Case Report

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Littoral Cell Angioma in the Last 33 Years

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ABSTRACT

Primary spleen neoplasms are rare diseases. Most often we find a tumorous involvement of splenic parenchyma as an accidental finding but sometimes it is a spontaneous spleen rupture. Littoral cell angioma (LCA) is a unique benign vascular neoplasm of splenic sinus-lining cells with unknown aetiology. LCA has no soft tissue counterpart. Patients with LCA has no age and sex predilection. In 1991, Stephen Falk and his colleagues first described LCA. Since then, according to the literature, 204 publications have appeared in the last 33 years. This article presents a short review of littoral cell angioma and a Hungarian case report. In Hungary our case is the first and the only.

Keywords: Spleen Rare Tumors; Spontaneous Spleen Rupture; Littoral Cell Angioma; Splenectomy; Hungarian Case

Key Messages: Littoral cell angioma is a rare, benign splenic tumor. The paper briefly summarizes the literature, reviewing the characteristics of the lesion and a unique Hungarian case in the international literature.

Introduction

Tumorous of the spleen are rare diseases. They are mainly associated with haematological malignancies, lymphomas or metastases. Primary spleen tumors are very rare. One of their larger groups is lymphoproliferative diseases, but even so, lymphomas of primary splenic origin account for only 1% of all lymphomas [1]. The non-lymphatic group is predominantly of vascular or mesenchymal origin. Vascular proliferations are the commonest primary connective tissue tumors of the spleen. Some resemble vascular tumors of other anatomical sites as lymphangiomas, hemangiomas, hemangioendotheliomas or angiosarcomas. Others appear unique to this organ such as Littoral Cell Angiomas (LCA) or hamartomas (so-called splenomas). All these lesions are rare in the spleen. Littoral cell angiomas are classified as vascular tumors. The littoral cells are actually long, spindle-shaped endothelial cells lining the red pulp sinuses, which line up like the dongles of barrels, hence the name littoral cells for sinus endothelial cells. The dongles formed by the endothelial cells are held together by the lattice fibres around the sinuses [2]. Littoral cell angioma is a predominantly benign tumor of the spleen and is very rare. It rarely causes symptoms and is usually detected incidentally. It was first described by Falk in 1991 in 17 cases [3].

Symptoms

The majority of littoral cell angiomas remain asymptomatic. Sometimes, however, it can cause uncertain abdominal pain, discomfort, and a rise in body temperature of unclear origin. But it may also cause symptoms due to hypersplenia, which may result in anaemia, thrombocytopenia, pancytopenia [4-7]. However, cases have been reported causing fever, chills, weakness, fatigue and pain, or anaemia for 5 years [8,9]. In 2004 pyrexia of unknown origin by a 36-year-old kidney transplanted woman was published [4].

Incidence

One of the most published Czech authors, with 25 cases, described the concomitant presence of another tumor in the majority of patients (15/25), predominantly colon or renal carcinoma [6]. A review of the literature shows that it may also occur along with other predominantly colorectal tumors [6,10,11] and renal tumors [6,11], but co-invasions with pancreatic adenocarcinoma [11,12], non-Hodgkin lymphoma, non-specific tumors of the liver, brain, epithelial ovarian cancer, non-small cell lung tumor [12], hepatocellular carcinoma [13] have also been described. In one case, a tumor mimicking metastasis of a preoperative papillary thyroid carcinoma was described, which was later found to be a littoral cell angioma [14]. Sometimes two rare

disorders occur like littoral cell angioma and Gaucher disease simultaneously, which involve the lysozymes. The statistical likelihood of chance occurrence of these in the same individual is quite low, especially they have similar and nonspecific clinical presentation [15]. The coexistence of littoral cell angioma and Von Willebrand's disease has also been reported [16]. The literature one LCA case described along with chronic hepatitis C virus infection, splenic marginal zone lymphoma and villous lymphocytic leukaemia in the same patient [17]. Another article reported a case of LCA found in liver cirrhosis [18]. In 2003, LCA was described in a patient with aplastic anaemia who developed marked splenomegaly and hypersplenism after multiple treatments [19]. Littoral cell angioma must be differentiated from splenic hamartoma, hemangioma, angiosarcoma, littoral cell angiosarcoma, and epithelioid and spindle cell hemangioendothelioma.

Littoral cell angioma is mostly a benign lesion, but malignant lesions have also been described [20]. Littoral cell hemangioendothelioma there is a risk of late abdominal and liver recurrence. It seems that the original splenic tumors are characterised by the presence of solid, clear cell areas, in comparing to the more typical benign littoral cell angiomas. In recurrent/metastatic lesions, solid clear cell areas predominate. Therefore, we recommend that all littoral cell angiomas should be carefully searched for such foci and, if present, the tumors should be classified as low malignancy and monitored for abdominal recurrence or metastasis [21].

