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Hepatic angiosarcoma: a transdisciplinary case study

Angiossarcoma hepático: estudo de caso transdisciplinar

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ABSTRACT: Hepatic Angiosarcoma is a rare malignancy of endothelial cell origin that is generally idiopathic and presents non-specific clinical manifestations. Hemoperitoneum can occur in 17-27% of cases and is a result of tumor rupture, which has a devastating prognosis. We present a 79-year-old female patient with history of diffuse right upper quadrant abdominal pain associated with syncope episodes and unintentional weight loss. Physical examination was unremarkable except for painful palpation of the right upper quadrant. Laboratory exams indicated chronic disease anemia, a 2.7 INR, decreased albumin, increased C-Reactive Protein and GGT, and normal AST, ALT, Alkaline Phosphatase and Bilirubin. Viral hepatitis serologies were negative. Abdominal ultrasonography revealed hepatomegaly and solid liver lesions of heterogeneous echogenicity and imprecise limits. Three-phase abdominal CT showed multiple liver masses of heterogeneous pattern of enhancement suggestive of atypical hemangioma associated with ascites. Chest CT revealed bilateral pulmonary nodules suggestive of metastasis. During hospital stay, the patient developed a massive hemoperitoneum that required emergency laparotomy. In this circumstance, liver and omentum biopsies were performed and the pathology reports ultimately indicated the possibility of hepatic angiosarcoma. The patient developed refractory hemoperitoneum and hemorrhagic shock and ultimately passed away, 48 days after hospital admission. Definitive diagnosis was only available posteriorly, with immunohistochemistry positivity for ERG, CD34 and Factor VIII-related antigen on both omentum and lung samples. This case study provides valuable clinical discussion and emphasizes how a transdisciplinary approach is essential to correctly diagnose and manage such complex cases.

Key words: Hemangiosarcoma; Hemoperitoneum; Liver neoplasms.

RESUMO: O Angiossarcoma Hepático é uma malignidade rara de origem endotelial que é geralmente idiopática e apresenta manifestações clínicas inespecíficas. Hemoperitônio pode ocorrer em 17-27% dos casos e resulta da ruptura tumoral, o que tem um prognóstico devastador. Apresentamos uma paciente de 79 anos, do sexo feminino, com história de dor difusa em quadrante abdominal superior direito, associada a episódios de síncope e perda de peso não intencional. O exame físico era pouco notável, exceto por palpação dolorosa do quadrante superior direito do abdome. Exames laboratoriais indicaram anemia de doença crônica, RNI de 2.7, Albumina reduzida, Proteina C-Reativa e GGT elevados e níveis normais de AST, ALT, Fosfatase Alcalina e Bilirrubinas. Sorologias para hepatites virais foram negativas. Ultrassonografia abdominal revelou hepatomegalia e lesões hepáticas sólidas de ecogenicidade heterogênea e limites imprecisos. TC abdominal em três fases mostrou múltiplas massas hepáticas com padrão de realce heterogêneo, sugestivo de hemangioma atípico, e ascite. TC de tórax revelou nódulos pulmonares bilaterais sugestivos de metástases. Durante a internação, a paciente desenvolveu hemoperitônio maciço e necessitou de laparotomia de emergência. Nessa circunstância, biópsias do fígado e do omento foram realizadas e os relatórios de estudo anatomo-patológico indicaram, em última análise, possibilidade de angiossarcoma hepático. A paciente desenvolveu hemoperitônio refratário e choque hemorrágico e, por fim, faleceu 48 dias após admissão hospitalar. O diagnóstico definitivo tornou-se disponível posteriormente, com estudo imuno-histoquímico positivo para ERG, CD34 e antígeno relacionado ao fator VIII nas amostras de omento e pulmões. Este estudo de caso proporciona valiosa discussão clínica e enfatiza como uma abordagem transdisciplinar é essencial para diagnosticar e manejar corretamente casos tão complexos.

