Check for updates

CLINICAL CASE

Littoral cell angioma of the spleen in a 70-year-old male patient with myelodysplastic syndrome: a case report

Angioma de células litorales del bazo en un paciente varón de 70 años con síndrome mielodisplásico: reporte de un caso

Ioannidis Orestis[1], Symeonidis Savvas[1], Aggeliki Koltsida[1], Papadopoulou Stauroula[2], Malliora Anastasia[1], Christidis Panagiotis[1], Ouzounidis Nikolaos[1], Kotidis Efstathios[1], Pramateftakis Manousos George[1], Mantzoros Ioannis[1], and Angelopoulos Stamatios[1]*

[1]Department of Surgery, School of Medicine, Aristotle University of Thessaloniki; [2]Department of Pathology, General Hospital of Thessaloniki "G. Papanikolaou". Thessaloniki, Greece

Abstract

Introduction: *Littoral cell angioma (LCA) is a new subtype of vascular tumor, which has been reported infrequently worldwide. It is associated with visceral malignancies and other immunologic conditions.* **Clinical case:** *We present a case of a 70-year-old Caucasian male with a 6-year history of myelodysplastic syndrome, which was investigated for splenomegaly and pancytopenia. Radiological and histopathological examinations revealed an LCA and an open splenectomy were performed. The patient had an uneventful post-operative recovery.* **Conclusion:** *LCA is a rare tumor, with atypical presentation often associated with other malignancies or immunologic conditions. Diagnosis is challenging, and so far, splenectomy is the gold standard treatment.*

Keywords: *Littoral cell angioma. Vascular tumor. Myelodysplastic syndrome. Spleen tumor. Case report.*

Resumen

Introducción: *El angioma de células litorales es un nuevo subtipo de tumor vascular, el cual ha sido reportado con poca frecuencia en todo el mundo. Se asocia con neoplasias malignas viscerales y otras condiciones inmunitarias.* **Caso clínico:** *Varón caucásico de 70 años con antecedentes de síndrome mielodisplásico de 6 años de evolución, que fue investigado por esplenomegalia y pancitopenia. Los exámenes radiológicos e histopatológicos revelaron un angioma de células litorales y se realizó una esplenectomía abierta. El paciente tuvo una recuperación posoperatoria sin incidentes.* **Conclusión:** *El angioma de células litorales es un tumor raro, con presentación atípica y frecuentemente asociado con otras neoplasias malignas o condiciones inmunitarias. El diagnóstico es un desafío y, hasta ahora, la esplenectomía es el tratamiento estándar.*

Palabras clave: *Angioma de células litorales. Tumor vascular. Síndrome mielodisplásico. Tumor de bazo. Reporte de caso.*

***Correspondence:**
Orestis Ioannidis
E-mail: telonakos@hotmail.com

Date of reception: 23-05-2022
Date of acceptance: 08-07-2022
DOI: 10.24875/CIRU.22000284

Cir Cir. 2024;92(6):829-834
Contents available at PubMed
www.cirugiaycirujanos.com

0009-7411/© 2022 Academia Mexicana de Cirugía. Published by Permanyer. This is an open access article under the terms of the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Littoral cell angioma (LCA) is a new subtype of vascular tumor, which has been reported variably and infrequently in the medical literature[1,2]. There are approximately 160 cases presented internationally and very few in the Hellenic Population. LCA has been recently associated with numerous autoimmune diseases and malignancies. In fact, there are only two previously reported cases of LCA in myelodysplastic syndrome (MDS) patients in the medical literature, none of these in Europe[3,4].

We report the case of a 70-year-old male patient with a history of MDS who presented with pancytopenia and splenomegaly. The following case report is presented in accordance with the Surgical Case Report guidelines[5]. We also review the relevant literature regarding the presentation and overall management of LCA.