Diagnosis

Despite sophisticated imaging techniques, it is not often possible to differentiate these primary splenic vascular neoplasms from pancreatic tumors [22]. Imaging most often shows an enlarged spleen with multiple nodules. Abdominal US by using a 5-MHz probe shows a lobulated splenomegaly of heterogeneous echogenicity without acoustic enhancement [8,23,24]. With a 7.5-MHz probe, multiple nodules are seen that are isoechogenic with the splenic parenchyma, some of them have anechoic areas inside. Abdominal MR imaging using spin echo proton density (PD) and T2-weighted MR images and unenhanced T1-weighted Spoiled Gradient Recalled Echo (SGRE) sequences shows hypointense lesions with respect to the liver and muscle in all sequences and some hyperintense areas in the PD and T2-weighted MR images, corresponding to the anechoic spaces seen in the US. [24] This finding reflects the presence of hemosiderin in the lesions due to the hematophagocytic capacity of the neoplastic cells [25]. CT scans show multiple, well-circumscribed, hypodense, non-enhancing splenic lesions. No significant increase in density after contrast administration [8,26]. Spiral-CT with oral and intravenous constrast material shows multiple low-attenuation nodular masses scattered throughout the spleen ranging from several millimeters to few centimeters in size [27,28]. Cases have also been published in which both early and late portal venous CT were performed and the lesions of the littoral cell angioma showed delayed contrast enhancement, making them isolated from adjacent splenic tissue [5,28,29].

This finding suggests that the vascular channels forming the littoral cell angioma perfuse more slowly with contrast than the normal splenic parenchyma and may help to delineate the differential diagnosis [25]. Lesions can be up to 9 cm in diameter and range in shape from spherical to geometrical. Most lesions have a defined margin, but poorly defined margins and fused lesions have been also detected [5]. No capsular lesions or small cystic spaces associated with nodular lesions detected on histological examination can be identified on CT. Significant abdominal adenopathy, typically seen in patients with splenomegaly and lymphoma, is not present in patients with littoral cell angioma. Large splenic masses with multiple nodular masses seen on LCA, including lymphoma, metastases, peliosis, sarcoid, and infection (especially fungal). The imaging features of these entities are usually non-specific and correlation with clinical findings is usually required to make a more accurate diagnosis. Macroscopically, the tumor forms solitary and multiple discrete nodules, which often appear spongy and filled with blood. In a series by Falk and his colleagues, spleens showed nodular lesions of 0.2-9.0 cm. These were usually multiple, except in two cases where solitary nodules were detected. These were typically dark red in colour, spongy and may have a cystic appearance. Rarely the lesion is a solitary white nodule [3]. Immunohistochemical staining showed reactivity against factor VIII-associated antigen (factor VIII R Ag), CD31, CD68, CD21 and PAS-positive intracytoplasmic inclusions antibodies, with no reactivity for vimentin, S-100 protein and CD34, CD8 [30-32].

Spleen LCAs were CD163+, with immunoreactivity present in the majority of the lining cells. Although considered a vascular tumor, the immunohistochemical features of the littoral cell angioma suggest histiocytic differentiation, as evidenced by positive immunoreactivity for histiocytic-associated antigens such as lysozyme and CD68 [3,33] and the positivity of CD163 [34].

Therapy

The diagnosis of littoral cell angioma is established retrospectively. It is often detected during histological examination of spleens removed during splenic rupture surgery. Sometimes splenectomy is performed for diagnostic and therapeutic purposes in cases of incidentally discovered splenomegaly. The procedure can be performed both by open abdominal surgery and laparoscopically [35-37].

Case Report

In December 2020, a 78-year-old female patient with a pacemaker was seen as an emergency patient for left shoulder pain and chest discomfort. The previous week she had abdominal pain, no trauma. Laboratory tests showed anaemia, thrombocytopenia, elevated D-dimer. Her blood pressure was 85/57 mm Hg, pulse rate 85/min, which showed an elevated shock index. A chest CT scan for suspected pulmonary embolism did not confirm pulmonary embolism, but the image of the mapped upper abdomen showed multiple small cysts, inhomogeneous contrast enhancement, with large amount of

fluid around the spleen, which raised the suspicion of splenic rupture. Urgent splenectomy was performed. During the operation, no abnormalities were found on inspection of the abdominal organs, but a large amount of blood was found in the abdominal cavity. The spleen was enlarged with multiple solid cysts and retraction on the surface. Postoperative supraventricular tachycardia resolved with pacemaker reprogramming. The patient's anaemia was corrected with a total of 4 E red blood cell masses. He received postoperative antibiotic therapy and vaccinations. The patient was discharged home in good general condition after an uneventful postoperative period on postoperative day 5. He was hospitalized again less than two weeks later for a Covid-19 infection and died of viral pneumonia on the 13th day of his care. Histopathological examination of the spleen confirmed a littoral cell angioma. The tumor showed CD-31 and CD-68 positivity, CD-34 negativity, CD-8 negativity, and KI-67 proliferation index was low, suggesting benignity. Hemisiderin pigment containing macrophages were also seen in several areas of the tumor, which were marked with Berlin blue.

Discussion

Littoral cell angioma is a very rare, benign spleen tumor. From its first description in 1991 to the end of 2023, 192 publications on littoral cell angioma was published in PubMed and 158 cases was published. A Chinese working group reviewed not only the English but also the Chinese language publications [12], resulting in a total of 204 publications and 443 patients [12]. In Hungary our case is the first and the only.

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