistik lenfanjiyomatozis, pansitopeni

ABSTRACT

Only a very few cases of splenic lymphangiomatosis have been published in the literature to date. Herein, we report the case of splenic lymphangiomatosis with unique characteristics. A woman in her 70s was referred to us due to worsening of her pre-existing pancytopenia. Abdominal computed tomography scan revealed an enlarged spleen (17 cm) and some hypodense lesions in the splenic parenchyma. These lesions were evaluated as benign cystic lesions. Then, splenectomy was performed. The lesions were diagnosed as lymphangiomatosis. Her thrombocytopenia, neutropenia, and lymphopenia were resolved postoperatively. Her anemia regressed but persisted likely due to underlying chronic illnesses. Lymphangiomatosis should be considered a rare cause in the differential diagnosis of hypersplenism and pancytopenia. Other potential causes of hypersplenism and pancytopenia should also be thoroughly investigated to arrive at an accurate diagnosis.

Keywords: splenic lymphangiomatosis, splenic cystic lymphangiomatosis, pancytopenia

Sending Date: 26.02.2024 **Acceptance Date:** 27.12.2024

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Cite as: Soyer AK, Civriz AH, Yaprak Bayrak B. A Rare Cause of Pancytopenia: Splenic Cystic Lymphangiomatosis, Case Report and Literature Review. Kocaeli Med J 2024; 13 (3): 219-222. doi: 10.5505/ktd.2024.87533

INTRODUCTION

Lymphangiomas are generally benign lesions occurring in the head and neck region. These lesions are characterized by abnormal proliferation of lymphatic vessels (1). Lymphangiomatosis is the term used to describe multiple lymphangiomas observed in the bone, soft tissues, and parenchymal organs. It rarely develops outside the head and neck region. Lymphangiomas can present with different symptoms depending on their location and size. Splenic lymphangiomatosis may present with abdominal pain and abdominal distention (2). Diagnosis can be difficult by the absence of typical symptoms. Surgery is the preferred definitive treatment and rules out the presence of malignancy. Very few cases of splenic lymphangiomatosis have been reported in the literature.

CASE REPORT

A woman in her 70s was referred to our department due to worsening of her pre-existing pancytopenia during her rheumatology follow-ups. She had a history of hypertension, ischemic heart disease, and rheumatoid arthritis. She complained of fatigue for>5 years. She had no B symptoms. She had no joint pain or stiffness. She had no alcohol intake or smoking habits. Her medications were doxazosin p.o. 1 × 4 mg, iron +2 p.o. 1 × 1, isosorbide dinitrate p.o. 1 × 5 mg, methylprednisolone p.o. 1 × 4 mg, acetylsalicylic acid p.o. 1 × 100 mg, calcium carbonate + D3 p.o. 1 × 1, alendronate 1 × 70/weekly, and carvedilol p.o. 1 × 12.5 mg.

During the examination, no palpable lymphadenopathy was noted. The spleen was palpated 4 cm below the costal margin.

Pancytopenia initially developed 5 years ago and persisted despite the discontinuation of leflunomide. In the initial imaging, the size of the spleen appeared normal. Multiple cystic lesions with occasional contrast enhancement were observed. The largest lesion measured 3 cm in diameter.

At the time of the presentation, laboratory values upon admission indicated normochromic anemia with hemoglobin value of 7.5 g/d L, MCV OF 84 fL, thrombocytopenia with platelet value of 73,600 × 103/µL, neutropenia with neutrophil value of 890 × 103/µL, and lymphopenia with lymphocyte value of 760 × 103/µL. HCT was 21% and WBC was 1795 × 103/µL. In the peripheral blood smear, platelets were observed as single entities. Anisocytosis and hypochromia were present in the red cell series. The platelet count was estimated to be approximately 70,000 × 103/µL. Abdominal CT and MRI scan revealed an enlarged spleen (17 cm) and some hypodense lesions in the splenic parenchyma. The largest lesion measured 33 mm in diameter. These lesions were evaluated as benign cystic lesions (Figure 1a & 1b & 1c).

