

Case Report

Anastomosing hemangioma of the liver containing eosinophilic hyaline globules

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Received October 9, 2015; Accepted December 8, 2015; Epub April 15, 2017; Published April 30, 2017

Abstract: Anastomosing hemangioma is a newly described variant of hemangioma that occurs primarily in the genitourinary tract, but can also be rarely found in other visceral organs, such as liver, adrenal gland, and gastrointestinal tract. Hepatic anastomosing hemangiomas have been rarely reported to-date in adults. Most cases are incidental findings during examinations for other processes. Here, we presented a case of hepatic anastomosing hemangioma arising in a 51-year-old man with the neoplastic endothelial cells containing numerous intra-cytoplasmic eosinophilic hyaline globules.

Keywords: Anastomosing hemangioma, inclusions, liver, vascular lesions

Introduction

Anastomosing hemangioma is a rare variant of capillary hemangioma mainly described in the genitourinary system, with a particular proclivity for the kidney [1-4] and it was first designated by Montgomery and Epstein in 2009 in a series of six cases of kidney and testis [1]. Rare cases of anastomosing hemangioma have been described in extra-urolologic tract, such as in the ovary [2], adrenal gland [5], gastrointestinal tract and liver [6]. Anastomosing hemangioma arising in the liver is quite uncommon with only 4 cases having been reported to date. Histologically anastomosing hemangioma has a background of non-endothelial supporting elements, an overall lobulated configuration and an association with anastomosing capillary-sized vessels. Additional vascular thrombi, extra-medullary hematopoiesis, and deposition of hyaline globules can be identified within the tumor. Herein, we present a unique case of anastomosing hemangioma arising from the liver with numerous eosinophilic hyaline globules within the cytoplasm of the tumorous endothelial cells.

Case presentation

A 51-year-old Chinese man referred to our hospital for further evaluation of an incidentally

found hepatic mass on abdominal ultrasonography during a health examination in a local clinic. There were no symptoms related to his liver disease. He had no history of surgery or trauma to the abdomen, and his past medical history was unremarkable with no known liver disease. He had no history of cigarette, alcohol or illicit drug use. Physical examination revealed no significant findings. Blood tests were all within normal limits, and hepatitis virus markers were negative. A abdominal computer tomography (CT) scan revealed a 5×3 cm circumscribed mass within the right liver lobe (**Figure 1A**). A segmental resection of the right liver lobe was performed. The patient recovered well after surgery. He has been followed for 36 months after surgery without any evidence of recurrence.

The resected right lobe of liver showed an unencapsulated and relatively circumscribed mass with a red brown color and spongy appearance, measuring 5×3 cm in diameter. The background liver parenchyma was macroscopically unremarkable without any evidence of nodularity. Histologic examination showed a rather homogeneous tumor composed of proliferation of anastomosing sinusoidal capillary-sized vessels that set in a variable degree of fibrous and edematous stroma (**Figure 1B**). The vessels were lined by a single layer of bland-looking endothelial cells which oftentimes

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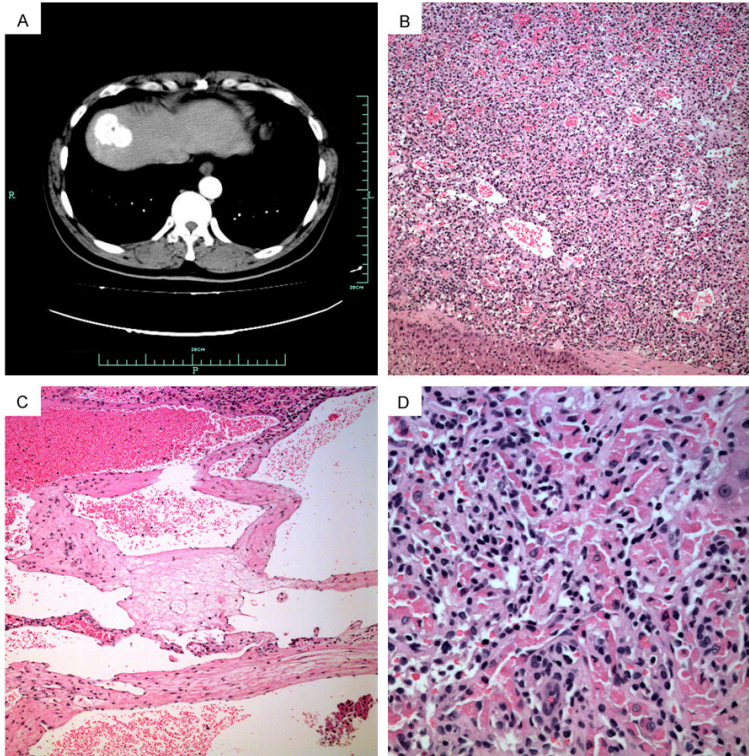


