

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Incidental littoral cell angioma of the spleen: cross-sectional imaging findings and review of the literature ☆

Pier Paolo Arcuri, MD^a, Stefano Taglianetti, MD^b, Barbara Vavalà, MD^a, Caterina Battaglia, MD^{b,*}, Domenico Laganà, MD^b, Francesco Manti, MD^b

^a Radiology Unit, Department of Radiology, Pugliese-Ciaccio Hospital, Catanzaro, Italy

^b Radiology Unit, Department of Experimental and Clinical Medicine, “Magna Graecia” University, Catanzaro, Italy

ARTICLE INFO

Article history:

Received 18 May 2022

Revised 13 June 2022

Accepted 21 June 2022

Keywords:

Littoral cell angioma

Spleen

Diffusion-MRI

FDG-PET/CT

ABSTRACT

Littoral cell angioma (LCA) is a primary splenic hemangioma found mostly in normal red sinus shore cells of the reticuloendothelial cell system of the spleen. In most cases is benign, but sometimes malignancies have been reported. This tumor displayed epithelial and histiocytic properties based on its cell of origin, splenic littoral cells. In this case report, we will describe a case of a 21-year-male presenting with an incidentally discovered LCA illustrated by cross-sectional imaging techniques, highlighting how the diffusional sequence and the positron emission tomography study, thanks to their greater specificity, have contributed to reaching a correct diagnostic orientation more than dynamic studies with contrast agent in both computed tomography and magnetic resonance.

© 2022 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Primary splenic tumors are uncommon and classified as lymphoid, non-lymphoid, and tumor-like lesions [1]. Primary vessel tumors are the most common type of non-lymphomatous tumor of the spleen, most of which are benign, mainly arising from the blood vessels, especially veins, and less commonly originating from red-pulp sinuses lined by littoral cells. Littoral cell angioma (LCA), first described in 1991 [2], is a rare vascular tumor of the spleen which displays both epithelial

and histiocytic properties based on their cell of origin, the splenic littoral cells lining the sinuses of the splenic red pulp. Initially thought to be benign, the biologic behavior of LCA has not been firmly established, as there have been several reports of LCA with malignant features [3–5]. LCA may occur at any age and has no gender predilection; this lesion may be accidentally found in patients with abdominal pain [6]. Moreover, LCA could be discovered as a splenic lesion in patients with laboratory evidence of hypersplenism, including anemia or thrombocytopenia, and constitutional symptoms including fever [2,7–10]. One hundred forty-seven cases

☆ Competing Interests: All authors declare no conflict of interest.

* Corresponding author.

E-mail addresses: pierpaoloarcuri@unicz.it (P.P. Arcuri), dtbattagliacat@gmail.com (C. Battaglia), domenico.lagana@unicz.it (D. Laganà), mantifra@unicz.it (F. Manti).

<https://doi.org/10.1016/j.radcr.2022.06.063>

1930-0433/© 2022 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)



Fig. 1 – Ultrasound shows the presence of multiple, solid-looking, focal hypoechoic lesions with regular margins.

have been reported in the international literature, but only one showed ultrasound, contrast-CT, contrast-MRI, and PET-CT imaging findings [11]. However, imaging findings of LCA (US, MRI, and CT) are nonspecific, and splenomegaly is a common finding. Due to the nonspecific imaging findings in the diagnostic work-up, splenectomy is often performed for diagnostic and therapeutic purposes [12]. Currently, both etiology as well as biological behavior, remains uncertain. Due to increasing numbers of LCA in association with autoimmune disorders such as Crohn's disease and inborn metabolic diseases such as Gaucher's disease, as with visceral organ tumors, immune system dysfunction has been postulated as a possible crucial pathogenic mechanism [2,13–16].

Case presentation

A 21-year-male was admitted to our hospital for abdominal trauma. The patient was asymptomatic without abdominal pain, fever, chills, weight loss, or other constitutional symptoms. No comorbidity was found in his past medical history. Both physical examination and biochemical tests were negative to pathological findings; he was not leukopenic, anemic, or thrombocytopenic. Ultrasound (Fig. 1) demonstrated no traumatic lesions of the liver, kidneys, and spleen. Still, it showed multiple solid hypoechoic nodules with regular margins, high vascularization (founded with the color Doppler examination), and without back wall reflections in the splenic parenchyma. Of note, the spleen presented average size.

