

Diffuse hemangiomas of the spleen – case report*

Nuket Eliyatkin¹, Sibel Demir Kececi², Arsenal Sezgin¹, Hakan Postaci¹, Tahsin Tekeli³, Ali Galip Denecli³

Departments of Pathology¹ and General Surgery², Izmir Research and Training Hospital, Izmir, Turkey

Department of Pathology³, Aegean Maternity Research And Training Hospital, Izmir, Turkey

Accepted for publication on 15 May 2006

**Presented at the XXIIIth World Congress of Pathology and Laboratory Medicine held on 26th-30th May 2005 in Istanbul, Turkey*

Background: Small localized hemangiomas are common neoplasms of the spleen. Isolated diffuse splenic hemangiomas is very rare. This lesion can be accompanied by severe hypersplenism and other complications.

Case: We report a case with significant splenomegaly caused by diffuse hemangiomas in a 58-year-old woman. After splenectomy, the normal parenchyma was found to be widely replaced by multiple dark-red, spongy nodules. Microscopic examination showed thin walled, cavernous vessels involving the entire spleen.

Conclusion: The differential diagnosis of diffuse splenic hemangiomas must include the other vascular tumors or tumor-like lesions of the spleen such as lymphangioma, littoral cell angioma, hemangioendothelioma and primary angiosarcoma, peliosis of the spleen, and hamartoma. We report this case of diffuse hemangiomas by virtue of its rareness and the presence of many other vascular lesions in the differential diagnosis.

Keywords: Diffuse hemangiomas, vascular tumors, spleen.

Background

The most common primary tumors of the spleen are benign and originate from the vascular endothelium. Hemangioma is the most common primary benign neoplasm of spleen^{1,2} and usually represents as a small, localized tumor.^{2,3} Diffuse hemangiomas is a variant of hemangioma, and splenic parenchyma is permeated and widely replaced by vascular proliferations. This condition may occur together with hemangiomas of the liver or it may occur as a manifestation of systemic angiomas, or less commonly, is confined to the spleen.^{2,4}

We present a patient with significant splenomegaly caused by diffuse hemangiomas. The patient had no clinical disorders resulting from the splenic vascular tumor.

Case

A 58-year-old woman was admitted to our hospital because of a 4-weeks history of fatigue, abdominal pain, weight loss, vomiting, left upper quadrant abdominal mass. Her medical history included diabetes mellitus Type 2 and oral antidiabetic therapy for the past seven years. There was no history of oral contraceptive usage.

Physical examination disclosed only a large, firm, non-tender spleen extending from the costal margin to the pelvis. The complete blood count, coagulation and liver function tests were within normal limits. Ultrasound examination of abdomen showed a significantly enlarged spleen including numerous, ill-defined, hyperechoic nodules and revealed a parenchymal heterogeneity and septation. Abdominal

CT demonstrated a splenomegaly caused by multiple nodules of variable size showing lower intensity. The findings were thought to represent an intrasplenic tumor, and in particular, splenic lymphoma was taken into consideration. For diagnostic and therapeutic purposes she underwent splenectomy. Her platelet count increased from 169.000/ μ l to 350.000/ μ l, postoperatively. The patient recovered uneventfully.

Grossly, the spleen weighed 1.770 g and measured 285x150x80 mm. The capsule was intact. On cut surfaces, parenchyma contained multiple dark red, spongy nodules (Figure 1). The material was fixed in 4% buffered formalin. Sections (5 μ) were cut from multiple paraffin-embedded tissue blocks and stained with hematoxylin-eosin. Immunohistochemical investigations were performed by avidin-biotin-peroxidase complex technique with vimentin, CD31, CD34, CD68 antibodies.

Microscopic examination showed an angiomatous lesion involving the entire spleen. Remnants of the red pulp were observed among the pathological vessels throughout the spleen (Figure 2a). The pathological vessels were mostly thin walled, cavernous vessels were lined by a flat to cuboidal endothelium without any cytologic atypia or mitosis (Figure 2b). The lumina contained weakly stained serum and erythrocytes. In some areas, red pulp persisted but sinuses were stretched. There was increased fibrosis in the residual red pulp. In some areas, there seemed to be a gradual transition from cystically dilated splenic



Figure 1. Gross appearance of tumor on cut section. Multiple dark-red, spongy nodules in the parenchyma.