Palavras-chave: Hemangiossarcoma; Hemoperitônio; Neoplasias Hepáticas

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INTRODUCTION

Hepatic angiosarcoma is the third most common primary malignancy of the liver. It is a rare but aggressive neoplasm of endothelial cell origin that presents with non-specific clinical manifestations like abdominal pain, fatigue and weight loss. The main differential diagnosis include benign and malignant hepatic neoplasms, particularly hemangioma and metastatic disease. Investigation must be comprehensive and requires a transdisciplinary approach in order to obtain accurate diagnosis and adequate treatment. In this case report, we aim to present the unusual clinical manifestations, diagnostic evaluation and initial management of a patient with hepatic angiosarcoma manifested as hemoperitoneum. Our objective is to share the knowledge we obtained from studying it and to emphasize the characteristics of this rare disease to contribute to education of future health care providers.

CASE REPORT

A 79-year-old female patient presented to the emergency room with a history of vague right upper quadrant abdominal pain for the past two months that became more intense in the past few days. In addition, she referred episodes of hypotension and syncope, that started two weeks before, and unintentional weight loss over the past few months. She denied fever, nausea, vomiting, diarrhea and external bleeding. Her comorbidities were hypothyroidism, atrial fibrillation and vitiligo. She denied alcohol consumption, smoking and drug use and her other aspects of her history were unremarkable. She routinely took the following medications: Rivaroxaban, Propafenone, Levothyroxine and Pantoprazole.

During initial evaluation she presented anicteric, acyanotic, with normal vital signs. Physical examination was unaltered except for an abdomen slightly rigid and painful to palpation of the right upper quadrant, with no palpable masses, no guarding or signs of peritoneal irritation.

An abdominal ultrasonography, a laboratory workup and Holter monitoring were requested. Her laboratory exams results were:

Hemoglobin: 8.1 mg/dl; Red Blood Cells: 2.71 millions/mm3; Hematocrit: 25.9%; MCV: 95.6 fL; MCH: 29.9 pg; MCHC: 31.3%, RDW: 15.2%; White Blood Cells: 10.02 x 109/L; 218.000 Platelets; Serum Iron: 38 mcg/dL; Ferritin: 322.3 ng/mL; Total Iron Binding Capacity: 185 mcg/dL; Transferrin Saturation: 17%; Prothrombin Activity: 32.5%; Prothrombin time: 27.9 seconds; INR: 2.7; Albumin: 2.8 g/dL; C-reactive Protein: 77 mg/dl; Urea: 49 mg/dl; Creatinine: 0.81 mg/dL; AST: 24 U/L; ALT: 27 U/L; GGT:106 U/L; Alkaline Phosphatase: 125 U/; 0.7 mg/dl Total bilirubin, 0.31mg/dl Direct bilirubin; Anti-HCV: Non-reactive; HBsAg: Non-reactive; Anti-HBs: 1000 mUI/ml; Anti-HIV 1 and 2: Non-reactive.

Abdominal ultrasonography showed presence of small ascites and an enlarged liver with expansive solid lesions of heterogeneous aspect and imprecise limits, on the right lobe and part of the left lobe, with modest vascularization on Doppler mapping. The largest lesions measured about 10 x 7,5 cm and 6,7 x 6 cm.

