

Hepatic Angiosarcoma: Probable Transformation From Cavernous Hemangioma An Autopsy Case Report And Review Of The Literature

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Citation

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Abstract

Hepatic angiosarcoma is a rare tumor with a fatal course. Although the etiology of hepatic angiosarcoma is unknown, it can occur after certain types of liver injury, and is associated with rare inherited disorders. We report here a rare case of high-grade angiosarcoma with autopsy findings and review of the literature. The patient was a 35-year-old Caucasian gentleman who presented with a history of pheochromocytoma, carotid body tumors, and intra-abdominal cavernous hemangioma involving the spleen, liver, gallbladder, and mesentery. Twenty years after his first resection, he presented with right-sided chest pain and progressive dyspnea. A massive hemothorax was found and a wedge biopsy of his right lung revealed angiosarcoma. There was no history of chemical carcinogen exposure or prior irradiation. The patient died three months after his admission to the hospital. Autopsy revealed marked hepatomegaly due to angiosarcoma admixed with benign cavernous hemangioma. Metastatic angiosarcoma was identified in the lungs, gallbladder, pancreas, small bowel, rectum, bladder, bone marrow, and lymph nodes. Tumor emboli were present in the brain. A literature search revealed few cases of hepatic angiosarcoma associated with a history of hepatic cavernous hemangioma/vascular malformation. The hepatic angiosarcoma in this patient likely represents malignant transformation of hepatic cavernous hemangioma.

INTRODUCTION

Hepatic angiosarcoma represents 1-2% of all primary hepatic tumors and it is the most frequent primary malignant mesenchymal tumor of the liver.¹ Hemochromatosis, von Recklinghausen's disease, and exposure to vinyl chloride, thorium dioxide, and arsenic are associated with angiosarcomas.^{2,3} However, more than half of the cases are idiopathic.³ So far, only a few cases of angiosarcoma have been reported from the transformation of benign hemangioma/vascular malformation.²

CASE REPORT

The patient, a 35 year-old Caucasian man presented at ages 15 and 17 with benign pheochromocytoma, which were resected. Two years later, he underwent surgery for a small bowel obstruction, and an exploratory laparotomy discovered a cavernous hemangioma on his spleen for which a splenectomy was performed. One year later, another exploratory surgery for cholecystitis revealed multiple hemangioma in the liver and gallbladder. At ages 23 and 25 he presented with bilateral carotid body tumors, which

were also resected. Due to a reactive tachycardia secondary to the resection of the carotid body tumors, he was subsequently treated with long-term low-dose β -blocker. The patient did well for 10 years, attended school, was married, had children, and was relatively asymptomatic on the β -blocker. He denied a history of exposure to radiation or any chemical carcinogens. He was adopted and his family history was unknown.

Three months prior to death, the patient developed rapidly progressive right-sided chest pain and dyspnea. He was admitted to the hospital and was diagnosed with a massive right hemothorax, a mediastinal cyst, and a right lower lobe lung mass. He underwent a right thoracotomy, complete decortications of the right lung, and partial parietal pleurectomy. At the same time the bleeding mediastinal cyst was resected and a wedge biopsy of the right lung was performed. A pathologic diagnosis of angiosarcoma was made from the resected and biopsied specimens. The patient continued to experience post surgical chest pain, which was barely controlled by oxycodone and other pain medications. Twelve days prior to death, the patient was readmitted to

hospital with severe chest pain, hemoptysis, recurrent respiratory distress, abdominal distention, and thrombocytopenia. A computed tomography scan of the chest, abdomen, and pelvis without contrast revealed nodular parenchymal infiltrates in the right lung, heterogeneous attenuation to the liver and extensive retroperitoneal adenopathy. His platelet count dropped from 200,000 to 33,000 in one month. Laboratory tests showed elevated liver functional tests, LDH, and bilirubin. He developed edema, jaundice, and severe anemia, necessitating multiple blood transfusions during the last week of his life. Review of the peripheral blood smear showed anisocytosis, poikilocytosis, acanthocytosis, and polychromasia. Bone marrow aspirate smear showed hypercellularity (80%) with advanced trilineage hematopoiesis. The myeloid: erythroid ratio was approximately 1. Megakaryocytes were increased up to 3 to 4 per high power field. High doses of morphine were used to control his chest pain. An autopsy was performed one day after death.

PATHOLOGIC FINDINGS

The patient was an overweight gentleman. Thoracic examination showed that the left pleural space contained 100 ml of serous fluid while the right side of the thorax revealed adhesions with evidence of decortications of the right lung and a partial parietal pleurectomy. Multiple hemorrhagic vascular tumors were located in the right middle and lower lobe of the lung as well as the mediastinum. One hundred fifty ml of straw-colored ascitic fluid was in the abdominal cavity. A 20 x 15 x 5 cm, large dark red organizing hematoma presented in the epigastric area, overlying the anterior surface of the liver. The liver appeared markedly enlarged, weighing 5700 gm. The outer surface and serial sections of the liver exhibited diffuse poorly circumscribed hemorrhagic dark red and brown vascular tumors of varied size. Multiple dark red, well-demarcated vascular nodules, 1 to 10 cm in diameter, were identified in the para-aortic area of the thoracic, abdominal, and pelvic regions, representing lymphadenopathy. In addition, multiple dark red, circumscribed, soft vascular tumors, 3 to 10 cm in diameter, grossly involved the mediastinum, gallbladder, tail of the pancreas, mesentery, paracolic tissues, and urinary bladder.

