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Case report

Case report: Infrequent littoral cell angioma of the spleen

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ABSTRACT

Introduction and importance: Littoral cell angioma is a rare solid spleen tumor with uncertain malignant potential. It is usually asymptomatic; therefore, its diagnosis is usually incidental. There are approximately 150 cases reported in the medical literature, but none of them in the Hispanic population.

Case presentation: We present a case of a 54-year-old woman who presented to our clinic with nonspecific abdominal pain. Imaging studies show a splenic mass with littoral cell angioma characteristics. The patient underwent an open splenectomy with subsequent histopathologic and immunohistochemical studies that confirmed the presence of a littoral cell angioma of a diameter of 8 × 4.5 × 3.5 cm. The patient was discharged after an uneventful postoperative recovery and was referred to the outpatient clinic for follow up.

Clinical discussion: This case report highlights the close relationship between the littoral cell angioma, neoplasias, and autoimmune diseases. Even though LCA has a good prognosis, there is still the possibility of malignant transformation, especially when the spleen weighs 1500 g; our patient's sample pointed towards a benign pathology. LCA has a positive IHC for endothelial and histiocyte tissues. The IHC results of our patient were positive for $CD34^{+}$ and $CD68^{+}$, confirming the LCA diagnosis.

Conclusion: Within red pulp spleen tumors, LCA should be highly considered as a differential diagnosis in all types of populations. In the case of a confirmed LCA, routine screening for neoplasias and autoimmune diseases should be performed.

1. Introduction

Primary tumors of the spleen can be classified by their origin: white pulp (lymphatic tissue) or red pulp (vascular tissue). Neoplasms arising from the lymphatic tissue can be divided into Hodgkin lymphoma and non-Hodgkin lymphoma. On the other side, vascular neoplasms can be divided into hemangiomas, angiomas, angiosarcomas, littoral cell angioma (LCA), and others [1]. Metastasis is considered secondary tumors.

LCA is a primary splenic hemangioma that arises from the lining cells of the trabeculated mesh in the reticuloendothelial system. Due to its marginal location, it acquired the name of *littoral* cell angioma. An important characteristic of this tumor is its dual endothelial and histiocytic differentiation versus the red pulp tumors, which only express an endothelial component [2].

LCA is an infrequent pathology. Until the year 2020, approximately 150 cases have been reported in the medical literature worldwide [1]. To our knowledge, in Ecuador and in Latin America this pathology has not yet been reported. Hence, it is important to share the findings and management with the medical community, so that this pathology can step up in the list of differential diagnosis.

The epidemiologic distribution is nonspecific, since patients from 1 to 77 years-old have been affected, with a greater predisposition in adulthood. In a case series of 13 patients in China, the mean age of presentation was 54.2 years old [3]. Regarding sex, no preference has been observed [1,2]. Most of the cases have been reported in Asian populations, and to some extent in North America, but no statistical studies have been made to determine if there is a specific predilection [3].

This case report was built and written based on the SCARE 2020 guidelines and alignments [12].

Abbreviations: LCA, Littoral cell angioma; CT, Computed Tomography; MRI, magnetic resonance imaging; IHC, immunohistochemistry.

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2. Case description

A 54-year-old female patient presented to the Emergency Department of a tertiary private center in Ecuador, complaining of dull abdominal pain for 24 h. The patient's medical history includes hypothyroidism and well-controlled diabetes mellitus with medication. The patient had a surgical history of hysterectomy, right oophorectomy, hemorrhoidectomy, cholecystectomy, and septoplasty.

The abdominal pain was described as a continuous mesogastrium and hypogastrium pain of moderate-intensity with radiation to the left iliac fossa and lumbar region. The patient recalls having similar episodes during the last three weeks with spontaneous remission. She did not report other accompanying symptoms like nausea, vomiting, or diarrhea.

The patient appeared diaphoretic with the following vital signs: BP 164/90 mmHg, HR 72 bpm, RR 20 rpm, Sat 91%. The patient's BMI was 25.56 kg/m^2. The physical exam revealed a non-distended, soft, depressible abdomen, painful to superficial and deep palpation in the epigastrium, which radiated to the hypochondrium and left flank. No signs of peritonitis were present. The rest of the physical evaluation was normal.

