Angiossarcoma Hepático: Caso Clínico
Hepatic Angiosarcoma: A Case Report

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Resumo:

O angiossarcoma hepático é um tumor vascular raro dentro do grupo das neoplasias malignas do fígado, tendo uma baixa prevalência. Não apresenta sinais/sintomas ou marcadores tumorais específicos. É uma patologia altamente agressiva, com uma taxa de mortalidade elevada. Os autores descrevem o caso de um doente do sexo masculino, 69 anos, com perda ponderal significativa, dor abdominal no quadrante superior direito, lesões petéquiais, rectorragias e epistáxis. Na ecografia abdominal foram objetivados múltiplos nódulos e a tomografia computorizada do abdómen mostrou trombose da veia porta e alterações sugestivas de hepatocarcinoma multifocal. A biópsia hepática, foi conclusiva para o diagnóstico final de angiossarcoma hepático.

Neste caso, malogradamente, o diagnóstico foi importante apenas em termos de exclusão de outras patologias, ao não permitir outra abordagem que não a da instituição de medidas paliativas, dada a agressividade e progressão célere da neoplasia em questão.

Palavras-chave: Hemangiosarcoma/diagnóstico; Hemangiossarcoma/diagnóstico por imagem; Hemangiossarcoma/patologia; Neoplasias do Fígado/diagnóstico; Neoplasias do Fígado/diagnóstico por imagem; Neoplasias do Fígado/patologia.

Abstract:

Liver angiosarcoma is a rare vascular tumor within the group of malignant neoplasms of the liver. It does not present with specific signs / symptoms or tumor markers. It has a high mortality rate due to its aggressive nature. The authors describe the case of a 69 - years - old male patient presenting with significant weight loss, abdominal pain in the upper right quadrant, petechial lesions, rectal bleeding and epistaxis. Abdominal ultrasound showed multiple nodules and there was portal vein thrombosis and changes suggestive of multifocal hepatocarcinoma on abdominal computed tomography. Liver biopsy was conclusive for hepatic angiosarcoma.

In this case, unfortunately, the diagnosis was important only in terms of excluding other pathologies, as it did not allow any approach other than the institution of palliative measures, given the aggressiveness and rapid progression of the neoplasm in question.

Keywords: *Hemangiosarcoma/diagnosis; Hemangiosarcoma/diagnostic imaging; Hemangiosarcoma/pathology; Liver Neoplasms/diagnosis; Liver Neoplasms/diagnostic imaging; Liver Neoplasms/pathology.*

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Introduction

Hepatic angiosarcoma is a rare vascular tumor within the group of malignant neoplasms of the liver, with a low prevalence (~ 2%).[1,2] However, it is considered the third most common primary hepatic tumor, representing 2%-3% of soft tissue sarcomas in adults.[3,4] Metastases are common at presentation, affecting lung, spleen and bones.[3] It has no specific signs/symptoms or tumor markers, leading to difficult and delayed diagnosis and precluding pharmacological or surgical curative approach.[3,5,6] It has a highly aggressive nature with a quick growth and spread, conditioning high mortality rates, even after early therapeutic measures.[4,5] It presents more frequently in men between the sixth and seventh decade of life and, in most cases, there is no carcinogen exposure history (vinyl chloride, arsenic, thorium dioxide and radiation, as examples), which makes its diagnosis more difficult.[1,2]

Case Report

A 69-year-old male was admitted to the emergency services due to abdominal pain in the right hypochondrium, continuous, without irradiation or factors of relief or aggravation and with an intensity of 6 out of 10 (numerical pain scale). His past medical history was significant only for hypercholesterolemia although he mentioned recent severe weight loss (14 kg in 4 months) and progressive anorexia. Concomitantly, on physical examination, he had scattered petechial lesions in the lower limbs (Fig. 1), rectal bleeding and epistaxis. Hepatomegaly was also evident as well as grade 2 ascites, without jaundice. Abdominal ultrasound identified solid hepatic nodules in the right hepatic lobe. Consequently, he was admitted to the Internal Medicine Unit for further study. Regarding laboratory tests they revealed mild cholestatic and hepatocellular injury – alanine aminotransferase (ALT) 116 U/L, alkaline phosphatase 130