Figure 1. A: Contrast-enhanced CT imaging shows a mass lesion in the liver. B: A vascular tumor with proliferation of anastomosing capillary-sized vessels. C: Foci of cavernous hemangioma were present. D: Numerous intracytoplasmic hyaline globules in endothelial cells.

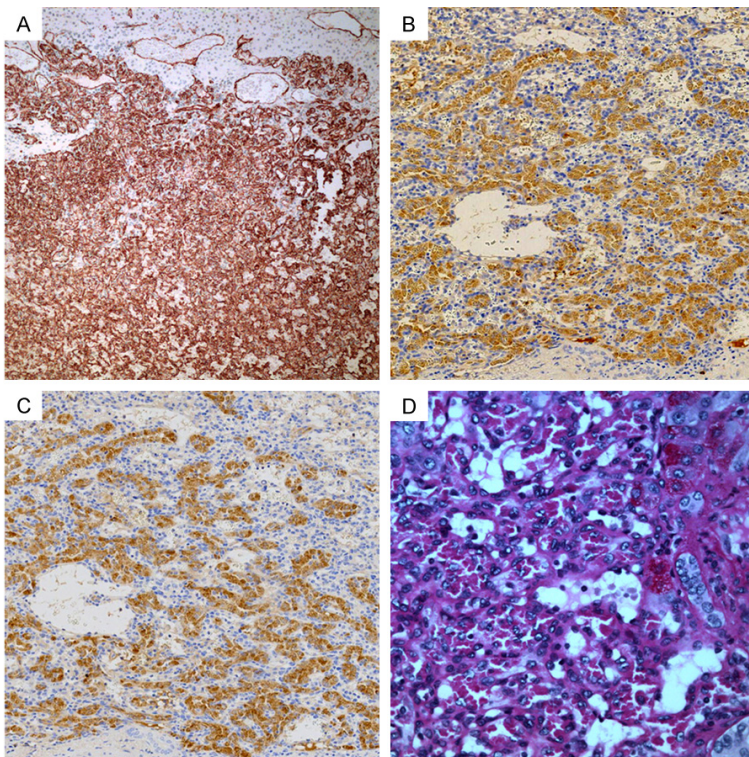


Figure 2. (A): Immunohistochemical analysis revealed that the tumor cells were diffusely positive for CD34. (B) and (C): Immunohistochemistry shows that light chain proteins are selectively present in the cytoplasm of endothelial cells with hyaline globules. Immunostaining for κ immunoglobulin light chain (B) and λ immunoglobulin light chain (C). (D): Intracytoplasmic hyaline globules in endothelial cells were intensively positive on PAS.

showing a hobnail appearance. The supporting stroma of the vessels was generally scant and dense, and in areas, the growth pattern was reminiscent of splenic parenchyma. There had minor zones consisting of more thin-walled channels lined by inconspicuous hobnail endothelial cells with loose or hyaline stroma. Additional foci of conventional cavernous hemangioma-like morphology was appreciated (**Figure 1C**). At the periphery of the lesion, the cytoplasm of the neoplastic endothelial cells had a swollen appearance due to the presence of numerous intra-cytoplasmic eosinophilic hyaline globules (**Figure 1D**). These eosinophilic hyaline globules presented with a globular shape and distributed as variable size and density across the tumor, with most being smaller than the size of an erythrocyte. They were largely confined to endothelial cells and some of these endothelia Blood bank inventory controls were completely stuffed with hyaline globules, which indented their nuclei and produced a scalloped nuclear outline or burst out of their cytoplasm. The endothelial cells lacked both nuclear atypia and mitoses, although a slight degree of nuclear enlargement was noted. Imm-

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Table 1. Summary of the reported cases of anastomosing hemangioma in the liver