Case report

A 70-year-old Caucasian man, with a known 6-year history of MDS and several previous hospital admissions for pancytopenia, presented to the Emergency Department due to pruritus and several ecchymoses all over the body. He was hemodynamically stable (blood pressure: 110/70 mmHg and heart rate: 95 bpm), oxygen saturation was 98% and temperature 36.7°C. Clinical examination revealed normal bowel sounds, soft and non-tender abdomen, dull to percussion left costal margin, without liver enlargement and non-palpable cervical, axillary and inguinal lymph nodes. His medical history included arterial hypertension, hypercholesterolemia, hypothyroidism on replacement therapy, allergic rhinitis, and asthma. The patient underwent laboratory examinations, which revealed normocytic normochromic anemia (hemoglobin = 8.8 g/dL), thrombocytopenia (88,000/μL), and leukopenia (2400 K/uL). The patient was admitted to the Department of Internal Medicine for further evaluation.

Additional blood results disclosed normal liver and kidney function, inflammatory markers within normal limits and negative serum immunological tests for *Toxoplasma*, Cytomegalovirus, Human Immunodeficiency Virus (HIV), and Epstein-Barr virus. In addition, a bone marrow biopsy revealed erythroid hyperplasia, although peripheral blood smear was normal. Further evaluation with an ultrasound of the upper abdomen was performed, demonstrating spleen enlargement (6 × 12 × 15 cm) and several hyperechoic lesions, without any other pathological findings. These results were subsequently confirmed with an abdominal computed tomography (CT) scan, where these multiple lesions appeared hypodense throughout the spleen (Fig. 1).

Taking all of the above into consideration, in combination with the patient's history of MDS, these multifocal splenic masses were believed to represent extramedullary involvement (EMI) of his blood cancer to the spleen. Moreover, the differential diagnosis included lymphoid and vascular spleen tumors. Thus, CT scans of the brain, lungs and neck were obtained and the possibility of metastasis was excluded from the study.

Following a surgical review, a decision was made to proceed with a splenectomy without obtaining a biopsy, due to its potential hemorrhagic complications. Vaccines against *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae* type b were administered 4 weeks before the elective surgery. Intraoperatively, we performed a midline incision and then entered the peritoneal cavity. An enlarged spleen with a reddish appearance and multiple tiny dark spots was recognized. We first clamped and lighted the splenic artery, and afterward, the splenic vein was clamped and lighted. The spleen was removed to its entirety and the abdomen was closed with a closed suction drain.

Subsequently, the spleen was sent for further histopathological and immunohistochemical studies. It measured a total of 14.5 × 9.5 × 7 cm, weighted 452 g and appeared reddish with homogenous texture. Macroscopically, sections through the specimen showed multifocal small dark lesions, the largest measuring 0.5 cm. Microscopically, the findings were consistent with a LCA of the spleen. More specifically, histopathological examinations revealed several non-encapsulated but well-circumscribed tiny masses, that consisted of anastomosing vascular channels (Fig. 2A), resembling splenic sinusoids, lined by histiocytes and eosinophils, with papillary projections (Fig. 2B) and cyst-like spaces (Fig. 3A), containing red blood cells (Fig. 3B), and widespread deposition of hemosiderin granules (Fig. 3C). No marked nuclear atypia or prominent mitotic figures were displayed (Fig. 4). Immunohistochemical characterization demonstrated that lining cells were positive for CD31 (Fig. 5A) and CD68 markers and negative for CD34, whereas cells within papillary projections were