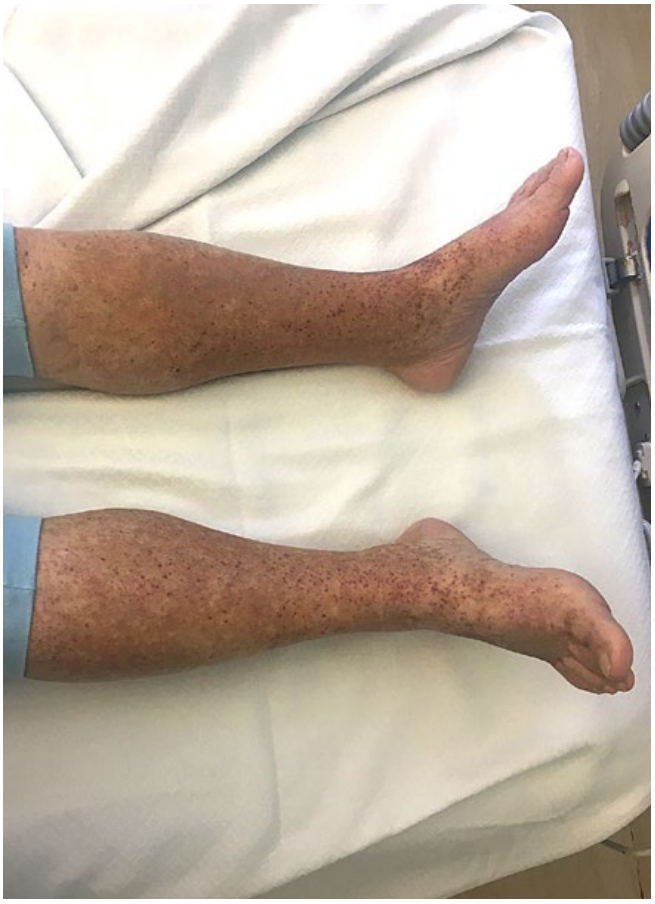

Figure 1: Petechial lesions in the lower limbs.

U/L, gamma-glutamyl transferase 160 U/L and total bilirubin 2.2 mg/dL; there was also increased prothrombin time (14.2 sec), thrombocytopenia (60.000x109 /L), negative alpha-fetoprotein and negative hepatitis B and C serologies (Table 1). Abdominal computed tomography (CT) scan showed complete portal vein thrombosis with superior mesenteric and splenic vein involvement, with cavernous transformation at the level of the hepatic hilum and hepatic parenchyma showed changes suggestive of multifocal hepatocarcinoma (Fig. 2). There were no extra-hepatic lesions, such as distant metastasis, on the whole-body computer tomography.

Subsequently, changes in liver parenchyma observed on computed tomography were approached through percutaneous liver biopsy to complement the study. Pathology results revealed a neoplasm with a predominantly solid pattern composed of sheets of pleomorphic cells. These neoplastic cells were composed of scant, eosinophilic cytoplasm and irregular nuclei with multiple nucleoli and mitotic figures, involving vessel structures with mild to moderate atypia. Immunohistochemistry study showed positivity of the neoplastic cells for vimentin and CD31, and negativity for CAM5.2, AE1/AE3, 34beta-E12, CK7, CK20, CD10, polyclonal CEA, HepPar1, S100, desmin, smooth muscle actin, HMB45, DOG1, CD117, ALK, CD23 and CD45. Proliferation index was 90% in Ki67 stain, and the final diagnosis was liver angiosarcoma (Fig. 3).

Furthermore, petechial lesions of the lower limbs and abdomen were becoming worse and confluent.

Table 1: Laboratory results on admission.

Blood Test	Results	Normal Value
Hemoglobin	11.7 g/dL	13 – 17.5 g/dL
Leucocytes	4.86 x 109/L	4 – 10 x 109/L
Platelets	60 x 109/L	150 – 400 x 109/L
Creatinine	0.85 mg/dL	0.72 – 1.18 mg/dL
Lactate dehydrogenase	1032 U/L	<248U/L
Aspartate aminotransferase (AST)	26 U/L	<35 U/L
Alanine aminotransferase (ALT)	116 U/L	<45 U/L
Alkaline phosphatase	130 U/L	30-120 U/L
Gamma-glutamyl transferase	160 U/L	< 65 U/L
Total bilirubin	2.2 mg/dL	0.2 – 1.2 mg/dL
Direct bilirubin	1.2 mg/dL	<0.5 mg/dL
Total proteins	7.8 g/dL	6.6 – 8.3 g/dL
Albumin	2.3 g/dL	3.5 – 5-2 g/dL
Prothrombin time	13.6 seg	10 – 14.2 seg
INR	1.36	<1.2
Activated partial thromboplastin clotting time	29.5 seg	25.1 – 36.5 seg