Case	Ref/Year	Age/Sex	Location	Size (cm)	Other Feature	Conventional Component of Cavernous Hemangioma	Follow-up Time (mo)
1	6/2013	64/F	Left	3	Thrombi	Present	67
2		62/F	Left	2.4	Thrombi	Present	14
3		48/M	Right	2	Thrombi	Absent	18
4		71/F	Left	6	None	Absent	96
5	This report	51/M	Right	5	Hyaline globule	Present	36

unohistochemistry revealed that the tumor cells were strongly and diffusely positive for CD31 and CD34 (**Figure 2A**). The neoplastic cells were negative for CK-pan, Hep-Par-1, SMA, desmin, D2-40 or CD8. The supporting stromal cells of the vessels were positive for SMA but not for desmin, CD31 or CD34. Proliferative marker (Ki-67) was less than 2%. The intracytoplasmic eosinophilic hyaline globules were strongly and diffusely positive for κ and λ immunoglobulin light chains (**Figure 2B, 2C**), as well as strongly positive for PAS staining (**Figure 2D**) and PAS with diastase resistant.

Discussion

Anastomosing hemangioma is a rare and recently recognized vascular tumor entity that was originally described by Montgomery and Epstein in 2009 [1] and showed a propensity for the genitourinary organs, such as kidney, testis, ovary, and adrenal gland [1-4]. Anastomosing hemangioma in the liver is uncommon, with only 4 cases having been documented in the English literature so far [6]. The clinicopathologic characteristics of all published cases of this kind of lesion in the liver are summarized in **Table 1**. Including the current one, the total of 5 patients included 3 women and 2 men with ages ranging from 48 to 71 years (mean 59; median 62). Tumor size ranged from 2 to 6 cm (mean 3.68 cm). Microscopically, it consisted of anastomosing sinusoidal capillary-sized vessels with scattered hobnail endothelial cells setting in a framework of non-endothelial supporting myoid cells. A component of conventional cavernous hemangioma was present in 3 cases, which suggests an intrinsic relationship between anastomosing hemangioma and cavernous hemangioma, the latter is the most common primary tumor of the liver. Vascular thrombi were seen in 3 cases, however, deposition eosinophilic hyaline globules, other commonly seen histologic features of

anastomosing hemangioma that had been previously well documented in the genitourinary system, was noted only in the current case in the liver series.

Hyaline globule is a commonly seen histologic feature in many different tumor types and benign or normal tissues. With regard to vascular tumors, hyaline globules have been described as a typical diagnostic clue in both benign and malignant lesions, such as glomeruloid hemangioma [7], papillary hemangioma [8], or Kaposi's sarcoma [9]. In glomeruloid hemangioma, the formation of hyaline globules were thought to represent depositions of polyclonal immunoglobulin E that was secreted by the tumor cells in a specific microenvironment. In papillary hemangioma, an electron microscopic study showed evidence of remnants of cell organelles in the hyaline globule structures, such as small lipid droplets and small membranous remnants, which fit into the concept of "thanatosome". The term "thanatosomes" was first proposed in 2000 by Papadimitriou et al [10] who hypothesized that, hyaline globules in the so-called thanatosomes is due to a blocked lysosomal degradation process in injured cells demonstrating membrane blebbing, increased influx of plasma proteins and elevated autophagocytic activity. In Kaposi's sarcoma, hyaline globules may be located intra-cellularly or extra-cellularly. Some of these hyaline globules were associated with erythrophagocytosis that lends further support to the finding of erythrocytes in phagolysosomes by ultrastructural analysis. In anastomosing hemangioma, eosinophilic intracytoplasmic hyaline globules has been observed in the neoplastic endothelial cells in a minority of the previously reported cases [1,6], however, this histologic feature has not been documented in anastomosing hemangioma of the liver. In the present case, endothelial cells containing PAS-positive and immunoglobulin light chains positive eosinophilic hyaline

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line globules also fit to thanatosomes, representing a degenerative phenomenon.

Anastomosing hemangioma should be distinguished from primary hepatic well-differentiated angiosarcoma which can also display anastomosing growth pattern and present with mild-to-moderated cytological atypia, and this distinction may be very challenging particularly in small core biopsies. In fact, 2 of the 4 cases of hepatic anastomosing hemangioma in Lin et al' report were initially interpreted as angiosarcoma because of the profound anastomosing appearance in biopsy [6]. However, the lack of a diffuse infiltrative border, with only mild cytologic atypia and low proliferative rate, and the absence of multilayering of endothelial cells can assist in distinguishing this rare variant of hepatic hemangioma from anigosarcoma [1, 6, 11].