Laboratory studies showed values within normal parameters. Cancer markers such as CEA and CA-125 were negative, antibodies to EBV and CMV were positive for IgG and negative for IgM, and acute phase reactants such as ESR were within normal ranges.

Simple and contrast abdominal CT showed an increase in splenic volume with a mass in the posterior-external region measuring 7.5 × 6.7 cm that partially captured the contrast, without stranding fat (Fig. 1). A mass continuation onto the hypogastrium of 2.6 cm was evidenced, with protrusion of the omentum, for which it was decided to perform a thoracic CT scan. No lymphadenopathy was found.

A nodular lesion with defined borders in the middle third of the spleen measuring 59 × 43 × 53 mm was observed on the simple and contrasted abdominal MRI. The mass presented a hyperintense focus in the T2 sequence and hypointense in T1, suggestive of blood content. After contrast administration, the affected area remained hypointense in the arterial, portal, and late phase. In the post-contrast phase, the periphery of the mass and the internal septa were enhanced. In addition, a smaller 10 mm lesion was observed in the upper third of the spleen (Fig. 1).

The differential diagnoses were LCA, metastatic lesions, and angiosarcoma. Based on the characteristic of the lesion: solid, single, non-lymphoid tissue, and symptomatic, an open splenectomy through a middle vertical incision was made. The surgery was performed by a general surgeon of the same institution who had 33 years of working experience. During the surgery, an adhered spleen measuring 11 × 8 × 6 cm with a weight of 227 g was obtained. No metastatic lesions, free fluid, or adenopathies were observed. A 6 cm incisional infraumbilical hernia was found, which was immediately corrected. A Jackson Pratt (JP) drainage was placed around the left hypochondrium. A clean surgery without complications, with an estimated blood loss of 200 cc. was performed.

On postoperative day 2, the patient's hemoglobin descended to 8.3 g/dL; hence, the patient was transfused with two RBC packages which helped raise her hemoglobin level to 11.8 g/dL. Besides this episode, the patient had a favorable recovery with an optimal oral intake and pain management. On postoperative day 4, the JP drainage was removed and the patient was discharged with no more than basic wound care and analgesia. The patient was referred for control in the outpatient surgery clinic.

In the macroscopic studies of the specimen, a principal multinodular mass with irregular and lobular borders and fibroelastic septi was observed with dimensions of 8 × 4.5 × 3.5 cm. The mass was localized 0.5 cm away from the splenic capsule (Fig. 2A). Additionally, other similar smaller masses were localized 0.4 cm away from the capsule and 1 cm away from the principal mass (Fig. 2B).

In the microscopic study, a vascular neoplasia of the red pulp was identified with multifocal proliferation of vascular canals. These canals had different dimensions, and some with cystic characteristics. Vascular canals were covered by flat endothelium and high endothelial venules (Fig. 3A and B). Immunohistochemistry was positive for CD34$^+$, CD68$^+$, CD8$^+$, and negative for S100$^-$ and D240$^-$ (Table 1). These findings pointed to a littoral cell angioma diagnosis.

On the 1st week post-operative follow up, the patient presented with a considerable amelioration of her pain and quality of life. She reported having no longer pain, besides her mild tenderness in the incision area. She did not report any negative changes in her bowel movements or appetite. The incision was in the expected phase of cicatrization, and there were no signs of infection. The patient was encouraged to follow up with her primary care physician to continue the treatment for her chronic pathologies, and to follow the usual screenings.

3. Discussion

Littoral cell angioma has an uncertain etiology, but due to its close relationship with other neoplasias and autoimmune diseases, it is believed that an immunologic deregulation is behind its cause. Some associated autoimmune conditions are ankylosing spondylitis, myelodysplastic syndromes, Crohn's disease, Wiskott-Aldrich, among others [1,2]. Among the associated neoplasms, lung, pancreas, kidney, and ovary malignancies have been found. In a study of 25 patients with littoral cell angioma, 15 of them had concomitant epithelial, mesenchymal, or hematologic malignancies [4]. In the case of our patient, an immunologic component was observed due to her history of