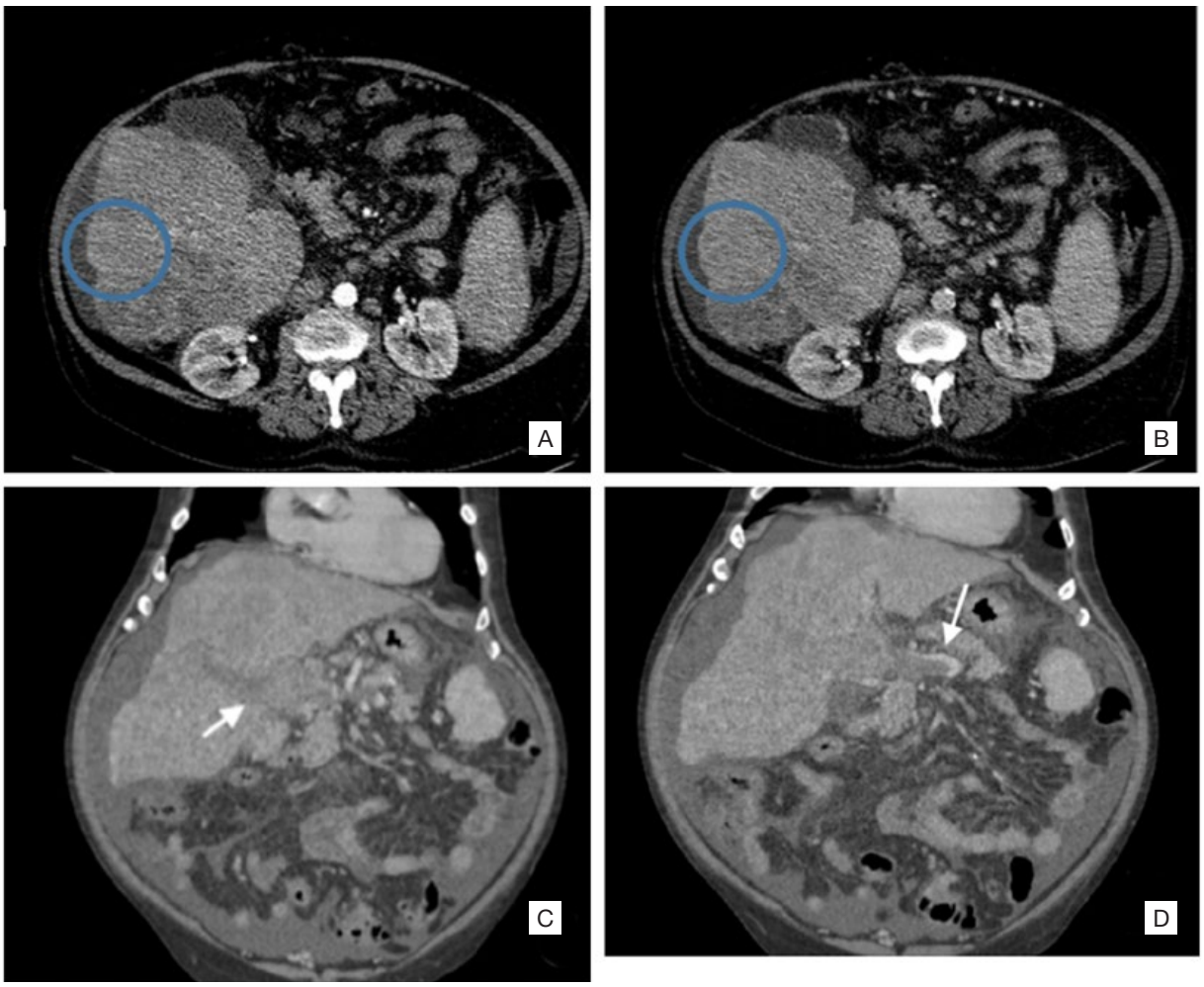

Figure 2: Abdominal and pelvic computed tomography images identifying a mass/conglomerate of solid nodular hepatic lesions involving almost the entire right lobe. The lesions have heterogeneous enhancement with areas of arterial phase enhancement (image A, example delimited by a circle), showing portal phase washout (images B and C). Additionally, complete portal vein thrombosis is observed with an image suggestive of cavernoma at hepatic hilum level (arrow in image C). The thrombus also involves the distal segment of the splenic veins (arrow in image D) and superior mesenteric vein.