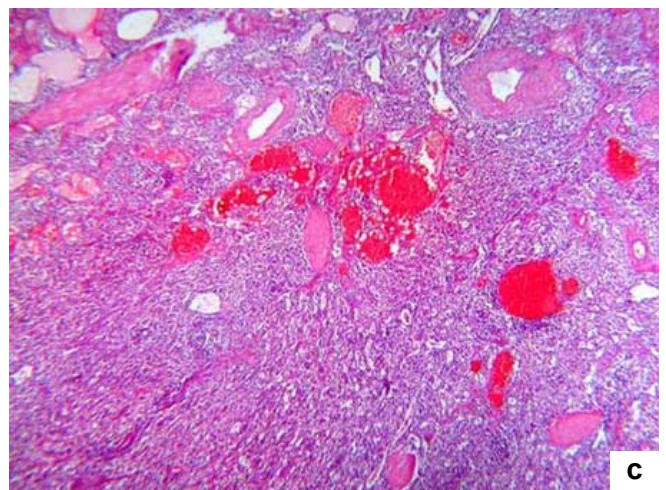
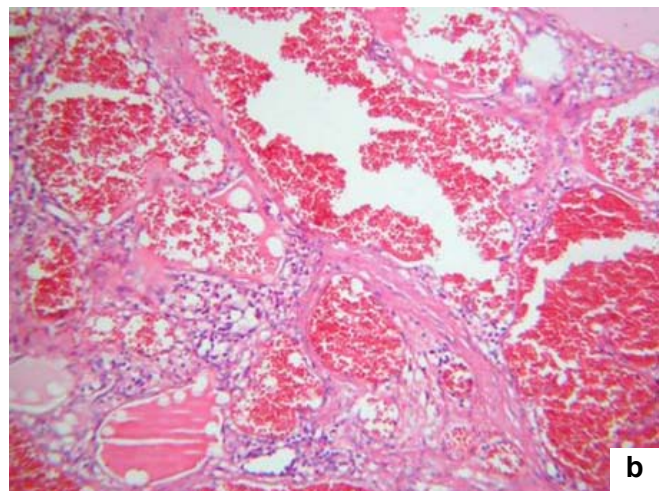
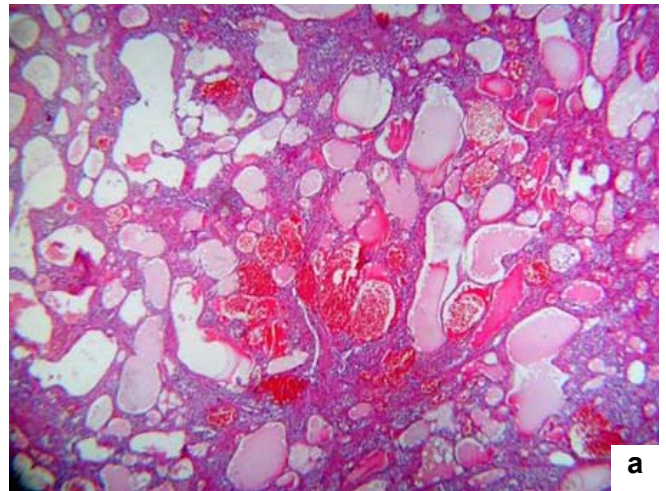


Figure 2. Spleen was infiltrated by an angiomatous tumor composed of thin walled and ectatic large vessels filled with erythrocytes and weakly stained serum (a). The neoplastic vessels were lined by flat endothelial cells containing oval nuclei that showed no mitotic activity (b). Normal splenic sinuses (below) and cavernous vessels (c).

sinuses to cavernous vessels (Figure 2c). Trabecular veins showed intimal thickening. The arteries were collapsed. The white pulp was atrophic.

Immunohistochemically, cavernous vessels of hemangiomas, splenic sinuses and all other splenic vessels showed a distinctly positive reaction with vimentin and CD34 (Figure 3a). CD31 expression was focally identified in cavernous vessels and splenic sinuses and was strongly positive in other splenic vessels (Figure 3b). In cavernous areas, a few cells lining the lumens exhibited an intracytoplasmic granular positivity for CD68 (Figure 3c).

Discussion

Diffuse hemangiomas of the spleen is a rare benign vascular condition.^{2,4,5} Splenic hemangiomas may be asymptomatic or cause complications such as disturbances of blood coagulation, rupture of the spleen and portal hypertension. Clinically, the diagnosis is usually difficult to make, but computed tomography and ultrasound can be useful methods for evaluating this vascular disorder.² In our case there was no radiologic or clinical evidence of other organ involvement and, therefore, the diagnosis of diffuse splenic hemangiomas was made.