After we have excluded post-traumatic lesions from being urgently managed, pre- and postcontrast CT examination was planned to define the nature of the lesions. An enhanced CT demonstrated multiple rounds, low hypoattenuating lesions in the spleen (Fig. 2a), significant contrast enhancement in the arterial phase, and slightly less noticeable in the venous stages (Figs. 2b and 2c). No significant abdominal adenopathy suggesting a possible lymphomatous etiology was found.

Furthermore, a pre- and postcontrast agent MRI study was performed to highlight the possible presence of any small "islands" of adipose tissue in the context of the lesions. The lesions were homogeneously hypointense on T1-weighted in-phase and out-of-phase (IP/OP) gradient-echo imaging sequences (Figs. 3a and b) and slightly hyperintense on T2-weighted images (TSE: Fig. 3c, STIR: Fig. 3d). The diffusion sequence (DWI) and the corresponding ADC map (Figs. 3e and f) showed a Diffusion coefficient equal to $1.43 \times 10^{-3} \text{ mm}^2 / \text{sec}$, compatible with benign lesions (cut-off: 1.21×10^{-3}) [17].

However, dynamic postcontrast MRI imaging (Gadoxetic acid) showed rapid wash-in with a peak at 2 minutes, followed by a significant wash-out at the 4th minute (Fig. 4); this behavior was suspicious for lesions with significant contextual neoangiogenesis. Therefore, our presumptive preoperative diagnosis was atypical hemangiomas, hamartomas, or diffuse low-grade hemangiosarcoma. In addition, a positron emission tomographic (PET) scan was performed and showed no increased fluorodeoxyglucose localization corresponding to the splenic abnormalities noted on the prior CT examination, suggesting a benign process (Fig. 5). Given the uncertain nature of this incidentally discovered splenic lesion, we proposed an operative resection with laparoscopic splenectomy for diagnostic and therapeutic purposes. The $12 \times 8 \times 4 \text{ cm}$ specimen (Fig. 2) showed multiple nodular lesions with a spongy appearance, varying from 0.5 to 3.5 cm. Microscopically, these lesions were described as a vascular neoplasm forming anastomosing papillary vascular channels with occasional papillary structure (Fig. 6). The lacunae were filled with edematous fluid and blood. Immunohistochemical staining was positive for endothelial (CD 31) and histiocytic (CD 68) markers. No cytologic atypia and mitotic figures were found. The combination of morphological and immunohistochemical analysis presenting this hybrid endothelial-histiocytic phenotype established the diagnosis of LCA. The operation and recovery were uneventful, and the patient was discharged on postoperative day 4. He will be followed up closely for the occurrence of visceral neoplasms.

Discussion

LCA is a rare vascular neoplasm that occurs exclusively in splenic tissue and was first described by Falk et al in 1991 [2]. It originates from the specialized endothelial cells lining the sinus channels of the splenic red pulp, called "littoral cells". LCA affects both men and women equally. Due to nonspecific clinical symptoms, LCA is most often found incidentally as a splenic mass on abdominal imaging. Two instances of LCA presenting splenic rupture and hemoperitoneum have been reported [18,19]. Moreover, about 50% of patients give splenomegaly or signs of hypersplenism like anemia or thrombocytopenia [2,7]. LCA is often multifocal, and lesions can vary in size [4]. Radiological diagnostic imaging can hardly achieve a definitive diagnosis of LCA because of its similar appearance to both benign splenic neoplasms (hemangiomas, lymphangiomas, hamartomas, hemangiopericytoma and hemangioendothelioma) and malignant tumors (angiosarcoma, lymphoma, Kaposi sarcoma, and metastasis).



