



## Metastatic Angiosarcoma of Liver: A Case Report

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### Abstract

*Angiosarcoma is a rare malignant tumour of endothelial origin with a poor prognosis; significantly, patients with intestinal angiosarcoma who survive over 1 year after diagnosis are extraordinarily rare. This article describes the case of a 43-year-old patient with HIV infection who presented with abdominal pain of 4 months duration along with swelling in the right upper part of abdomen which had increased in severity 4 weeks prior to presentation. After a complicated diagnostic process, the diagnosis of metastatic liver angiosarcoma was made by history and imaging. We reviewed previous cases of angiosarcoma described in the English literature to determine their risk factors, diagnosis and treatment, and we found that angiosarcoma is extremely rare, especially metastatic liver angiosarcoma. To the best of our knowledge, this may be the first case of primary angiosarcoma of the large intestine with metastasis to the liver reported in the English literature.*

**Keywords:** Large intestine, Primary angiosarcoma, Hepatic metastasis, Hepatectomy.

### Introduction

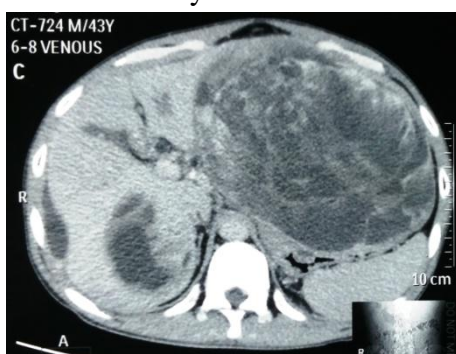
Angiosarcomas, which account for only 1 to 2% of all soft tissue sarcomas, are rare malignant tumours of endothelial origin <sup>(1,2)</sup> These tumour occur most commonly in the skin and soft tissue and less commonly in breast, liver, bone, and spleen <sup>(3)</sup>. Hepatic angiosarcoma is a very rare disease, accounting for only 2% of primary liver malignancy <sup>(4,5,6)</sup>; however, it still ranks as the third place in the list of most common primary liver malignancies <sup>(5,6)</sup>. Hepatic angiosarcoma originates from endothelial cells and usually presents as an abdominal mass with unspecific symptoms and signs <sup>(7)</sup>, making it difficult to

diagnose in the early stage. The survival of hepatic angiosarcoma is very poor, which is attributable to its rapid progress, high recurrence rate, and resistant to traditional chemotherapy and radiotherapy. Even liver transplantation could not benefit patients with liver angiosarcoma <sup>(8)</sup>. To date, the therapeutic guideline for liver angiosarcoma has not been set up; partial liver resection to remove tumor radically still remains to be the cornerstone of treatment options <sup>(9)</sup> Here, we report a 43-years-old patient with HIV infection who presented with abdominal pain of 4 months duration, along with rapidly increasing swelling right upper part of the abdomen prior to 3

weeks before admission and treated by partial liver resection.

### Case Presentation

A 43 years old patient with known HIV infection complained upper abdominal pain of 4 months duration which was gradual in onset, associated with nausea, vomiting and fatigue. Pain was of dull aching type, with no aggravating factors but relieved by taking oral analgesics. There was no associated fever, loose stool, passing of black coloured stool or vomiting of blood. At the beginning of pain, he was admitted in our Hospital at Medicine ward during 29/11/15 – 11/12/15 where he was found to have complex cystic lesion involving segment VI of liver and focal mesenteric and bowel wall thickening. He was treated conservatively and his condition was slightly improved and discharged with stable condition. He was re-admitted into our hospital under Surgery Department on 26/2/2016 with rapidly increasing swelling in right upper part of the abdomen with pain at the site of lump for about 1 month associated with weakness and loss of appetite. On examination, he was an average well-built body with poor nutritional status and ECOG performance status of 3. On per abdominal examination, there was a huge non-tender lump extending from the right hypochondrium to the left hypochondrium measuring approximately 24x10 cms, smooth surface, smooth round margin and firm in consistency. Ascites was also noted.



**Figure 1** Computed tomography scan of the whole abdomen showed evidence of well defined, large, vessels attenuating enhancing mass lesion involving both lobes of liver (segments V, VI, II & III)

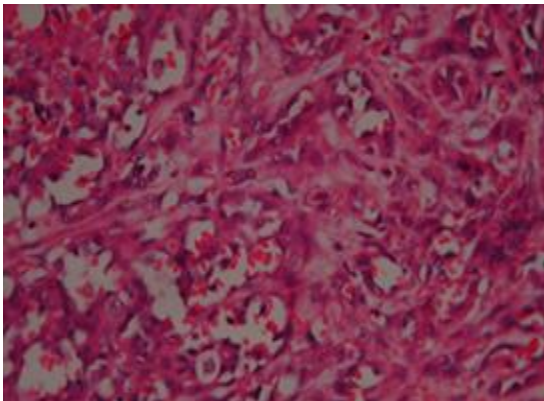
The patient was diagnosed to have HIV and HCV infection and was on ART since 2007. He gave history of right hemicolectomy on 15/09/2014 due to angiosarcoma of ascending colon and intestinal TB (for which he was taking 6 months course of ATT) with no other documents except HPE of right hemicolectomy specimen report.