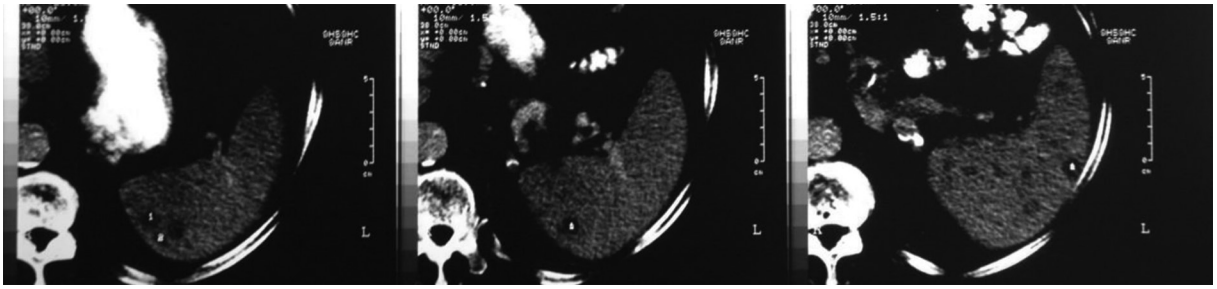

Figure 1. *Abdominal computed tomography scan showing multiple hypodense lesions throughout the spleen.*

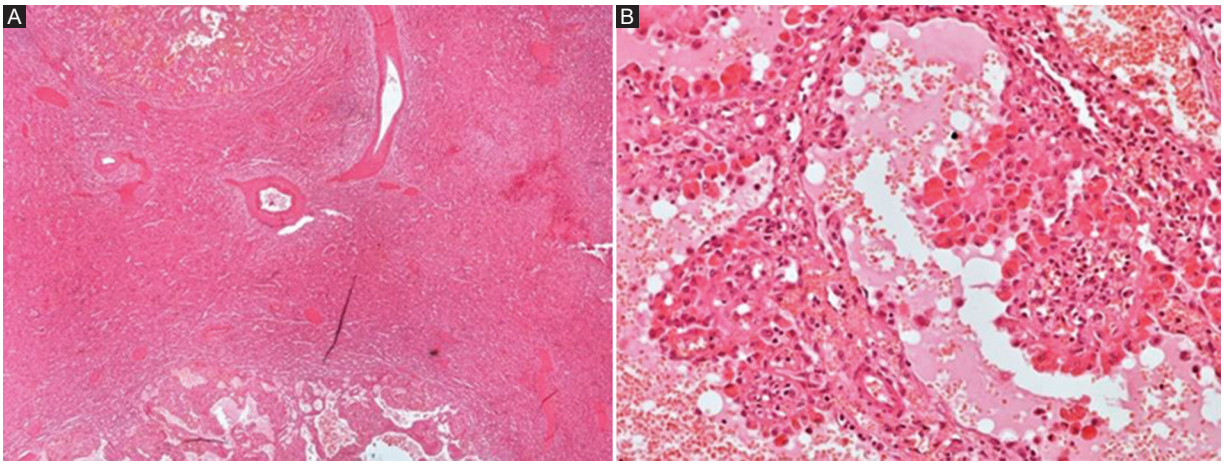

Figure 2. *Histopathological examinations revealed several non-encapsulated but well-circumscribed tiny masses, that consisted of anastomosing vascular channels* **(A)** *with papillary projections lined by tall endothelial cells* **(B)**.

positive for CD34 (Fig. 5B). The final diagnosis of LCA was established. The patient had an uneventful post-operative recovery and remained well at 12 months of post-operative follow-up.

Prophylactic antimicrobial therapy was indicated and oral amoxicillin was prescribed to be taken twice daily in the 1st 2 years after the splenectomy.

Discussion

LCA, first described by Falk et al.[6] in 1991, is a very rare vascular tumor located only in the spleen, that arises from the littoral cells of the red pulp sinuses[7], which have features similar to both endothelial cells and macrophages[2]. According to literature, it occurs mostly in the age range of 35-60 years, without sex-based predilection[8]. Here, we present a case of a 70-year-old Caucasian male, aiming to emphasize the rarity of the tumor, its atypical presentation with a MDS background and its diagnostic challenges.

Despite its uncertain etiology, it has been suggested that immunologic deregulation may play a significant role in the development of the tumor. Indeed, ankylosing spondylitis, Crohn's disease, Wiskott-Aldrich syndrome, and MDS are, among others, medical conditions associated with LCA. At first, it was thought to be a benign neoplasm; however, recent studies have proved that it exhibits malignant potential[9]. Moreover, it may be associated with several visceral malignancies, such as colorectal, pancreatic, renal, and lung carcinomas[10].