Fig. 2 – (A) Baseline CT confirms the presence of multiple focal splenic lesions, homogeneously hypodense with clear margins. Absence of loco-regional lymph adenomegaly. The spleen is of regular size. (B) CT (arterial phase) shows intense enhancement of the previously reported focal splenic lesions. (C) CT (portal phase) shows moderate persistence of the contrast medium in the lesions.

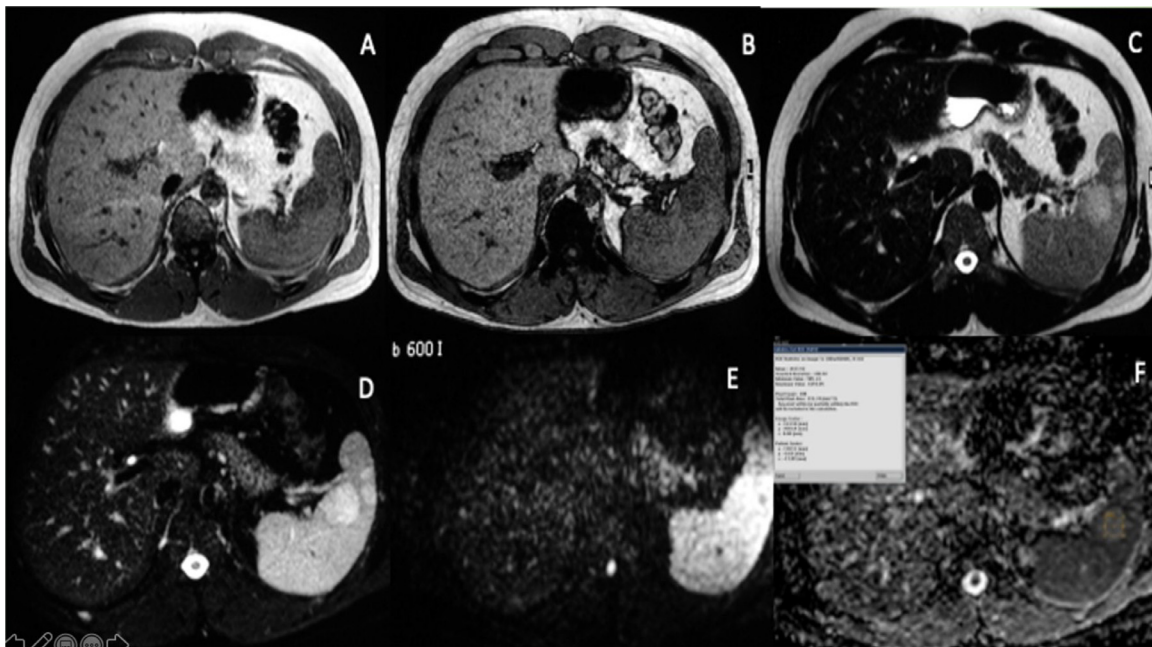


Fig. 3 – (A) MRI (SE T1 in-phase) shows homogeneous hypo-intensity of splenic lesions. (B) MRI (SE T1 out-phase) shows homogeneous hypo-intensity of splenic lesions. (C) MRI (TSE T2 W) shows homogeneous hyperintensity of splenic lesions. (D) MRI (STIR sequence) shows homogeneous hyperintensity of splenic lesions. (E) MRI (DWI sequence, b value = 600) shows homogeneous hyperintensity of splenic lesions, compatible with the absence of significant lesion restriction phenomena. (F) MRI (ADC Map). The ADC map shows a value = 1.43×10^{-3} confirming the absence of restriction.

Multiple imaging modalities have been used to evaluate LCA. However, there does not seem to be a superior option, and findings are inconsistent because of the vascular nature and variability of the tumor [11]. Sonography is rarely helpful because the findings vary widely. The sonographic features of LCA are variable and range from heterogeneous echotexture without specific nodules [20] to hyperechogenic [21], hypoechogenic [9], or echogenic [22] appearing lesions [8,10,23]. LCA masses are only rarely visible; however, early-phase contrast-enhanced CT may appear as multiple low-attenuation lesions related to the surrounding splenic parenchyma. On delayed images, they are generally isodense with the surrounding enhancing splenic tissue [11,24–26]. In contrast with most liter-

ature, our CT scan showed significant enhancement in the arterial phase, disorienting us toward a correct diagnostic hypothesis.