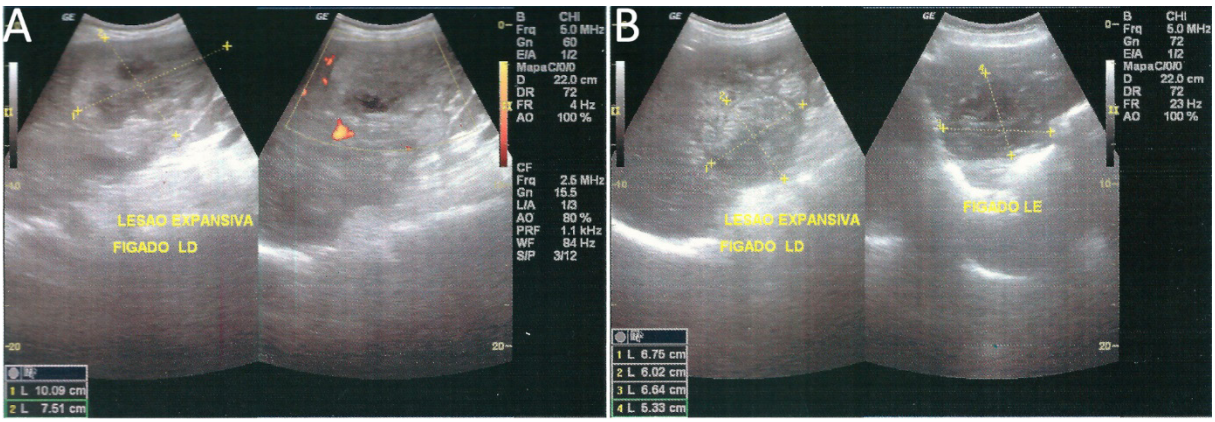

Figure 1. Abdominal Ultrasonography. A: expansive lesion on the right lobe of the liver of heterogeneous echogenicity and imprecise limits. B: Expansive lesion on the left lobe of the liver of heterogeneous echogenicity

In sequence, the patient was admitted and Rivaroxaban was suspended. She received intramuscular vitamin K and was started on daily 40 mg subcutaneous enoxaparin.

Chest and abdomen CT were requested in sequence. Abdomen CT was performed with intravenous contrast in three phases. It indicated hepatomegaly associated with multiple hepatic nodules in both right and left lobes, some with central hemorrhagic areas, suggestive of secondary dissemination; Small ascites containing hyperdense material in the right paracolic gutter, likely corresponding to blood; Mesoabdominal fat hyperdensity.

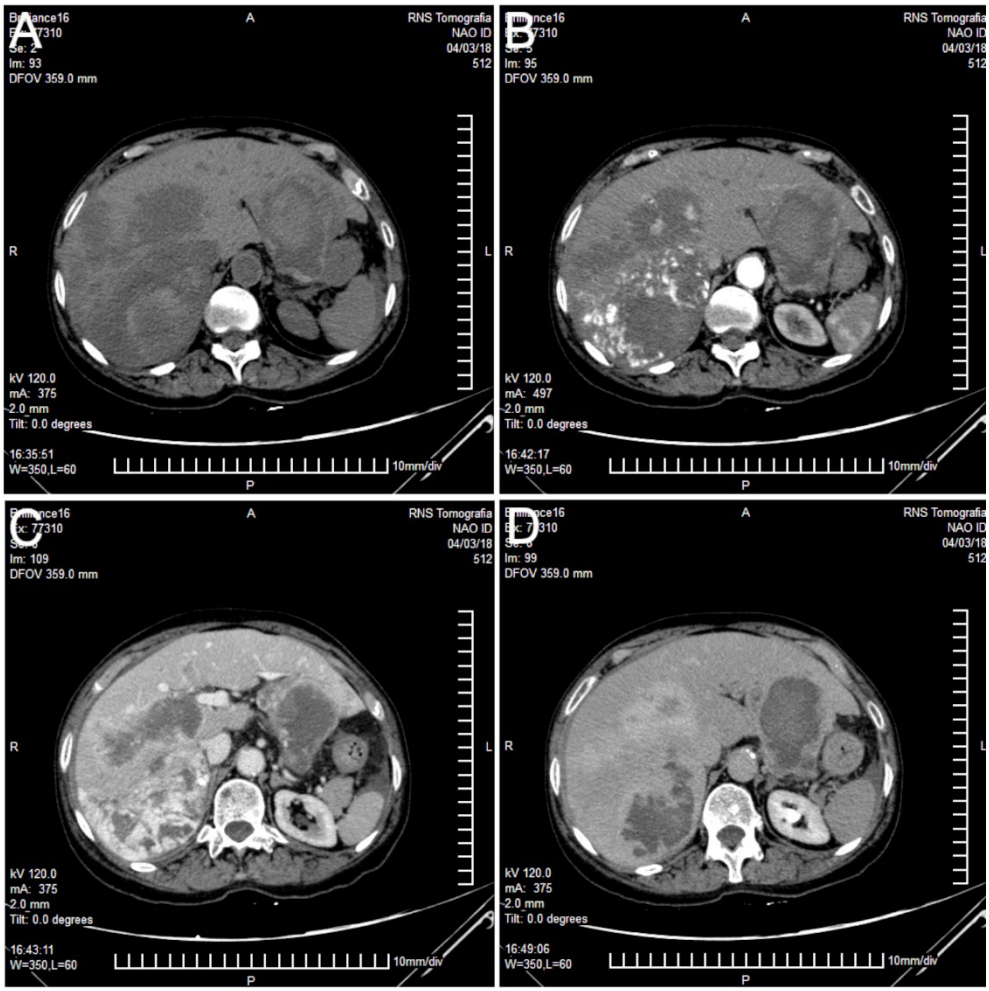

Figure 2. Abdominal CT Scan. A: Non-enhanced Abdominal CT Scan. B: Enhanced CT scan during early hepatic arterial phase. C: Portal venous phase. D: Equilibrium phase