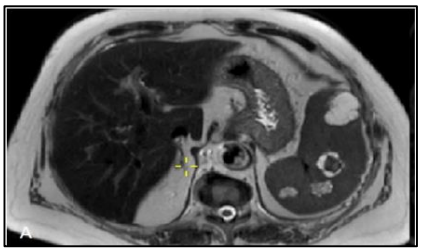
Her other laboratory values were as follows: total protein, 71.56 g/L; albumin, 41.2 g/L; urea, 29 mg/dL; creatinine, 0.76 mg/dL; AST (SGOT), 24.7 U/L; ALT (SGPT), 19,3 U/L; LDH, 367 U/L; sodium, 137.6 mmol/L; potassium (K), 5.30 mmol/L; calcium, 10.48 mg/dL; complete urinalysis, normal; total bilirubin, 1.86 mg/dL; indirect bilirubin, 1.45 mg/dl; corrected reticulocyte percentage, 1.9%; INR, 1.26; transferrin saturation, 33%; iron, 81 ug/dl; ferritin, 505 ng/ml; B12, 360 pg/ml; folic acid, 33 ng/ml. Her HbsAg, anti HCV, anti HIV, toxoplasma IgM, CMV IgM, EBV IgM, rubella IgM, syphilis panels and parvovirus PCR were negative. The FLAER test for paroxysmal nocturnal hemoglobinuria (PNH) was negative. The bone marrow biopsy showed normocellular bone marrow with a mild increase in reticulin fibers (1+). PET/CT scan revealed an enlarged spleen with mildly increased metabolic activity areas (SUVmax 4.3). The liver SUVmax value was 3.6. Several hypodense lesions were observed within the spleen, which did not show any metabolic activity (Figure 1d).

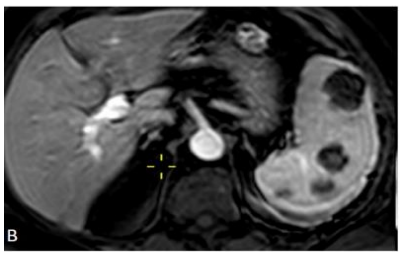
Leflunomide was previously discontinued due to pancytopenia, but no response was observed. Hypersplenism was considered as the possible cause of worsening pancytopenia.

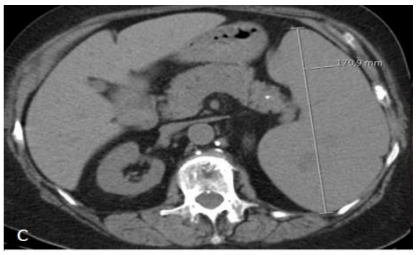
Splenectomy was performed without complications. The spleen weighed 870 g and measured 17 × 17 × 7.5 cm in size. In the macroscopic examination, six cystic lesions were observed in the splenic sections. The largest lesion was 3 cm in diameter (Figure 1e & 1f). Upon closer examination, these cystic areas tended to merge with each other. They had a cystic and multilobulated appearance, clearly separated from the splenic parenchyma with well-defined borders. The cyst walls were beige. In the hematoxylin eosin-stained sections, large cysts were lined with a single layer of a squamous epithelium. Beneath the epithelium, fibrous thickenings were observed. Among these cysts and within their walls, smaller structures were observed that were lined with similar epithelium. These structures appeared as thinner vascular formations and sometimes exhibited a cleft-like appearance. The interior of the cystic structures was filled with serous fluids. The cysts did not contain erythrocytes. Additionally, in the area between these structures, extravasated erythrocytes and hemosiderin-laden macrophages were observed (Figure 2). In the immunohistochemical examinations, diffuse and strong cytoplasmic reactions were observed in the cyst epithelium with CD34, CD31, and D2.40. Immunohistochemical examinations with CD8 and HHV-8 showed negative reactions in the cyst epithelium. Considering the morphological, immunohistochemical, clinical, and radiological findings together, the patient was finally diagnosed with lymphangiomatosis.

At 1 month postoperatively, her laboratory values were as follows: PLT, 349.5 × 103/µL; NEU, 5,048 × 103/µL; WBC, 8,687 × 103/µL; MCV, 90.60 fL ; LYM, 2,356 × 103/µL; and HGB, 10.51 g/dL. Anemia is likely to persist due to the underlying chronic illnesses. The patient's weakness has improved, and no additional complaints have been observed.