Magnetic resonance imaging of the spleen may further help in the diagnosis by showing hypointense lesions on both T1-weighted and T2-weighted scans [27]. In our case, MRI imaging demonstrated the hypointense lesions on T1 weighted and hyperintense on T2-weighted images. Maybe due to an inferior hemosiderin content of LCA. Moreover, DWI sequence, ADC map, and dynamic contrast graphic images may be helpful as diagnostic tools in the differential diagnosis among malignant and benign splenic processes; in our case, DWI images and relative diffusion coefficient showed

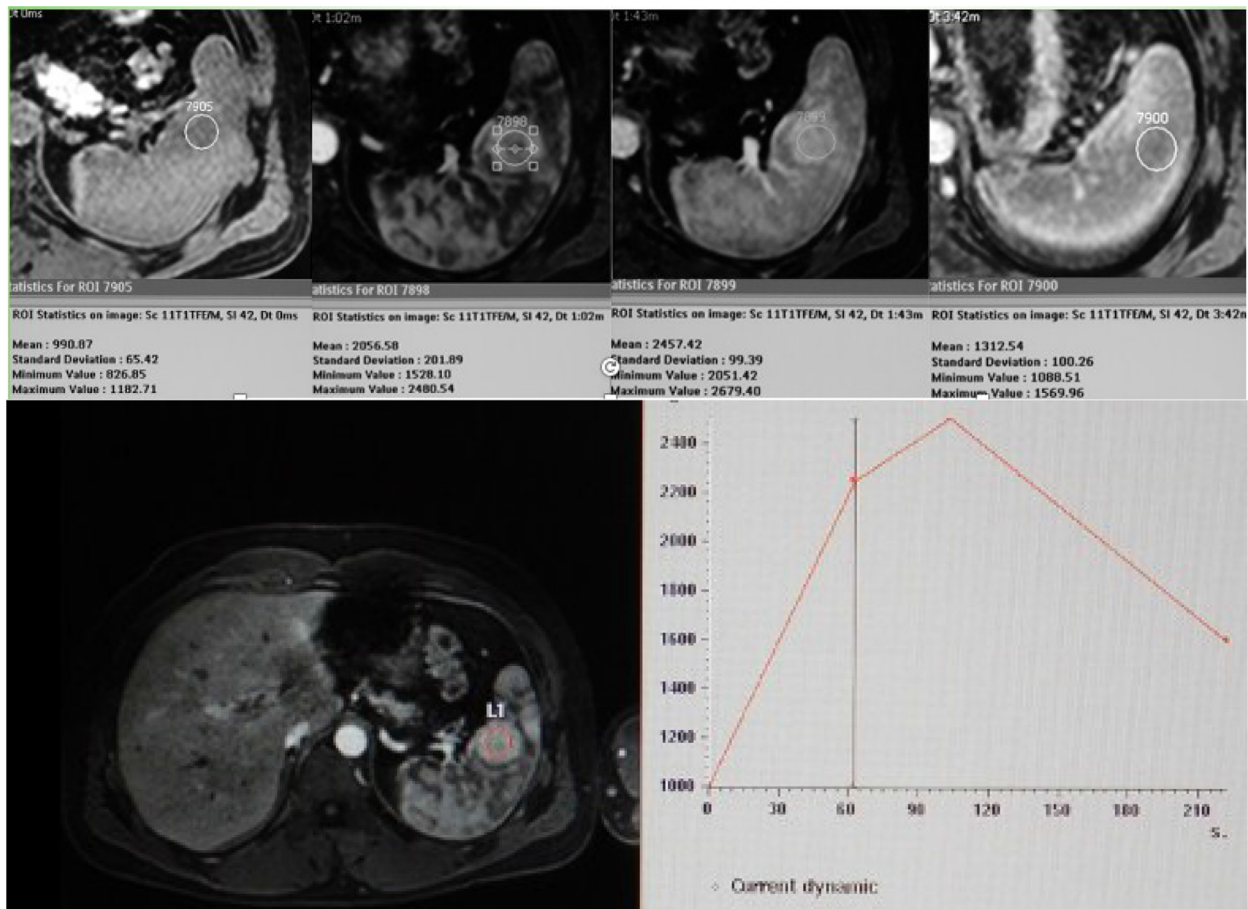


Fig. 4 – The dynamic study with MRI shows intense enhancement after contrast agent with significant wash-out in the subsequent phases.