More specifically, MDS are clonal hematopoietic disorders involving morphologic defects and peripheral-blood cytopenias, with a high risk of progression to acute myeloid leukemia (AML)[11]. EMI in AML is reported in 2.5-9.1% of affected patients. The involved sites include soft tissue, gastrointestinal tract, bone and lymph nodes, where spleen counts for 2% of all the locations. The appearance of EMI in the course of AML is a very complex phenomenon, and it is associated with several clinical and laboratory features,

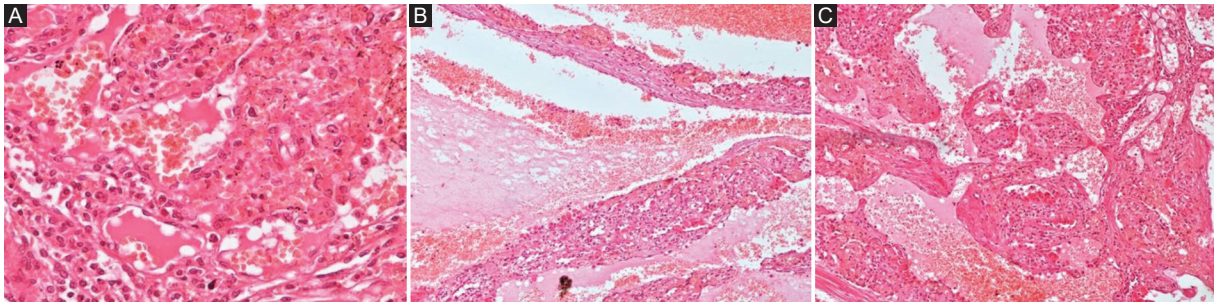

Figure 3. A: *irregular channel lumina and cystic spaces.* **B:** *cystic spaces filled with blood. Few sloughing endothelial cells.* **C:** *intracytoplasmic hemosiderin pigment.*

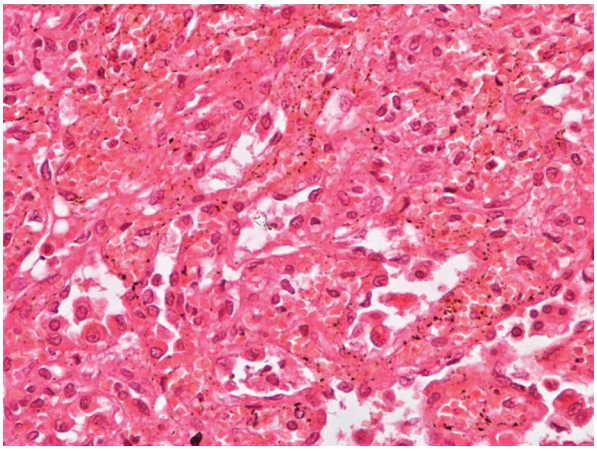

Figure 4. *No prominent mitotic figures were displayed.*

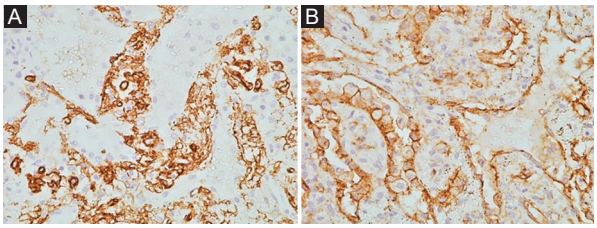

Figure 5. *Immunohistochemical characterization of littoral cell angioma.* **A:** *lining cells positive for CD31.* **B:** *papillary projections positive for CD34.*

such as increased levels of lactate-dehydrogenases (LDH) and leukocytosis[12]. As a result, spleen lesions in our case could be considered as extramedullary sites of blood cancer, but neither LDH levels nor leucocyte count was significantly associated with EMI, excluding this possibility.