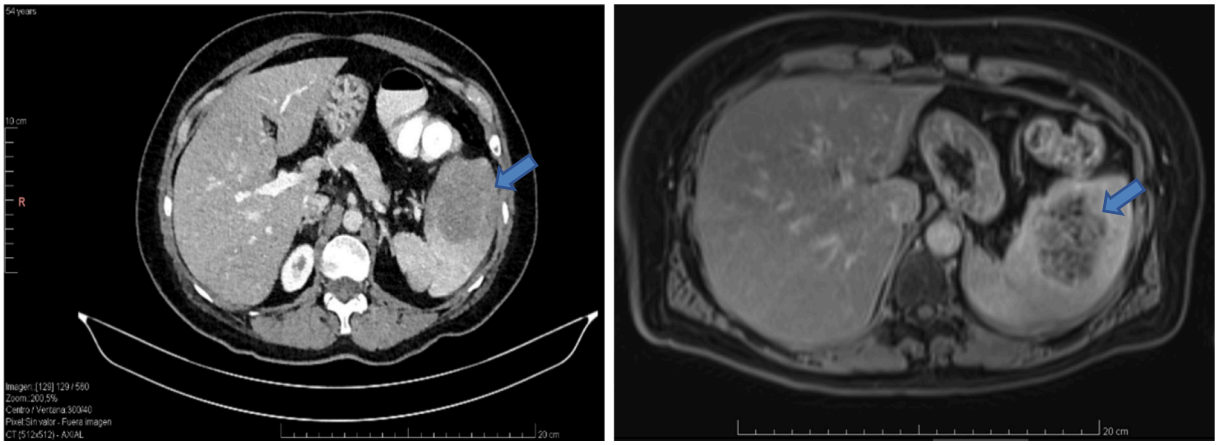

Fig. 1. Multinodular and septated splenic mass (arrow) on CT and MRI.

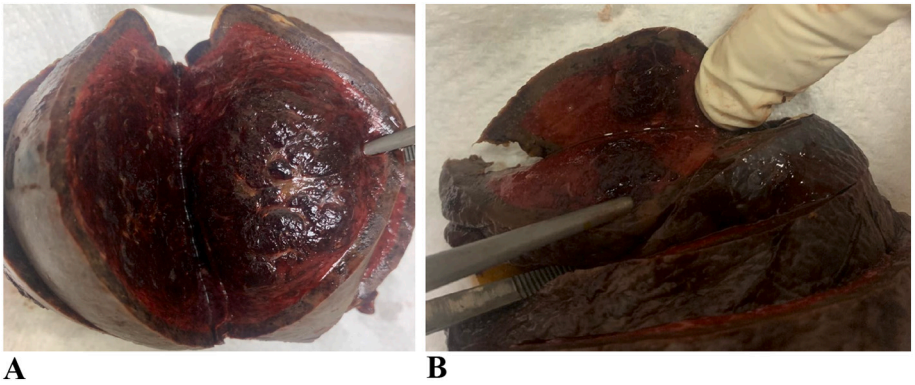

Fig. 2. Spleen with littoral cell angiosarcoma. A) Principal multinodular and septated mass in the center of the specimen. B) Secondary masses with diameters of 1.5 × 1.2 × 1 cm.

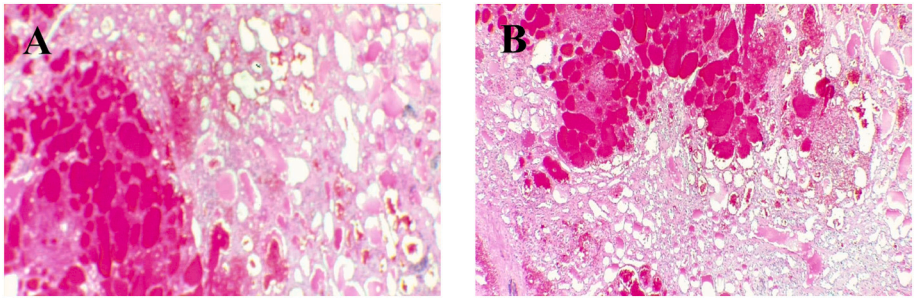

Fig. 3. Histologic study of LCA. A) Vascular proliferation within the red pulp. B) Prominent endothelial cells desquamating from the vascular walls.

Table 1
Immunohistochemistry results.

IHC	Result	Comments
CD34	+++/+++	*Present in endothelial cells of tumoral capillaries*
CD68	++/+++	*Interspersed between high endothelial cells and desquamated cells from the capillary lumen*
CD8	+	*Intracapillary presence of $CD8^{+}$T lymphocytes*
S100	–	*Negative for endothelial cells of tumoral capillaries*
D240	–	*Negative for endothelial cells of tumoral capillaries*

hypothyroidism and diabetes.