the average value typical for benign lesions, while the dynamic postcontrast images showed, after an early arterial wash-in, an average early wash-out (already significant at the 4th minute), therefore, suspicious for malignant neoplasia (intensely vascularized). Hence, the need to perform a further diagnostic test, a PET scan. PET scan showed no increased fluorodeoxyglucose localization corresponding to the splenic abnormalities noted on the prior CT examination in the only case reported in the literature [11]. Percutaneous biopsy of splenic lesions, with both CT and US guidance, has been successfully performed in many instances of LCA [28,29]. Still, this approach is controversial because of the risk of hemorrhage pneumothorax and other complications [30]. Radiological findings are rarely sufficient for making a definitive diagnosis because many other splenic neoplasms can mimic LCA. Several differential diagnoses must be considered. These include benign neoplasms like hamartoma, hemangioma, or lymphangiomatosis, as well as malignant tumors such as lymphoma or angiosarcoma, but also metastatic diseases or disseminated infections such as fungal disease, septic emboli, and granulomatous diseases [20]. Mycobacterium avium-intracellular complex, Pneumocystis carinii, and disseminated Kaposi sarcoma may also cause splenic masses but are typically seen in immunocompromised individuals. Since our patient did not present any adenopathy or diseases in

other organs, metastatic disease was considered an unlikely diagnosis. However, a definite diagnosis is often difficult to obtain, and splenectomy is subsequently performed for diagnostic and therapeutic purposes. Pathologically, LCA typically shows multiple focal blood-filled nodules, and microscopic examination reveals anastomosing vascular channels lined with tall endothelial cells and papillary projections [2,8,12]. Since the littoral cells have features intermediate between endothelial cells and macrophages, they show a hybrid endothelial-histiocytic phenotype on immunohistochemical staining. Immunohistochemically, LCA is characteristically CD 34 negative, CD 68 positive, CD 31 positive, 21 positive, and 8 negatives [31].

Additionally, the epithelial cells in LCA do occasionally express S-100 protein [32]. High expression of forming homology domain protein 1 (FHOD1), a typical feature of normal littoral cells, not of LCA, distinguished these [33]. Further research has been done evaluating molecular markers and LCA to help aid in the accurate diagnosis of LCA tumors. LCA has most commonly been described as a benign lesion even if there are some reports of LCA with malignant features: a low-grade variant (littoral cell hemangioendothelioma) [4] and the tumor's malignant counterpart, littoral cell angiosarcoma [34].

Furthermore, in one case, metastatic lesions were found in the liver and retroperitoneum 4 years after splenectomy