1A **1B** **1C**







1D 1E 1F

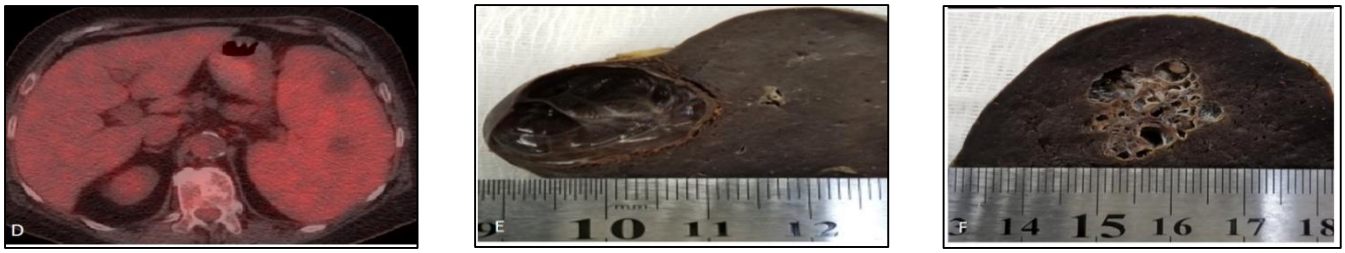


Figure 1. CT, MRI, PET images and macroscopic photographs.
a & b & c) Abdominal CT and MRI scans revealed an enlarged spleen (17 cm) and some hypodense lesions in the splenic parenchyma. The largest lesion measured 33 mm in diameter. These lesions were evaluated as benign cystic lesions.
d) PET/CT scan revealed an enlarged spleen with mildly increased metabolic activity areas (SUVmax 4.3). The liver SUVmax value was 3.6. Several hypodense lesions were observed within the spleen, which did not show any metabolic activity.
e & f) In the macroscopic examination, six cystic lesions were observed in the splenic sections. The largest lesion was 3 cm in diameter.