In face of the clinical worsening with rapid progression to hepatic failure and evident cachexia, palliative care was instituted after a multidisciplinary decision. Unfortunately, the patient died two months after diagnosis.

Discussion

Angiosarcoma is a malignant tumor arising from spindle cells of endothelial origin.[1-3] Predominantly it presents in older men and is related to exposure to carcinogens although, in most cases, the risk factor is not identified.[1-5] Initial symptoms are nonspecific, such as abdominal discomfort and distension, fatigue and weight loss.[1,2] Physical examination typically shows hepatic involvement with abdominal pain, hepatomegaly, jaundice and ascites.[2] Changes in liver enzymes and severe thrombocytopenia are usual, but clinical evolution to fulminant liver failure is rare.[1,2] This case showed some of the typical signs and symptoms described above, but with a fatal and unexpected progression to acute liver failure, considering the mild laboratory alterations on admission; as already mentioned no tumor markers were identified.[2]

Regarding petechial lesions, they may be interpreted as a manifestation of paraneoplastic vasculitis. Despite hematologic disorders constitute the most common group of malignancies associated with cutaneous vasculitis some are related to solid organ tumors. Hepatocarcinoma is one of those reported tumors.[7] In these cases, the presence of cytopenias and immature cells can be a warning. However, considering the galloping progression of the disease, the authors could not confirm this hypothesis, namely by performing a skin biopsy or excluding other causes of vasculitis. Furthermore, this vasculitic lesions and multiple vascular thrombosis described on liver CT, besides thrombocytopenia and increased prothrombin time, as well as the above-mentioned epistaxis and rectal bleeding, may also raise the possibility of slow development of a disseminated intravascular coagulation process, as primarily venous thrombotic and embolic manifestations are common features; once