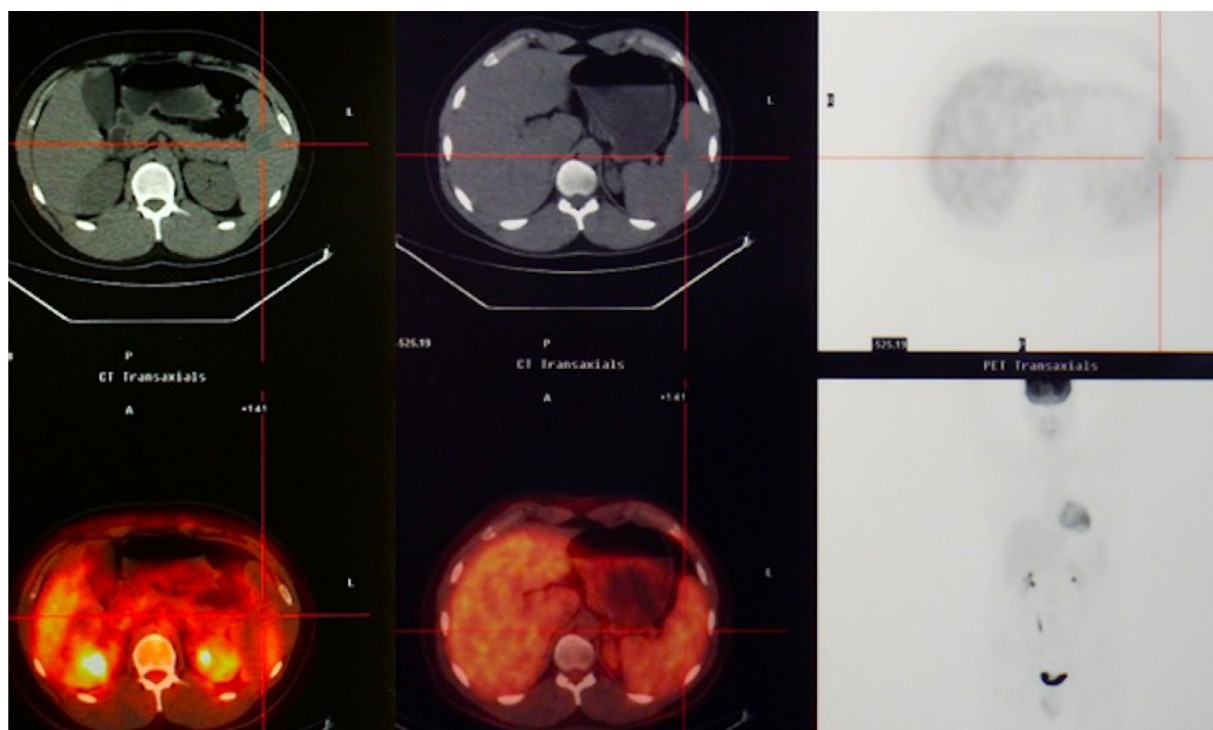


Fig. 5 – The CT-18 FDG-PET examination shows the absence of FDG uptake in spleen lesions.

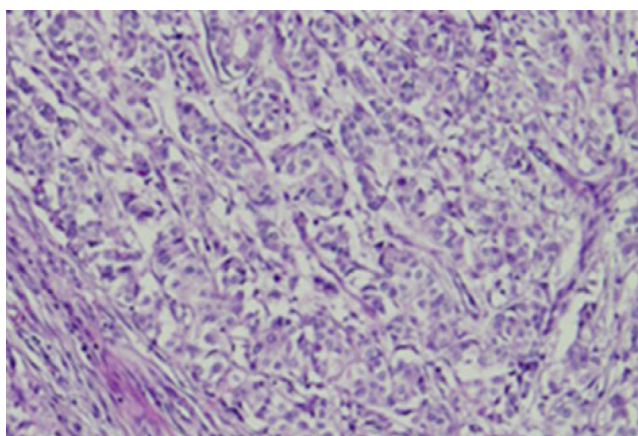


Fig. 6 – Photomicrograph of the littoral cell angioma (hematoxylin-eosin, original magnification 50 x). Microscopically, the lesion shows vascular neoplasms forming anastomosing vascular channels lined by histiocytes with occasional papillary structure, consistent with littoral cell angioma. These cells expressed vascular markers by immunohistochemistry (FVIII, CD31, and CD34).

for LCA [35]. The etiology of this neoplasm remains unclear. A few reports in the international literature have described association with visceral organ tumors, including colorectal adenocarcinoma, hepatocellular carcinoma, non-small cell lung cancer, renal cell cancer, pancreatic cystadenocarcinoma, pancreatic neuroendocrine tumor, seminoma, ovarian cystadenocarcinoma, papillary thyroid cancer, and transitional

cell carcinoma of the bladder [1,7]. Other reports have shown an association between LCA and immunological disorders, such as ankylosing spondylitis, myelodysplastic syndrome, aplastic anemia, non-Hodgkin lymphoma, Crohn's disease, and Gaucher's disease [7,34,36] so that an etiological association with immune dysregulation has been proposed [2,13–16]. Due to possible malignant features of LCA and the described association with other malignancies, patients with suspected LCA should undergo close follow-up after splenectomy. LCA is typically an incidental finding on diagnostic imaging workup, as in our case, without specific imaging features. Even if DWI sequences and PET scans may be other useful diagnostic tools in differentiating benign from malignant spleen lesions, a specific radiological diagnosis of LCA seems impossible. So, a particular diagnosis requires histologic examination [12].