Microscopically, thin anastomosing vascular channels lined by prominent atypical endothelial cells with pleomorphic, hyperchromatic nuclei and high mitotic activity reminiscent of high-grade angiosarcoma composed virtually all of the

vascular tumors, lymphadenopathy and the hematomas identified grossly in the lung, the liver, and multiple organs in the thorax, abdomen, and pelvis. Multiple foci of the liver and gallbladder showed features of cavernous hemangioma that were admixed with high-grade angiosarcoma (Figure 1). Mild extramedullary hematopoiesis was present in the liver. These vascular tumors appeared strongly positive for the vascular marker, CD31 (Figure 2) by immunohistochemical stain. The metastasis of angiosarcoma was also identified in small bowel, rectum, and spinal bone marrow. Tumor emboli were identified in the brain. Post-mortem specimens from blood, liver, and skin were sent for cytogenetic analysis. Unfortunately, the cells failed to grow in culture so no cytogenetic evaluation was available.

Figure 1

Figure 1: Right lobe of the liver showing angiosarcoma admixed with cavernous hemangioma suggestive of possible origin from the transformation of previous cavernous hemangiomata. (Hematoxylin-eosin. Original magnification x 100.)

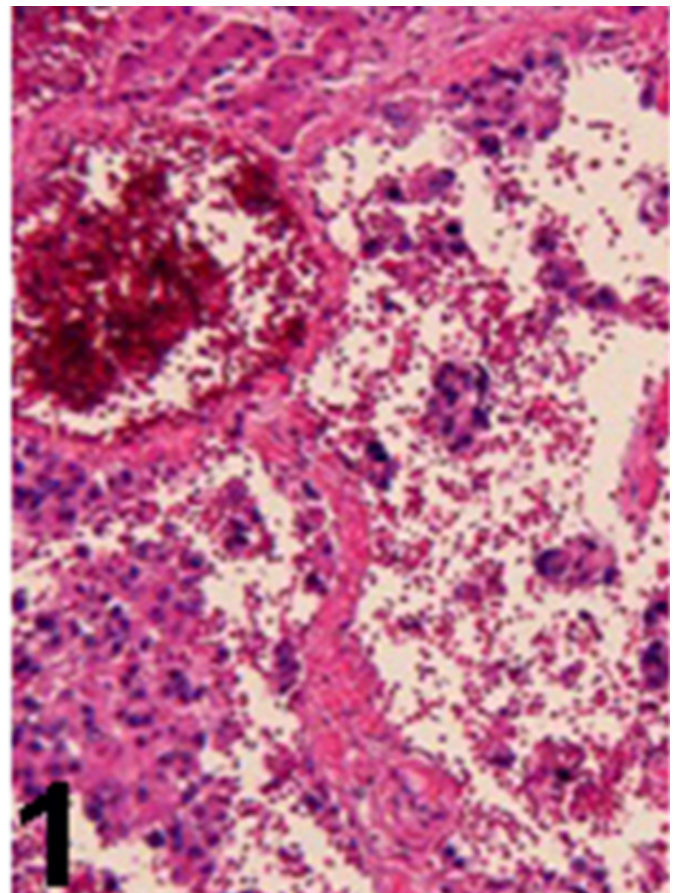
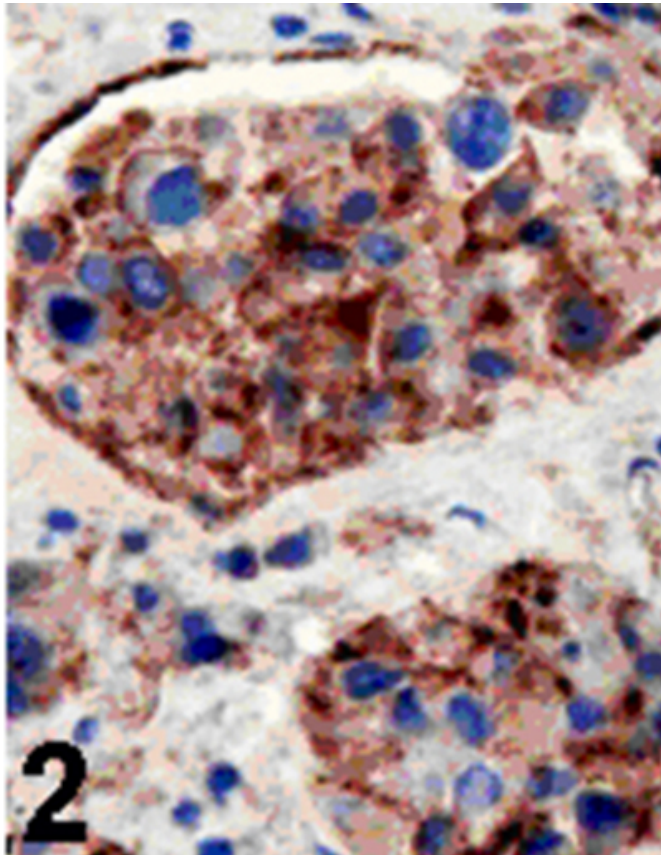