Chest CT indicated bilateral pulmonary nodules, compatible with secondary neoplastic lesions; Soft-tissue density nodules, varied in size, with random distribution across the pulmonary parenchyma bilaterally; The largest nodules are located in the apical-posterior and basal posterior segments of the superior and inferior left lobe, respectively; Cyst in the superior right lobe; Cystic mediastinal formation alongside the pericardium, likely corresponding to pericardial cyst; Minimal pleural effusion to the right; Cardiomegaly. Hiatal hernia; Discrete aortic atheromatosis.

Within 36 hours of hospital admission, the patient developed hemodynamic collapse with tachycardia, tachypnea, severe pallor and important decline of mental status, associated with severe abdominal distention. There was significant hemoglobin decrease from admission to 5.2 mg/dl, mild thrombocytopenia, acidosis and elevated lactate level.

An exploratory laparotomy was conducted, revealing a massive hemoperitoneum. Large solid liver lesions with hemangioma aspect were spotted, as well as smaller lesions on the omentum of similar aspect. About four liters of blood were drained but there were no signs of active bleeding. Intraoperative biopsy of liver and omentum lesions was performed.

The patient was admitted to the ICU, where she received blood transfusions and was maintained stable with the use of vasopressors until post-operative day 8, after which she was discharged from the ICU and awaited further diagnostic evaluation.

Histopathologic analysis results were available a week after surgery. Hepatic sample was a 1,5 x 1 x 0,5 cm irregular fragment. Microscopic examination indicated capsular thickening; hematic and lymphatic lakes in the subcapsular parenchyma; sinusoidal dilation; thick fibrous septae, lymphocyte and monocyte infiltration; no signs of neoplasia; cannot exclude possibility of fibrous cyst. Omental sample was a 2 x 2 x 1 cm irregular fragment that indicated fibroadipose tissue with cavernous hemangioma.

After considering the patient's clinical manifestations, the natural history of hemangiomas and the adverse conditions in which the biopsies were obtained,

a review of the analysis was requested and a biopsy of the pulmonary nodules was planned and performed about ten days later, after patient's clinical stabilization.

Ten days after the pulmonary biopsy, the patient developed new hemodynamic collapse and severe abdominal distention. She received 900 ml of packed red blood cells and 600 ml of frozen plasma and was urgently submitted to laparotomy. About 5 liters of blood were drained from the peritoneal cavity and a large hepatic mass on the segment 7 of the liver was encountered, with active signs of bleeding. Hemorrhagic spots were seen on the omentum as well. A damage control surgery approach was adopted: Extensive hepatorrhaphy was performed and the abdomen was packed in the site of hepatic bleeding and temporarily closed, to be assessed again in 48 hours once the patient was stable.

Two days later the patient was reassessed and the packs were removed from the abdomen. The abdominal cavity was re-evaluated and showed no signs of hemorrhage, allowing the surgeons to proceed to definitive closure of the abdominal wall.