Conclusions

This rare case presented, atypical for some imaging aspects, highlighting the imaging features in the different methods, allowed us to define the decisive role of DWI sequence and PET study in orienting the diagnosis toward benign lesions. Moreover, gold standard management remains splenectomy, and long-term follow-up for the development of synchronous tumors or metastatic lesions is advised.

Patient consent statement

Written informed consent was obtained from the patient.

REFERENCES

- [1] Bailey A, Vos J, Cardinal J. Littoral cell angioma: a case report. *World J Clin Cases* 2015;3(10):894–9.
- [2] 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.
- [3] Emir S, Sozen S, Yazar MF, Altinsoy HB, Arslan Solmaz O, Ozkan Z. Littoral-cell angioma of the spleen. *Arch Iran Med* 2013;16:189–91.
- [4] Ben-Izhak O, Bejar J, Ben-Eliezer S, Vlodavsky E. Splenic littoral cell haemangioendothelioma: a new low-grade variant of malignant littoral cell tumor. *Histopathology* 2001;39:469–75.
- [5] Meybehm M, Fischer HP. Littoral cell angiosarcoma of the spleen. Morphologic, immunohistochemical findings and consideration of histogenesis of a rare splenic tumor. *Pathologe* 1997;18:401–5.
- [6] Kutok JL, Fletcher CD. Splenic vascular tumors. *Semin Diagn Pathol* 2003;20:128–39.
- [7] Harmon RL, Cerruto CA, Scheckner A. Littoral cell angioma: a case report and review. *Current Surgery* 2006;63(5):345–50.
- [8] Levy AD, Abbott RM, Abbondanzo SL. Littoral cell angioma of the spleen: CT features with clinicopathologic comparison. *Radiology* 2004;230:485–90.
- [9] Ziske C, Meybehm M, Sauerbruch T, Schmidt-Wolf IG. Littoral cell angioma as a rare cause of splenomegaly. *Ann Hematol* 2001;80:45–8.
- [10] Goldfeld M, Cohen I, Loberant N, Mugrabi A, Katz I, Papua Papua, Noi I. Littoral cell angioma of the spleen: appearance on sonography and CT. *J Clin Ultrasound* 2002;30:510–13.
- [11] Sarandria J J, Escano M, Kamangar F, Farooqui S O, Montgomery E, Cunningham S C. Littoral cell angioma: gastrointestinal associations. *Gastrointest Cancer Res* 2014;7(2):63–4.
- [12] Abbott RM, Levy AD, Aguilera NS, Gorospe L, Thompson WM. Primary vascular neoplasms of the spleen: radiologic-pathologic correlation. *Radiographics* 2004;24(4):1137–63.
- [13] Gupta MK, Aguilera NS, Pastores GM. Littoral cell angioma of the spleen in a patient with Gaucher disease. *Am J Hematol* 2001;68:61–2.
- [14] Suvajdzic N, Cemerikic-Martinovic V, Saranovic D, Petrovic M, Popovic M, Artiko V, et al. Littoral-cell angioma as a rare cause of splenomegaly. *Clin Lab Haem* 2006;28:317–20.
- [15] Tholouli E, Roulston JA, Byers R, Burton I, Liu Yin JA. Littoral cell angioma of the spleen in a patient with severe aplastic anemia. *Haematologica* 2003;88(11):ECR33.
- [16] Tan YM, Chuah KL, Wong WK. Littoral cell angioma of the spleen. *Ann Acad Med Singapore* 2004;33:524–6.
- [17] Jang K M, Kim S H, Hwang J, Lee SJ, Kang TW, Lee MW, et al. Differentiation of malignant from benign focal splenic lesions: added value of diffusion-weighted MRI. *AJR* 2014;203:803–12.