Routine investigations were found within normal limits. USG guided FNAC of Liver SOL reports was inconclusive with features suggestive of an organizing inflammatory lesion. Hepatomegaly with multiple liver complex SOL with Splenomegaly were noted in USG Abdomen. CT Abdomen was repeated again where it showed multiple complex SOL liver involving segments II, III and VI.

Under the impression of liver tumor, highly suspected as metastatic angiosarcoma based on the past history of intestinal angiosarcoma and findings in abdominal CT of the patient, laparotomy was performed. Left lobe of liver with huge pocket like tumor measuring approximately 24x20x10 cms, right lobe of liver containing 2 pockets of tumor size approximately 5x3x2cms & 4x3x2cms respectively and anterior surface of stomach densely adhered to the left lobe of liver, were noted. Left hepatectomy with non-anatomical resection of posterior part of right lobe of liver along with partial gastrectomy were done. 4 units of packed red cells and 4 units of fresh frozen plasma were transfused intraoperatively due to huge amount of blood loss.

The multiple sections studied show liver tissue with a malignant tumor composed of spindle cells arranged in sheets, short fascicles and predominantly in loosely scattered singles in a myxoid stromal background. Individual tumor cells have moderate amount of cytoplasm and highly pleomorphic vesicular nuclei. Good number of cells displays phagocytosed erythrocytes. Numerous multinucleated tumor giant cells with bizarre grotesque nuclei are seen. Many areas show large dilated hemorrhagic areas resembling peliosis hepatitis like areas. Also seen are numerous blood vessels lined by plumped endothelium.

Kaposiform-like areas displaying extravasated RBC's are seen. Extensive areas of haemorrhage, necrosis and infarction are identified. Features are of metastatic angiosarcoma.

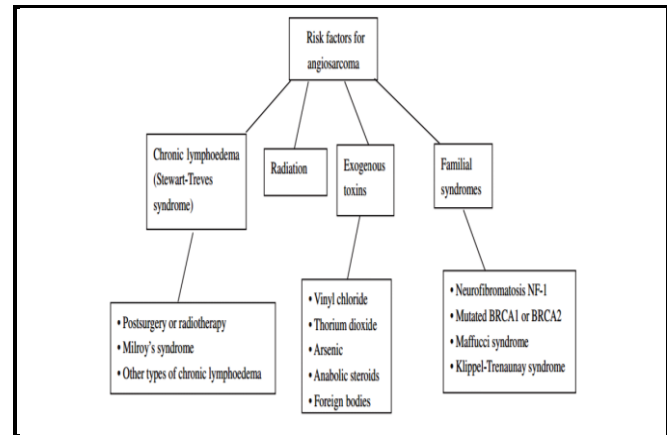


**Figure 2** Microscopic examination showed a malignant tumor composed of spindle shaped cells arranged in sheets (haematoxylin and eosin stain; x 400)

The early post-operative period was uneventful. Abdominal drain was removed on 5<sup>th</sup> post-operative day. Patient complained of passing of black coloured stool and haemoglobin was found to be low for which 2 units of packed red cells was transfused subsequently. He was put on oral feeding from POD 7, developed wound dehiscence since POD 9. Abdominal stitches was removed on POD 23 and discharged with satisfactory condition on POD 27.

### Discussion

Angiosarcoma, a subtype of soft tissue sarcoma, an aggressive malignant disease deriving from endothelial-type cells of lymphatics or blood vessels, is characterized by aggressively proliferating and widely distributed tumour cells. (9,10) Angiosarcoma occurs most commonly in head and neck, followed by breast. Liver angiosarcoma, occurs mainly in elders, is ranked as fifth in the list of most common seen sites of angiosarcoma and is very rare. (2,4) Young and colleagues reviewed angiosarcoma with a focus on clinical trials and outlined its risk factors. According to these authors, the risk factors for angiosarcoma were varied and are listed in Figure.(2)



Majority of patients have symptoms and signs mimicking chronic liver disease. (11) Although the symptoms are usually nonspecific, abdominal distension and discomfort/ pain, weakness, fatigue, and weight loss are the most prominent clinical symptoms. Hepatosplenomegaly, ascites, jaundice, and anemia are the most common clinical signs and these are frequently associated with advanced liver angiosarcoma. (12,13) The spontaneous rupture of hepatic angiosarcoma (HA) with intraperitoneal hemorrhage has been reported in 15–27% of patients. (4,14)