The differential diagnosis of diffuse splenic hemangiomas must take into account the other vascular tumors or tumor-like lesions of the spleen such as lymphangioma, littoral cell angioma, hemangioendothelioma and primary angiosarcoma, peliosis of the spleen, and hamartoma.^{2,4,5} Lymphangioma and lymphangiomas are readily separated because they are often subcapsular and lymphatic channels contain eosinophilic, proteinaceous material without erythrocytes.^{2,3,4,5} In contrast to our case, the cells lining lymphatic channels are stained negatively for CD34. Localized hemangiomas possessing a nodular pattern are easily eliminated.

Littoral cell angioma, first described as a tumor of the cells lining the splenic sinus by Falk et al., is a vascular proliferation unique to the spleen.⁶ Grossly, it appears as a solitary nodule or as multiple spongy, blood-filled nodules.^{1,2,6} Histologically, the lesion is composed of anastomosing vascular channels resembling splenic sinus with irregular lumina, often featuring papillary projections and cyst-like spaces.^{2,6} Lining cells are not only flat but also enlarged, protruding in the sinus lumen, with large, somewhat hyperchromatic nuclei and moderately abundant clear

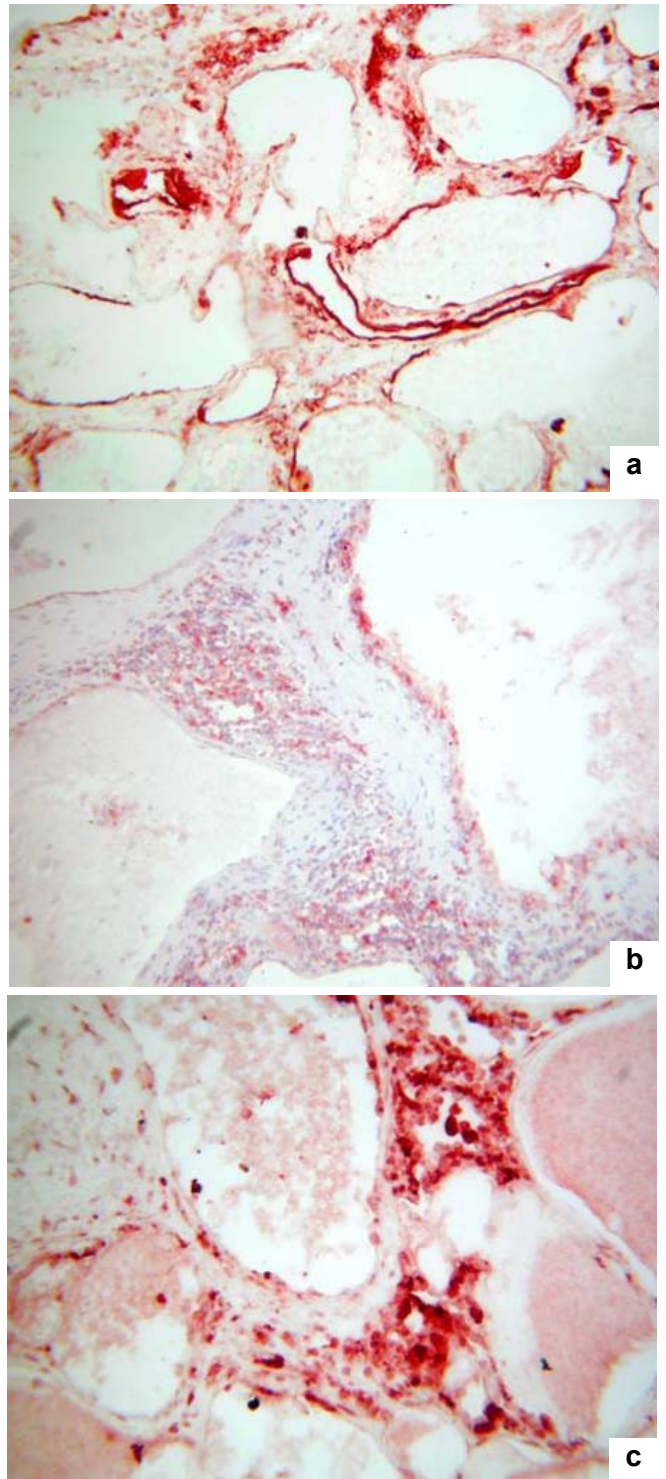


Figure 3. Immunohistochemically, cavernous vessels show a positive reaction with CD34 (a), CD31 (b), and a few cells lining the lumens of the cavernous vessels exhibited intracytoplasmic granular positivity for CD68 (c).

to eosinophilic cytoplasm with a variable papillary pattern and sloughing of lining cells into vascular spaces.^{1,4,6} Although cases of malignant littoral cell tumor had been reported, littoral cell angioma usually shows a benign clinical course.⁷ Since there is an

association between littoral cell angioma and visceral malignancies, careful and close follow-up of patients diagnosed with littoral cell angioma is proposed.⁸ According to Arber et al., the immunohistochemical phenotype of lining cells of littoral cell angioma is factor VIII (+), CD34 (-), CD21 (+), CD68 (+), CD8 (-).¹ In our case, lining cells are factor VIII (+), CD34 (+) and CD68 focally positive.