- [18] Pilz JB, Sperschnieder T, Lutz T, Loosli B, Maurer CA. Littoral cell angioma in primary and accessory intrapancreatic spleen presenting as splenic rupture. *Am J Surg* 2011;201:e15–17.
- [19] Yamane H, Ohashi K, Suzuki T, Takigawa N. Ruptured littoral cell angiosarcoma causing hemoperitoneum. *Intern Med* 2012;51:337–8.
- [20] Kinoshita LL, Yee J, Nash SR. Littoral cell angioma of the spleen: imaging features. *AJR* 2000;174:467–9.
- [21] Espanol I, Lerma E, Fumanal V, Palmer J, Roca M, Domingo-Albòs A, et al. Littoral cell angioma with severe thrombocytopenia. *Ann Hematol* 2000;79:46.
- [22] Oliver-Goldaracena JM, Blanco A, Miralles M, Martin-Gonzalez MA. Littoral cell angioma of the spleen: US and MR imaging findings. *Abdom Imaging* 1998;23:636–9.
- [23] Bhatt S, Huang J, Dogra V. Littoral cell angioma of the spleen. *AJR American J Roentgenol* 2007;188:1365–6.
- [24] Bisceglia M, Sickel JZ, Giangaspero F, Gomes V, Amini M, Michal M. Littoral cell angioma of the spleen: an additional report of four cases with emphasis on the association with visceral organ cancers. *Tumori* 1998;84:595–9.
- [25] Hanna T, Baumgarten D, Friedman T. Littoral cell angioma: a case and review of the literature. *Radiol Case Rep* 2011;6:324–6.
- [26] Rana Netra, Ming Z, Hui M S, Bin Y. Case report: littoral cell angioma of spleen. *Indian J Radiol Imaging* 2009;19(3):210–12.
- [27] Jun D, Shen Q, Yin H, Zhou X, Wu B. Littoral cell angioma of the spleen: report three cases and literature review. *Int J Clin Exp Pathol* 2015;8(7):8516–20.
- [28] Nagarajan P, Cai G, Padda MS, Selbst M, Kowalski D, Proctor DD, et al. Littoral cell angioma of the spleen diagnosed by endoscopic ultrasound-guided fine-needle aspiration biopsy. *Diagn Cytopathol* 2011;39:318–22.
- [29] Shah S, Wasnik A, Pandya A, Bude RO. Multimodality imaging findings in image-guided biopsy-proven splenic littoral cell angioma: three cases. *Abdom Imag* 2011;36:735–8.
- [30] Singh AK, Shankar S, Gervais DA, Hahn PF, Mueller PR. Image-guided percutaneous splenic interventions. *Radiographics* 2012;32:523–34.
- [31] Johnson C, Goyal M, Kim B, Wasdahl D, Nazinitsky K. Littoral cell angioma. *Clin Imaging* 2007;31:27–31.
- [32] Bhatt S, Simon R, Dogra VS. Littoral cell angioma: sonographic and color Doppler features. *J Ultrasound Med* 2007;26:539–42.
- [33] Ogembo JG, Milner DA, Mansfield KG, Rodig SJ, Murphy GF, Kutok JL, et al. SIRP α /CD172a and FHOD1 are unique markers of littoral cells, a recently evolved significant cell population of red pulp of the human spleen. *J Immunol* 2012;188:4496–505.
- [34] Rosso R, Paulli M, Gianelli U, Boveri E, Stella G, Magrini U. Littoral cell angiosarcoma of the spleen. Case report with immunohistochemical and ultrastructural analysis. *Am J Surg Pathol* 1995;19:1203–8.
- [35] Fernandez S, Cook GW, Arber DA. Metastasizing splenic littoral cell hemangioendothelioma. *Am J Surg Pathol* 2006;30:1036–40.
- [36] Chourmouzi D, Psoma E, Drevelegas A. Littoral cell angioma, a rare cause of long-standing anemia: a case report. *Cases J* 2009;2:9115.