Figure 2

Figure 2: Right lobe of the liver showing neoplastic cells which are strongly positive for CD31. (Immunoperoxidase, anti-CD31. Original magnification x 400.)



COMMENT

Hepatic angiosarcoma is a rare, deadly vascular malignant tumor. Patients with hepatic angiosarcoma most commonly present with vague complaints of abdominal pain, weakness, fatigue, and weight loss.^{2,3} Physical examination and laboratory tests are often indicative of hepatic dysfunction but are not specific for angiosarcoma. Hepatosplenomegaly, ascites, and jaundice are common.² Hepatic angiosarcoma may manifest as congestive heart failure and cause fatal spontaneous rupture of the liver.^{2,4} Vennarecci (1997) documented 6 patients with primary hepatic angiosarcoma in which no apparent predisposing factors were present. At presentation, symptoms, signs, and liver function tests were not specific. Four patients presented with metastatic disease to lung, peritoneum, bone, and spleen. The longest survival was 10 months with liver transplantation.¹ So far, most of the predisposing interest in angiosarcoma has been focused upon the association of chemical exposure and radiation therapy. However, only two cases of postradiation angiosarcoma had been reported among the 5,100 breast

cancer patients treated in the period 1980-1994. The incidence of chest wall and breast angiosarcoma after radiotherapy was found to be 0.46 per 1,000, a slightly higher risk for developing a secondary angiosarcoma as compared to the healthy population.⁵ A rare case of high grade angiosarcoma arising from skeletal haemangiomatosis was found in a 72 year old man who had a history of atomic bomb irradiation more than 50 years prior to disease presentation.⁶

A hypothesis of eventual malignant transformation from cavernous hemangioma of the liver was developed in 1991, when a case of a solitary and encapsulated hepatic tumor demonstrated a cavernous hemangioma surrounded by an angiosarcoma.⁵ Recently more evidence of transformation of benign vascular neoplasm to angiosarcoma has been documented. Four cases of angiosarcoma arising in a hemangioma/vascular malformation (HVM) were described in 2002.³ All these patients were in the 6th or 7th decade of life. Development of an enlarging deep-seated soft tissue mass was the main presenting symptom. No patient had a history of prior radiotherapy at the same site.³ A rare case of laryngeal angiosarcoma arising from the malignant transformation in a laryngeal hemangioma was documented.⁸ A woman with angiosarcoma arising from a benign congenital hemangioma of the parotid gland was also reported. She had a history of congenital hemangioma surgically removed 8 years previously. No radiotherapy had been administered at the time of primary excision.⁹ Some angiosarcomas have arisen from cutaneous hemangiomatosis in Maffucci and Kasabach-Merritt syndromes.^{10,11}

More recently, researchers are working on identifying gene mutations which are associated with neoplasm. A study in 2006 reported that 83% of angiosarcomas had allelic loss at 17p13 (p53), 66% at 13q14 (RB), and 50% at 11p13 (WT-1). In comparison, 60% of hemangiomas had allelic loss at 17p13 and 13q14, but only in 20% at 11p13. This evidence provides some insight into the potential pathogenesis of angiosarcomas and benign hemangiomas. It also shines a light on potential transformations of benign vascular tumors to malignancy, since they share the same genes but have different degrees of gene mutation.¹² Thus far, the definitive predisposing factors causing angiosarcoma are still questions waiting to be explored and answered.

Where was the primary site from which the angiosarcoma originated in this current patient? Most likely it would be that his angiosarcoma developed from the malignant

transformation of the cavernous hemangiomas found in the liver during his exploratory surgery. The rationale is as follows. First, the liver is one of the many sites involved in the hemangiomatous process, as recognized during his teenage years. Second, the liver showed remarkable hepatomegaly and diffuse infiltration of angiosarcoma while no other organs demonstrated complete infiltration by the tumor. Third, the liver is a much more common site for the origin of angiosarcoma than lungs or other organs.

Angiosarcoma can spread via the blood stream into virtually every organ and develop diffuse metastasis to lymph nodes, as was shown in this patient. Unfortunately, there was no cytogenetic data available from this patient. A latent time span of fifteen years existed between his benign cavernous hemangiomas to the development of symptomatic fatal angiosarcoma in this relatively young patient. Within three months of the initial presentation of spontaneous massive hemothorax and progressive dyspnea, the patient died.

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