The diagnosis of HA is difficult, particularly if the patient does not present a history of exposure to carcinogens, since HA is not characterized by any specific tumour marker (16). Morphologically, HA may appear as multiple nodules, dominant masses, or a diffusely infiltrating lesion, and its appearance may vary slightly in computed tomography (CT) and MRI. (17) Follow-up imaging studies should be performed, and a diagnosis of angiosarcoma should be suspected if there is rapid enlargement. (15,18) Pathological diagnosis is very necessary. Epithelioid haemangioma (HEH), a rare, usually low-grade malignant tumor, should be considered for differential diagnosis of HA. Elongated or round tumoural endothelial cells exhibit severe nuclear atypia and frequent mitoses, and grow along dilated sinusoids, separated by surviving atrophic or hyperplastic hepatocytes. (19,20) The combination of CD31 and factor VIII-related antigen was the most sensitive, with 90% of cases expressing one of the two markers. (21) Pathological and immunohistochemical examinat-

ions can contribute to the definitive diagnosis of angiosarcoma. <sup>(22)</sup> Liver biopsy is thought to be nondiagnostic and treacherous. Failure to make diagnosis and complications like bleeding or subcapsular hematoma may occur. <sup>(8, 11)</sup> Therefore, nonsurgical biopsy is generally avoided, and open liver biopsies or laparoscopy will be more accurate and safe.

There are various treatment regimens for patients with HA. However, due to the high recurrence rate and poor post-transplant survival rate of patients, liver transplantation is no longer provided. According to European Liver Transplant Registry experience, HA is an absolute contraindication to liver transplant; the median overall survival of 22 patients who underwent liver transplant is 6 months, five (23%) patients died of infectious complications and 17 (77%) patients died of tumour recurrence. <sup>(24)</sup> Kim et al <sup>(25)</sup> reported that a combination of chemotherapy resulted in an improved outcome for 2 out of 4 patients, suggesting the potential usefulness of palliative chemotherapy to improve the survival rate of patients

Currently, the best treatment option for HA is partial surgical resection of the liver to remove the tumor. <sup>(11, 26)</sup> Zhou et al <sup>(27)</sup> reported that out of 6 patients with HA with solitary masses, 3 patients underwent right hepatectomy (2 patients survived for >1 year; 1 patient succumbed to disease perioperatively), 1 patient underwent extended right hepatectomy (survived for 6 months) and 2 patients underwent left hepatectomy (1 patient survived for 10 months; 1 patient was alive without recurrence 29 months later). Unfortunately, HA is often diagnosed unexpectedly after surgical procedures that do not meet oncological treatment standards. <sup>(28)</sup>

However, most HA cases are discovered at an advanced stage actually, and less than 20% of the patients receive surgery. <sup>(28)</sup> Emergent TAE is used for deadly intra-abdominal bleeding. TACE is a palliative treatment for unresectable HA patients. <sup>(11)</sup> Park et al. used emulsion of iodized oil and cisplatin treating four HA patients, and the

survival time was 2, 5, 8, and 12 months, respectively. <sup>(29)</sup> Huang et al. reported a patient receiving hepatic arterial infusion chemotherapy after TAE survived for 24 months. <sup>(30)</sup>

### Conclusion

The findings of this case report are of extreme significance. To our knowledge, this may be the first report of primary angiosarcoma of the large intestine with metastasis to the liver, particularly in patient with HIV infection. One should focus on similar cases in the future to ensure early diagnosis and proper treatment.

**Conflict of interest:** None

**Funding:** None

### Consent

Written consent was taken from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-chief of this journal on request.

### References

1. Al Ali J, Ko HH, Owen D, Steinbrecher UP: Epithelioid angiosarcoma of the small bowel. *Gastrointest Endosc* 2006, 64:1018–1021.
2. Young RJ, Brown NJ, Reed MW, Hughes D, Woll PJ: Angiosarcoma. *Lancet Oncol* 2010, 11:983–991.
3. Brown CJ, Falck VG, MacLean A: Angiosarcoma of the Colon and Rectum: Report of a case and review of literature. *Dis Colon Rectum* 2004;47: 2202 – 2207
4. Mani H, Van Thiel DH: Mesenchymal tumors of the liver. *Clin Liver Dis* 2001, 5:219-257, viii.
5. Molina E, Hernandez A: Clinical manifestations of primary hepatic angiosarcoma. *Dig Dis Sci* 2003, 48:677-682.
6. Locker GY, Doroshow JH, Zwelling LA, Chabner BA: The clinical features of hepatic angiosarcoma: a report of four