Intrahepatic splenosis [12] should also be considered in the differential diagnosis in needle biopsies because of the "spleen-like" appearance in anastomosing hemangioma. However, there is no white pulp in anastomosing hemangiomas, lack CD8 immunological reaction of the endothelial cells and the absence of medical history of splenic trauma or surgery can avoid a misdiagnosis of splenosis.

All the 5 cases were treated with surgery. The follow-up information is available for all 5 cases, and none have experienced tumor recurrences, metastases, or dead due to the tumor. The summarized follow-up evidence suggest that anastomosing hemangioma in the liver seems to be a benign tumor, however, there have several potential limitations, such as the small sample size and the relatively short-term follow-up, long-time surveillance of more cases is warranted to arrive at any definitive conclusion on its biological behavior.

Conclusion

In summary, we herein present a rare case of anastomosing hemangioma of the liver containing eosinophilic hyaline globules and summarize the clinicopathologic features of all the 5 such lesion in this location reported in the literature. Careful morphologic study with ancillary immunohistochemical studies should allow for confident distinction of anastomosing hemangioma from morphologic mimics. As with

other hemangiomas involving the liver, simple surgical excision is typically curative, and the prognosis for patients with these tumors is excellent.

Acknowledgements

This work was supported by Education Department of Zhejiang Province research project (Y201534684).

Disclosure of conflict of interest

None.

Authors' contribution

KS and JW analyzed the data and wrote the manuscript as a major contributor. MZ and XT helped to revise the discussion section of this manuscript. All authors have read and approved the final manuscript.

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References

- [1] Montgomery E, Epstein JI. Anastomosing hemangioma of the genitourinary tract: a lesion mimicking angiosarcoma. *Am J Surg Pathol* 2009; 33: 1364-1369.
- [2] Kryvenko ON, Gupta NS, Meier FA, Lee MW, Epstein JI. Anastomosing hemangioma of the genitourinary system: eight cases in the kidney and ovary with immunohistochemical and ultrastructural analysis. *Am J Clin Pathol* 2011; 136: 450-457.
- [3] Wetherell DR, Skene A, Many K, Manecksha RP, Chan Y, Bolton DM. Anastomosing haemangioma of the kidney: a rare morphological variant of haemangioma characteristic of genitourinary tract location. *Pathology* 2013; 45: 193-196.
- [4] Zhao M, Li C, Zheng J, Sun K. Anastomosing hemangioma of the kidney: a case report of a rare subtype of hemangioma mimicking angiosarcoma and review of the literature. *Int J Clin Exp Pathol* 2013; 6: 757-765.
- [5] Ross M, Polcari A, Picken M, Sankary H, Milner J. Anastomosing hemangioma arising from the adrenal gland. *Urology* 2012; 80: e27-28.
- [6] Lin J, Bigge J, Ulbright TM, Montgomery E. Anastomosing hemangioma of the liver and

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- gastrointestinal tract: an unusual variant histologically mimicking angiosarcoma. *Am J Surg Pathol* 2013; 37: 1761-1765.
- [7] Calonje E, Fletcher CD. Sinusoidal hemangioma. A distinctive benign vascular neoplasm within the group of cavernous hemangiomas. *Am J Surg Pathol* 1991; 15: 1130-1135.
- [8] Suurmeijer AJ, Fletcher CD. Papillary haemangioma. A distinctive cutaneous haemangioma of the head and neck area containing eosinophilic hyaline globules. *Histopathology* 2007; 51: 638-648.
- [9] Fukunaga M, Silverberg SG. Hyaline globules in Kaposi's sarcoma: a light microscopic and immunohistochemical study. *Mod Pathol* 1991; 4: 187-190.
- [10] Papadimitriou JC, Drachenberg CB, Brenner DS, Newkirk C, Trump BF, Silverberg SG. "Thanatosomes": a unifying morphogenetic concept for tumor hyaline globules related to apoptosis. *Hum Pathol* 2000; 31: 1455-1465.
- [11] Maluf D, Cotterell A, Clark B, Stravitz T, Kauffman HM, Fisher RA. Hepatic angiosarcoma and liver transplantation: case report and literature review. *Transplant Proc* 2005; 37: 2195-2199.
- [12] Casulo C, Day B, Dawson KL, Zhou X, Flowers CR, Farber CM, Hainsworth JD, Cerhan JR, Link BK, Zelenetz AD, Friedberg JW. Intra-hepatic splenosis as an unexpected cause of a focal liver lesion in a patient with hepatitis C and liver cirrhosis: a case report. *Cases J* 2009; 2: 8335.