Atipical immunophenotype in a littoral cell angioma
Atipični imunofenotip kod angioma litoralnih ćelija

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Abstract

Background. Littoral-cell angioma (LCA) is a recently described benign vascular tumor of the spleen, whose imaging and pathologic characteristics have been discussed only by a few authors. The tumor is characterized by a mixture of papillary and cystic areas lined by neoplastic cells deriving from normal splenic lining — littoral cells. The neoplastic LCA cells express both endothelial and histiocytic antigens associated with CD8 negativity, compared with the normal endothelium of the venous sinuses of the spleen red pulp that only expresses endothelial antigens and CD8 positivity. Therefore, the typical and characteristic immunohistochemical pattern of the LCA is as follows: CD31, CD68, CD163, CD21, FVIII antigen positive; CD34, CD8 negative.

Case report. We reported a 60-year-old male with moderate nodular splenomegaly with one large hypoechoic solid lesion and mild thrombocytopenia in whom the diagnosis of LCA was made after the elective splenectomy. Namely, histopathological and immunohistochemical data allowed a final diagnosis of classical LCA in spite of CD21 negativity. As far as we know this is the first reported CD21-negative LCA patient. Histological specimens were presented and differential diagnoses discussed.

Conclusion. Littoral-cell angioma is a very rare benign splenic neoplasm that should be considered in the differential diagnosis of multinodular splenomegaly, particularly if the patient has the signs of hypersplenism.

Key words: splenic neoplasms; immunohistochemistry; histology; antigens, CD; splenectomy.

Apstrakt

Uvod. Angiom litoralnih ćelija (ALČ) nedavno je opisan benigni tumor slezine vaskularnog porekla o čijim patohistoloskim i radiološkim karakteristikama ima malo podataka u medicinskoj literaturi. Tumor se odlikuje prisustvom papilarnih i cističnih tvorevina sastavljenih od tumorskih ćelija koje vode poreklo od litoralnih ćelija slezine koje oblažu venske sinuse crvene pulpe. Za razliku od normalnih litoralnih ćelija slezine koje eksprimiraju samo endotelne antigene, ćelije ALČ eksprimiraju istovremeno endotelne i histiocitne antigene uz odsustvo bojenja na CD8 koje je inače prisutno kod normalnih litoralnih ćelija. Stoga, imunofenotipski profil ALČ jedinstven je i karakterističan: CD31, CD68, CD163, CD21, FVIII antigen pozitivni; CD34, CD8 negativni.


Ključne reči: slezina, neoplazme; imunohistohemija; histologija; antigeni, CD; splenektomija.

Introduction

Littoral-cell angioma (LCA) is a very rare primary tumor of the spleen arising from normal endothelial cells lining the venous sinuses of the spleen red pulp (littoral cells). The neoplastic LCA cells express both endothelial and histiocytic antigens, compared with the normal endothelium of the venous sinuses that only expresses endothelial antigens. Therefore, the immunophenotypic signature of CD31, CD68, CD163, FVIII antigen and CD21 on the lining cells of the LCA is unique to this tumor. Typically, CD34 and CD8 are negative. The tumor is considered benign, though the litera-
ture has described a patient with disseminated disease and an apparent response to the therapy, and two other cases have shown histological atypia, though without fully malignant histological features\textsuperscript{1-3}. 

**Case report**

A 60-year-old male was referred to our institute in December 2006 due to spleen tumor. He complained of intermittent blunt pain of moderate intensity under his left costal margin lasting for a few years but it was not before November 2006 that the abdominal ultrasound (US) scan was performed revealing an enlarged spleen of 15.5 cm with a large hypoechogenic solid lesion. Computerized tomography (CT) without contrast confirmed splenomegaly (17 × 12.4 cm), nonhomogenous and hypodense without clear delineation of tumor.

Physical examination identified an enlarged, firm, non-tender spleen extending 3 cm below the left costal margin. The patient's medical history besides arterial hypertension was unremarkable. He was not aware of any familial related diseases and had not recently visited a foreign country. The patient had been constitutionally well and denied suffering from fever, weight loss or night sweats. All hematological values were normal except for a mild thrombocytopenia (60−70 × 10\(^9\)/L). Clotting tests were within normal limits, excluding a disseminated intravascular coagulopathy. No biochemical or immunological abnormalities were found and viral serological tests were negative.

For diagnostic purposes the patient underwent splenectomy. The 900-gram resected spleen (16 × 13 × 8.7 cm) had an intact and sturdy capsule (Figure 1). Splenic tissue was completely replaced by a solitary nodular lesion of spongy appearance measuring 11.5 × 10 × 8.5 cm. Microscopically, the lesion consisted of dilated anastomozing vascular channels, with multiple papillary projections and cyst-like spaces (Figure 2). These channels were lined with tall endothelial cells positive for FVIII antigen, CD68 (Figure 3), CD31 (Figure 4) and lysozyme showing their mixed endothelial-

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histiocytic phenotype. The endothelial cells were CD21, CD34 and CD8 negative. Littoral cells exhibited homophagocytosis and an intracellular hemosiderin. Additional feature was a focus of extramedullar hematopoiesis. No atypical cells or mitotic figures were seen. Although the endothelial cells in our patient lack CD21 positivity, which is typically at least focal in LCA, the pathohistological finding in our case is consistent with the immunophenotype of a classical LCA. Bone marrow and liver biopsies were normal. The patient recovered well from surgery and his platelet count normalized. Six months after the surgery, the patient remains asymptomatic.

Discussion

Littoral-cell angioma represents a rare and distinct clinico-pathological benign tumor of the spleen. It is a lesion unique to the spleen and always situated within the splenic red pulp. It is seen throughout a wide age range and occurs equally in the sexes. The clinical presentation can include splenomegaly, hypersplenism with thrombocytopenia and/or anemia as in our case, pyrexia of unknown origin or could be an incidental finding. Littoral-cell angioma has been associated with synchronous malignancies (colorectal, renal and pancreatic adenocarcinoma, ovarian cancer and seminoma and lymphoma), autoimmune (aplastic anemia, Crohn’s disease) and Gaucher’s disease, indicating a possible pathological-physiological association.

Neither clinical signs nor symptoms of either malignant disease or any other disease were detected during the 18-month follow-up of the patient. The combination of morphologic and immunohistochemical analyses showing a hybrid endothelial-histiocytic phenotype established the diagnosis of LCA in the patient in spite of CD21 negativity.

Primary tumors of the spleen other than lymphoid and hematological tumors are quite rare, and LCA should be considered in the differential diagnosis of multinodular splenomegaly. The most difficult differential diagnosis from which to distinguish LCA is angiosarcoma. LCA, however, lacks the irregular growth pattern of the anastomosing vessels, nuclear atypia, increased mitotic activity and necrosis seen in angiosarcoma. Radiological diagnosis is difficult as the findings on US, CT and Technitium scanning are fairly nonspecific.

Conclusion

Littoral-cell angioma itself is a rare benign splenic neoplasm that should be considered in the differential diagnosis of nodular splenomegaly, particularly if the patient has clinical symptoms of hyperplenism.

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REFERENCES


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