If there is no cytologic atypia in hemangiomas and Ki-67 is negative, the diagnosis of hemangioendothelioma and primary angiosarcoma of the spleen can be ruled out.^{2,4,6}

Peliosis of the spleen is an extremely rare entity of unknown pathogenesis. It can be localized to spleen or may occur with hepatic peliosis,^{2,4} is often associated with wasting diseases such as tuberculosis and cancer, or presents after treatment with steroid hormones.⁴ Grossly, the spleen is usually small. Macroscopically dark red dots from 2 to 10 mm can be observed dispersed in splenic parenchyma.⁴ Microscopically, the lesion is characterized by blood-filled cystic spaces predominantly in parafollicular areas.² There are cystic spaces with well-defined margins, surrounded by splenic tissue with no endothelial lining.^{4,9} However, in our case the cystic cavities were lined by a continuous layer of endothelium which expressed vascular endothelial markers.

Splenic hamartoma also referred to as splenoma or splenadenoma is composed of normal red pulp elements in abnormal quantity, developing a well-circumscribed mass.² There is also a lack of organized lymphoid tissue within the hamartoma; lymphoid cells, if present, are haphazardly distributed.⁴ Typical histological features include irregular and tortuous vascular formations lined by endothelium, which exhibit immunohistochemical characteristics of splenic sinus endothelium.^{2,4,5} In our case, since the lesion is diffuse and microscopically lymphoid tissue (white pulp) can be seen, diagnosis of hamartoma is not taken into consideration. The origin and pathogenesis of diffuse hemangiomas of the spleen still remains debated. It is controversial whether the origin is malformative or neoplastic. According to many pathologists diffuse hemangiomas has a neoplastic

origin and may be classified as a benign proliferation of endothelial cells.^{1,4}

In conclusion if there is splenic vascular proliferation, diffuse hemangiomas should be taken into consideration as well as lymphangioma, littoral cell angioma, hemangioendothelioma and primary angiosarcoma, peliosis of the spleen, and hamartoma. In many studies, different results about the immunohistochemical phenotype of splenic vascular lesions have been reported. Further studies are needed to elucidate the importance of the immunohistochemical findings in the pathogenesis and differential diagnosis of the splenic vascular lesions. We report this case of diffuse hemangiomas by virtue of its rareness and the presence of many other vascular lesions in the differential diagnosis.

References

1. Arber DA, Strickler JG, Chen YY, Weiss LM. Splenic vascular tumors: a histologic, immunophenotypic, and virologic study. *Am J Surg Pathol* 1997; 21: 827-835.
2. Steininger H, Pfofe D, Marquardt L, Sauer H, Markwat R. Isolated diffuse hemangiomas of the spleen: case report and review of literature. *Pathol Res Pract* 2004; 200: 479-485.
3. Burke JS. The Spleen. Sternberg's Diagnostic Surgical Pathology fourth edition. Philadelphia Lippincott Williams&Wilkins 2004: 849.
4. Dufau JP, le Tourneau A, Audouin J, Delmer A, Diebold J. Isolated diffuse hemangiomas of the spleen with Kasabach-Merritt-like syndrome. *Histopathology* 1999; 35: 337-344.
5. Atasoy P, Bozdoğan Ö, Ereku S. Diffuse hemangiomas of the spleen associated with pregnancy: A case report. *Turkish Journal of Cancer* 2004 34: 85-87.
6. Falk S, Stutte HJ, Frizzera G. Littoral cell angioma. A novel splenic vascular lesion demonstrating histiocytic differentiation. *Am J Surg Pathol* 1991; 15: 1023-1033.
7. Ben-Izhak O, Bejar J, Ben-Eliezer S, Vlodavsky E. Splenic littoral cell haemangioendothelioma: a new low-grade variant of malignant littoral cell tumour. *Histopathology* 2001; 39: 469-475.
8. Collins GL, Morgan MB, Taylor FM 3rd. Littoral cell angiomas with poorly differentiated adenocarcinoma of the lung. *Ann Diagn Pathol* 2003; 7: 54-59.
9. Tsokos M, Puschel K. Isolated peliosis of the spleen: report of 2 autopsy cases. *Am J Forensic Med Pathol* 2004; 25: 251-254.