Furthermore, LCA has specific immunophenotypic and morphologic characteristics, which differentiate it from other vascular splenic neoplasms, such as lymphangioma, hemangioma, hemangioendothelioma, and hemangiosarcoma[13].

LCA has no characteristic clinical manifestations and it might be incidentally detected during imaging studies in asymptomatic patients. However, in some cases, LCA may be manifested with splenomegaly, abdominal pain, weakness and fatigue, fever of unknown origin, or pancytopenia[8,14]. In our case, LCA manifested with spleen enlargement and laboratory evidence of hypersplenism.

Due to its atypical clinical appearance, imaging studies, such as ultrasonography, CT and magnetic resonance imaging (MRI) scan, could play a significant role in differential diagnosis, as they can detect splenic lesions. More specifically, the sonographic appearance is variable, including hypoechoic, isoechoic or hyperechoic lesions in an enlarged spleen[2]. On abdominal CT scans, obtained without contrast material, LCA typically appears as well- or poorly-circumscribed multiple hypodense lesions, while after contrast material administration, they may be presented as hypoattenuating in the early portal venous phase. However, these features may also be presented in other primary splenic neoplasms, metastatic disease, lymphoma, Kaposi's sarcoma, sarcoidosis or infectious processes, which lead to microabscess formation[1]. In our patient, absence of abdominal and thoracic neoplasm, lymph nodes' involvement or granulomas on CT scans, as well as negative screening tests for HIV and other infections, led the diagnosis primarily to splenic neoplasms. On MRI, it mostly appears slightly hypointense on T1- and T2-weighted pulse sequences, a finding that reflects the presence of hemosiderin in the lesions due to the hemophagocytic capacity of neoplastic cells[2,8,15]. Unfortunately, this fairly specific imaging feature is present only in a few cases[16]. One case shows inhomogeneously

hyperintensity on unenhanced T2-weighted images, as well as in hemangioma of the spleen[15]. We did not proceed to an MRI in our case, due to patient's right knee arthroplasty implants.

Histopathologically, non-encapsulated multiple or solitary nodules, variant in terms of size, texture and color, are revealed in macroscopic examination[8]. As for the color, it ranges from red to black, an appearance which reflects the presence of blood products of variable age[17].

Microscopically, the lesions contain several anastomosing vascular channels, lined with flat and tall endothelial cells, and irregular lumina, usually accompanied by papillary projections and cyst-like spaces. They might slough off into the vascular lumina and show hemophagocytosis. The neoplastic LCA cells, due to their dual endothelial and histiocytic differentiation, express antigens of both types. In contrast to normal endothelial cells, LCA cells express not only factor VIII antigen but also CD31, CD68, KP1, lysozyme, CD21, and CD163. The immunohistochemical pattern is negative for CD8, CD34, and S-100 antigens[8]. Our case was not an exception, as anastomosing vascular channels, resembling splenic sinusoids, with widespread deposition of hemosiderin were observed.

Taking into consideration the atypical clinical and imaging characteristics of LCA, as well as the high risk of hemorrhage after performing a fine-needle aspiration biopsy, the final diagnosis of this rare tumor depends on histological and immunohistochemical examinations post-operatively[8].

Regarding the treatment of LCA, open splenectomy or hand-assisted laparoscopic total splenectomy is the gold standard. This is mandatory due to the tumor's large size or diffuse nature, while it also serves the purpose of preserving enough tissue for histological and immunohistochemical examinations[18]. Although total splenectomy, both diagnostic and therapeutic, is the most widely performed procedure, there has been described a case in the international literature where a partial splenectomy was preferred for a localized tumor, preserving the advantage of patient's post-operative intact immune function[19]. Regarding the best surgical approach, recent studies have shown laparoscopic splenectomy to be superior to open splenectomy, in terms of decreased need of pain relievers and length of stay, as well as earlier oral intake[1]. However, in our case, we proceeded with an open approach, due to surgeon's preference, followed by an uneventful post-operative course.