2A 2B

2C 2D

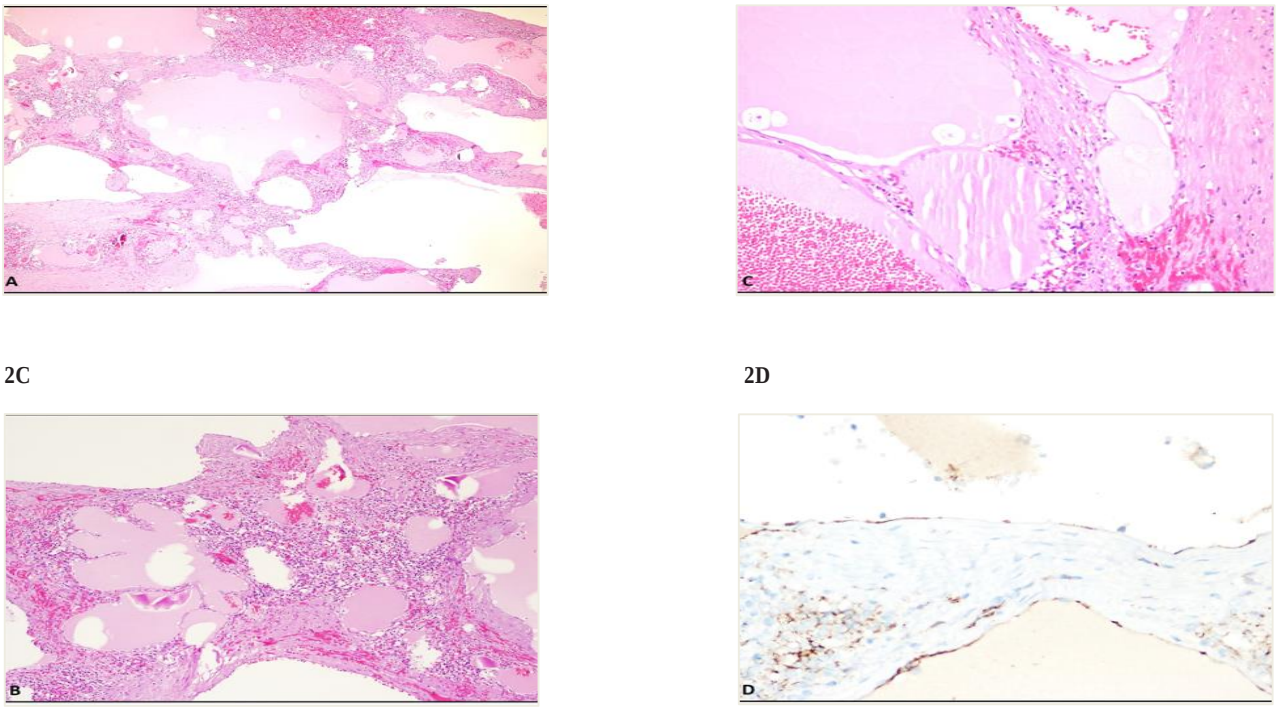


Figure 2. Microscopic Photographs. a & b & c & d) Cystic areas tended to merge with each other. They had a cystic and multilobulated appearance, clearly separated from the splenic parenchyma with well-defined borders. The cyst walls were beige. In the hematoxylin eosin-stained sections, large cysts were lined with a single layer of a squamous epithelium. Beneath the epithelium, fibrous thickenings were observed. Among these cysts and within their walls, smaller structures were observed that were lined with similar epithelium. These structures appeared as thinner vascular formations and sometimes exhibited a cleft-like appearance. The interior of the cystic structures was filled with serous fluids. The cysts did not contain erythrocytes. Additionally, in the area between these structures, extravasated erythrocytes and
hemosiderin-laden macrophages were observed.

DISCUSSION

Lenfangioma is typically observed in children but very rarely in adults. While it is most commonly found in the neck (75%) and axilla (20%), cases of lymphangiomatosis located in the spleen are extremely rarely reported. Although cystic lesions in the spleen are rare, their differential diagnosis is crucial for shaping the treatment approach. Nonepithelial-lined pseudocysts, squamous cysts, and mesothelial cysts are included in the differential diagnosis of splenic cystic lesions. In our case, flattened endothelial cells were found in the cyst lining. When these cells were examined immunohistochemically, they exhibited diffuse cytoplasmic positive reactions with CD31, CD34, and D2.40. These results indicate that the lesion in our patient is of lymphatic origin. When considering the differential diagnosis of lymphatic origin lesions, kaposiform lymphangiomatosis is one of the primary conditions that should be considered. These lesions are borderline tumors, and their diagnosis is crucial for shaping the treatment approach due to their local aggressiveness. They exhibit similar immunohistochemical staining patterns. Differentiation between the two lesions can be made based on histomorphological features such as increased cellularity and a cleft-like growth pattern (3).

Lymphangiomas can present with different symptoms depending on their location and size. We have compiled the clinical findings of 26 cases of isolated splenic lymphangioma reported in the literature for adults: The average age of 26 patients was 41.6 years, with the youngest being 22 and the oldest being 76 years. In our patient, splenic cystic lymphangiomatosis was initially detected at 67 years old, which is significantly higher than the average age reported in previous cases. Among the mentioned patients, 23 were females and 3 were males. The following symptom distribution was observed: abdominal pain (n = 15), anemia (n = 4), massive splenomegaly (n = 3), massive splenomegaly associated with anemia and thrombocytopenia (n = 2), palpable mass (n = 2), massive splenomegaly associated with portal hypertension and omental varices (n = 1), spontaneous splenic rupture (n = 1), post-traumatic splenic rupture (n = 1), chronic back pain (n = 1), dyspnea (n = 1), and asymptomatic (n = 5).

In our patient, splenomegaly and pancytopenia occurred due to splenic cystic lymphangiomatosis. It was considered that pancytopenia was associated with hypersplenism. Although reported cases in the literature showed anemia and thrombocytopenia with hypersplenism (4,5), we have not come across cases specifically attributed to pancytopenia. In the reported case with massive splenomegaly accompanied by omental varices and portal hypertension (5), although it caused anemia and thrombocytopenia, it did not result in neutropenia and lymphopenia. Our patient is unique in this regard. Furthermore, although isolated splenic lymphangiomatosis has been reported in Turkey, no reports of the cystic form of this disease. In this regard, our case is also unique.

Lymphangiomatosis should be considered a rare cause in the differential diagnosis of hypersplenism and pancytopenia. Other potential causes of hypersplenism and pancytopenia should also be thoroughly investigated to arrive at an accurate diagnosis.

Informed Consent: Informed consent was obtained from the patient.

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