- cases and a review of the English literature. *Medicine (Baltimore)* 1979, 58:48-64.
7. Selby DM, Stocker JT, Ishak KG: Angiosarcoma of the liver in childhood: a clinicopathologic and follow-up study of 10 cases. *PediatrPathol* 1992, 12:485-498.
  8. 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.
  9. Chien CY, Hwang C, Yeah C, Chen H, Wu JT, Cheung CS, Lin CL, Yen C, Wang W, Chiang KC: Liver Angiosarcoma, a rare liver malignancy, presented with intra-abdominal bleeding due to rupture – a case report: *WJ SurgOncol* 2012: 10:23
  10. Antonescu CR: Targeted therapies in gastrointestinal stromal tumors. *Semin Diagn Pathol* 2008, 25:295–303.
  11. Zheng Y, Zhang X, Zhang J, Hui Z, Du W, Li R and Xiu-bao, Ren X : Primary hepatic angiosarcoma and potential treatment options. *J GastroHep*, 29 (2014) 900 – 911.
  12. Timaran CH, Grandas OH, Bell JL: Hepatic angiosarcoma: long-term survival after complete surgical removal. *AmSurg* 2000, 66:1153-1157.
  13. Forbes A, Portmann B, Johnson P, Williams R: Hepatic sarcomas in adults: a review of 25 cases. *Gut* 1987, 28:668-674.
  14. Leowardi C, Hormann Y, Hinz U et al. Ruptured angiosarcoma of the liver treated by emergency catheter-directed embolization. *World J. Gastroenterol.* 2006; 12: 804–8.
  15. Okano A, Sonoyama H, Masano Y et al. The Natural History of a Hepatic Angiosarcoma that was Difficult to Differentiate from Cavernous Hemangioma. *Intern. Med.* 2012; 51: 2899–904.
  16. Wang ZB, Yuan J, Chen W and Wei LX: Transcription factor ERG is a specific and sensitive diagnostic marker for hepatic angiosarcoma. *World J Gastroenterol* 20: 3672-3679, 2014.
  17. Koyama T, Fletcher JG, Johnson CD, et al: Primary hepatic angiosarcoma: Findings at CT and MR imaging. *Radiology* 222: 667-673, 2002.
  18. Arima-Iwasa S, Chijiwa K, Makino I, Tanabe R, Ohuchida J, Kondo K. A case of hepatic angiosarcoma surviving for more than 16 months after hepatic resection. *Hepatogastroenterology* 2007; 54: 533–5.
  19. Benign and malignant vascular tumors of the liver in adults. *SeminLiver Dis.* 2008; 28: 302–14.
  20. Cho NH, Lee KG, Jeong MG. Cytologic evaluation of primary malignant vascular tumors of the liver. One case each of angiosarcoma and epithelioid hemangioendothelioma. *ActaCytol.* 1997; 41:1468–76.
  21. Rao P, Lahat G, Arnold C et al. Angiosarcoma: a tissue microarray study with diagnostic implications. *Am. J. Dermatopathol.* 2013; 35: 432–7.
  22. Khalil MF, Thomas A, Aassad A, Rubin M, Taub RN: Epithelioid angiosarcoma of the small intestine after occupational exposure to radiation and polyvinyl chloride: a case report and review of literature. *Sarcoma* 2005, 9:161–164.
  23. Rademaker J, Widjaja A, Galanski M. Hepatic hemangiosarcoma: imaging findings and differential diagnosis. *Eur. Radiol.* 2000; 10: 129–33.
  24. Orlando G, Adam R, Mirza D, et al: Hepatic hemangiosarcoma: An absolute contraindication to liver transplantation - the European Liver Transplant Registry experience. *Transplantation* 95: 872- 877, 2013.
  25. Kim HR, Rha SY, Cheon SH, et al: Clinical features and treatment outcomes of advanced stage primary hepatic angiosarcoma. *Ann Oncol* 20: 780-787, 2009.

26. Timaran CH, Grandas OH and Bell JL: Hepatic angiosarcoma: Long-term survival after complete surgical removal. *Am Surg* 66: 1153- 1157, 2000.
27. Zhou YM, Li B, Yin ZM, et al: Results of hepatic resection for primary hepatic angiosarcoma in adults. *Med SciMonit* 16: CR61- CR66, 2010.
28. Leowardi C, Hormann Y, Hinz U et al. Ruptured angiosarcoma of the liver treated by emergency catheter-directed embolization. *World J. Gastroenterol.* 2006; 12: 804–8.
29. Park YS, Kim JH, Kim KW et al. Primary hepatic angiosarcoma: imaging findings and palliative treatment with transcatheter arterial chemoembolization or embolization. *Clin. Radiol.* 2009; 64: 779–85.
30. Huang NC, Wann SR, Chang HT, Lin SL, Wang JS, Guo HR. Arsenic, vinyl chloride, viral hepatitis, and hepatic angiosarcoma: a hospital-based study and review of literature in Taiwan. *BMC Gastroenterol.* 2011; 11: 142.