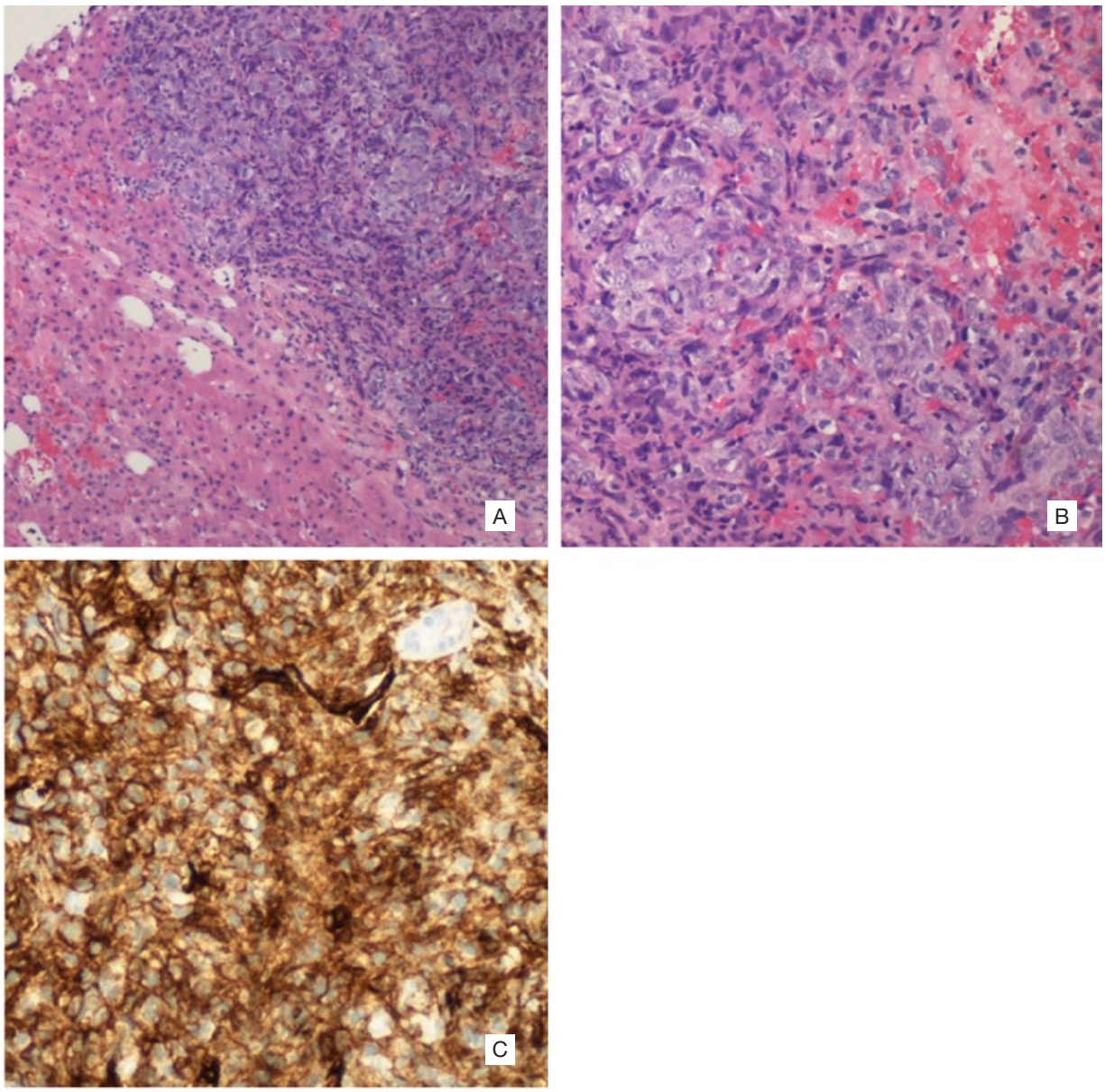

Figure 3: Pathology of liver biopsy.
(A)The neoplasia presents a predominantly solid pattern (HE 100x). (B) The neoplastic cells are composed of scant, eosinophilic cytoplasm and marked nuclear pleomorphism with prominent nucleoli
(→), involving vessel structures (HE 200x). (C) Positivity for CD31 in the neoplastic cells (CD31 200x).

more, there is no enough data to confirm it although its plausibility should be considered.

In terms of imaging tests, hepatic angiosarcoma has a variable appearance on both CT and magnetic resonance imaging (MRI), reflecting the pleomorphic histological nature.[8] Most commonly present as multiple masses but can occur as a single heterogeneous mass.[8] On CT it presents as hypoattenuating masses (some may be hyperattenuating reflecting hemorrhage) on both non-contrast and contrast--enhanced CT, with nodular enhancement being common, as seen in our case.[8] On MRI in T1/T2 they have heterogeneous areas of high signal reflecting mixed tumor and hemorrhage with heterogeneous enhancement with progressive filling.8 Notwithstanding what literature describes, this patient had no distant metastatic disease.

Liver biopsy, allowing a thorough anatomopathological study, is essential for full diagnosis.[1,5] In the immunohistochemical tests, one or more tumor markers must be identified - CD31, CD34, factor VIII antigen, vimentin, among others.[3,4] In the presented clinical case, histopathological examination required a wide immunohistochemistry study due to the atypical morphology of the neoplasm that revealed a positivity for CD31, considered the most specific marker for hepatic angiosarcoma.[9,10]

At the moment, liver angiosarcoma medical and surgical treatment is limited, with a fatal outcome in all similar clinical

conditions.[4,5] Even liver transplantation shown no benefit in survival, therefore it is presently contraindicatedin.[1,3] There are a few clinical cases in which liver resection was successful but the tumor mass was unique and there were no metastasis.[2,5] In our patient, supportive care was implemented, due to rapid worsening of the clinical condition. In conclusion, hepatic angiosarcoma has no specific presentation compared to other liver tumors, requiring a thorough study with imaging and biopsy exams for its diagnosis. It has a poor prognosis in the short term and there is no specific therapy at the moment.[1]

Conclusion

This case exposes a rare oncological entity with nonspecific clinical presentation nor pathognomonic imaging findings, though biopsy is essential for a definitive diagnosis. It is a disease that must be considered in the differential diagnosis when we have a patient with no history of liver disease, exposure to carcinogens or presence of specific tumor markers. Timely suspicion is crucial as it can definitely change the initial approach, for example, if the tumor is confined to one lobe, possible impacting on life expectancy, despite knowing its reserved prognosis due to rapidly progression, metastasis development and high recurrence rate. ■

Declaração de Contribuição

TA, CT, CF – Elaboração do manuscrito
RR, JP – Elaboração e revisão do manuscrito
FS – Revisão do manuscrito

Contributorship Statement

TA, CT, TF – Preparation of the manuscript
RR, JP – Preparation and review of the manuscript
FS – Manuscript review

Responsabilidades Éticas

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