LCA is an asymptomatic pathology in more than 55% of cases [6]. In the rest of the patients, it can present diffuse abdominal pain and fever. It can also be associated with splenomegaly, anemia, and thrombocytopenia [5]. The patient in this case report presented with nonspecific abdominal pain. Regarding epidemiology, our 54-year-old patient was within the range of the expected age based on the literature. The majority of the LCA published cases have been from Asia or North America, but to our knowledge this pathology has not been reported in South America. This is important to highlight because it gives us a clue regarding this tumor behavior. Does it have some genetic predilection, or does it have a more sporadic conduct? Of what we know until today, the age, sex, nor race are determinant factors for developing this pathology, therefore, surgeons should start placing LCA into their differential diagnosis whenever there is a case of red pulp splenic neoplasia.

Even though LCA has a good prognosis, there is still the possibility of malignant transformation, especially when the spleen weighs 1500 g or is larger than 20 cm^2. In addition, littoral cells can transform into angiosarcoma, worsening its prognosis. In our patient, the spleen weighted 227 g and the microscopic studies pointed towards a benign pathology.

For the diagnosis, imaging such as MRI or CT cannot differentiate between angioma, angiosarcoma, lymphoma or metastasis. On CT, it is expected to observe a well-demarcated and hypodense mass. On T2, the mass would be hyperintense, while in T1, it would be hypointense [7]. In theory, doing a fine needle aspirate cytology could help with the diagnosis. Still, the risk of bleeding is high and in the case of malignant neoplasia; it could promote its dissemination [8]. Based on the aforementioned, the best diagnostic method is postoperative pathologic studies.

Benign and asymptomatic tumors are treated conservatively. However, in the case of splenomegaly, symptomatology, and chronic consumption coagulopathies like in the case of hemangiomas, LCA, and lymphangioma, a splenectomy is indicated [9]. Between open and laparoscopic splenectomy, open is the most recommended approach due to its lower risks of capsule rupture and tumoral cells' dissemination [2]. Reports have been published regarding successful open splenectomies without recurrence in the next 32.3 months [10,11]. In our case, our decision was based on the spleen's size of 11x8x6 cm. These dimensions were generating mass effects and discomfort to our patient.

Regarding our differential diagnosis, angiosarcoma was discarded because it usually presents with large hyperchromatic nuclei, poor cytoplasm, and a high mitotic index. The splenic hamartoma was also discarded because it presents on histology with fusiform cells with a hemorrhagic background [8]. None of these descriptions were found on our patient.

One of the most important tools for the diagnosis is immunohistochemistry (IHC). LCA has a combined pattern of endothelial and histiocytic cells. It shows a positive pattern for $CC68^{+}$, $CD31^{+}$, vWF^{+}, $CD21^{+}$, $CD34^{-}$, and $CD8^{-}$ [8]. Endothelial markers are $FVIII^{+}$, CD31, vWF^{+}, $CD34^{+}$, while the histiocytic markers are CD68 [2]. The IHC results of our patient were positive for endothelium, $CD34^{+}$, and histiocyte, $CD68^{+}$, confirming the LCA diagnosis.

The importance of sharing these findings and concising scattered information regarding infrequent pathologies, highlights the multidisciplinary approach needed in most of them. Even though the direct treatment is a splenectomy, the postoperative management must be

focused on malignancy screening and autoimmune diseases due to its close relationship with those conditions.

4. Conclusion

Within red pulp spleen tumors, LCA should be highly considered as a differential diagnosis due to its sporadic behavior. Race, sex and age are not a determinant factor for developing this pathology. Even though a great quantity of cases hse been reported in Asia, this pathology is still prevalent in other areas, like South America. In the case of a confirmed LCA, routine screening for neoplasias and autoimmune diseases should be performed.

Ethical approval

N/A

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CRediT authorship contribution statement

The authors conceptualized, designed the study, coordinated, interpreted data, drafted, and critically reviewed the manuscript for important intellectual content. Finally, all the authors agreed to be accountable for all aspects of the work in ensuring questions related to accuracy or integrity of any part of the work.

Guarantor

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Research registration

N/A

Declaration of competing interest

The authors declare not having competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Patients consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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