Conclusion

LCA is a recently described vascular tumor of the spleen, associated with other malignancies, and may itself also have malignant potential. Its diagnosis is very challenging to make pre-operatively, but it should always be considered in the differential diagnosis of splenic lesions. So far, splenectomy is the gold standard treatment of vascular splenic tumors, including the LCA.

Funding

No funding was received for the present study.

Conflicts of interest

The authors declare no competing financial interests.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

References

1. Blansfield JA, Goldhahn RT Jr., Josloff RK. Littoral cell angioma of the spleen treated by laparoscopic splenectomy. JSLS. 2005;9:222-4.
2. Liu YP, Cheng SM, Huang JK. Littoral cell angioma of the spleen: a case report. Chinese J Radiol. 2005;30:241-6.
3. Erçin C, Gürbüz Y, Hacıhanefioğlu A, Karakaya AT. Multiple littoral cell angioma of the spleen in a case of myelodysplastic syndrome. Hematology. 2005;10:141-4.
4. Bierenbaum J, Alapat DV, Godinez C, Park AE, Zhao XF, Baer MR. Littoral cell angioma: a correctable cause of progressive pancytopenia in a patient with myelodysplastic syndrome. Leuk Res. 2010;34:e117-9.
5. Agha RA, Fowler AJ, Saeta A, Barai I, Rajmohan S, Orgill DP et al. The SCARE statement: consensus-based surgical case report guidelines. Int J Surg. 2016;34:180-6.
6. Falk S, Stutte HJ, Frizzera G. Littoral cell angioma. A novel splenic vascular lesion demonstrating histiocytic differentiation. Am J Surg Pathol. 1991;15:1023-33.
7. Borch WR, Aguilera NS, Brissette MD, O'Malley DP, Auerbach A. Practical applications in immunohistochemistry: an immunophenotypic approach to the spleen. Arch Pathol Lab Med. 2019;143:1093-105.
8. Lin XY, Li JM, Wang QX, Feng JZ, Zhao MQ, Zhong WX, et al. Littoral cell angioma of the spleen: report of three cases and a review of the literature. Chin Med J (Engl). 2011;124:3423-6.
9. Tee M, Vos P, Zetler P, Wiseman SM. Incidental littoral cell angioma of the spleen. World J Surg Oncol. 2008;6:87.

10. Roldan-Vasquez E, Roldan-Vasquez A, Jarrin-Estupiñan X, Roldan-Crespo J. Case report: infrequent littoral cell angioma of the spleen. Int J Surg Case Rep. 2021;85:106242.
11. Cazzola M. Myelodysplastic syndromes. N Engl J Med. 2020;383: 1358-74.
12. Fianchi L, Quattrone M, Criscuolo M, et al. Extramedullary involvement in acute myeloid leukemia. A single center ten years' experience. Mediterr J Hematol Infect Dis. 2021;13:e2021030.
13. Kinoshita LL, Yee J, Nash SR. Littoral cell angioma of the spleen. Am J Roentgenol. 2000;174:467-9.
14. Tan YM, Chuah KL, Wong WK. Littoral cell angioma of the spleen. Ann Acad Med Singapore. 2004;33:524-6.
15. Schneider G, Uder M, Altmeyer K, Bonkhoff H, Gruber M, Kramann B. Littoral cell angioma of the spleen: CT and MR imaging appearance. Eur Radiol. 2000;10:1395-400.
16. Wang YJ, Li F, Cao F, Sun JB, Liu JF, Wang YH. Littoral cell angioma of the spleen. Asian J Surg. 2009;32:167-71.
17. Chourmouzi D, Psoma E, Drevelegas A. Littoral cell angioma, a rare cause of long standing anaemia: a case report. Cases J. 2009;2:9115.
18. Du J, Shen Q, Yin H, Zhou X, Wu B. Littoral cell angioma of the spleen: report of three cases and literature review. Int J Clin Exp Pathol. 2015;8:8516-20.
19. Mac New HG, Fowler CL. Partial splenectomy for littoral cell angioma. J Pediatr Surg. 2008;43:2288-90.