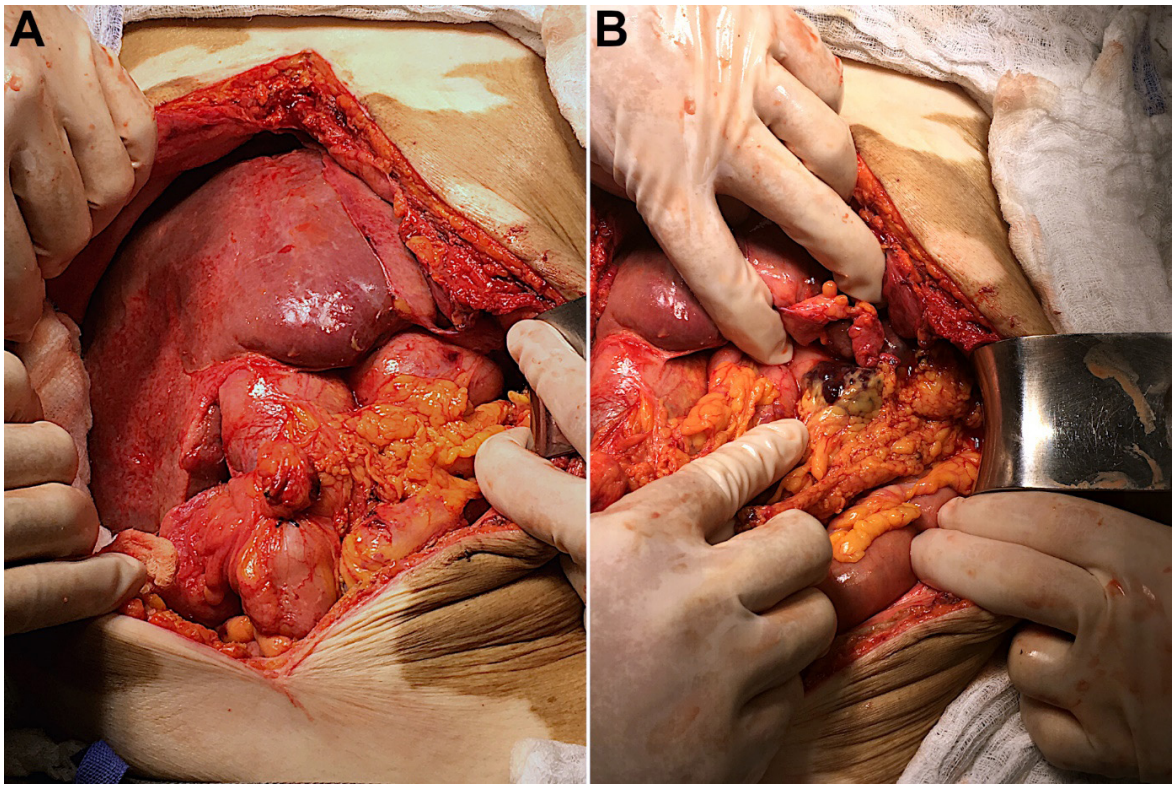

Figure 3. Macroscopic appearance of the liver during second-look laparotomy following a massive hemoperitoneum. A: Enlarged liver with no signs of active hemorrhage. B: Omental metastatic lesion, or "omental cake", spotted during laparotomy

Results of the review of the omentum sample pathological analysis were available five days after her last laparotomy, and showed: circumscribed neoplasm composed of anastomosing vascular channels that formed cavernous structures of varied sizes, with abundant hemorrhagic material and necrotic foci; the cells lining the vascular channels are fusiform and present oval nuclei, with discrete atypia and evident nucleoli. The conclusion was that the findings were suggestive of angiosarcoma.

Histopathologic examination of the pulmonary biopsy revealed various small nodules composed of small anastomosing vascular channels, at times forming cavernous structures. They are lined by fusiform cells with elongated nuclei, with discrete pleomorphism and evident nucleoli. The conclusion was that the findings were suggestive of angiosarcoma.

In order to confirm the diagnosis, an immunohistochemistry study was requested. Concurrently, an Angio-CT was planned to provide anatomical study of the tumor vasculature.

The case was considered surgically unresectable due to multiple, infiltrative, hepatic masses and metastasis to other organs. The therapeutic proposal offered was embolization, to reduce size and risk of hemorrhage, and palliative chemotherapy. However, shortly after the patient developed another episode of hemorrhagic shock, which ultimately resulted in her death, 48 days after admission.

Immunohistochemistry analysis reports posteriorly informed: Both the omentum and pulmonary samples tested positive for ERG, CD34, Factor VIII-related antigen and negative to cytokeratin and epithelial membrane antigen; 50-60% of omentum sample cells and only 25-30% of pulmonary cells were positive to Ki 67. The diagnosis of angiosarcoma was, therefore, confirmed.

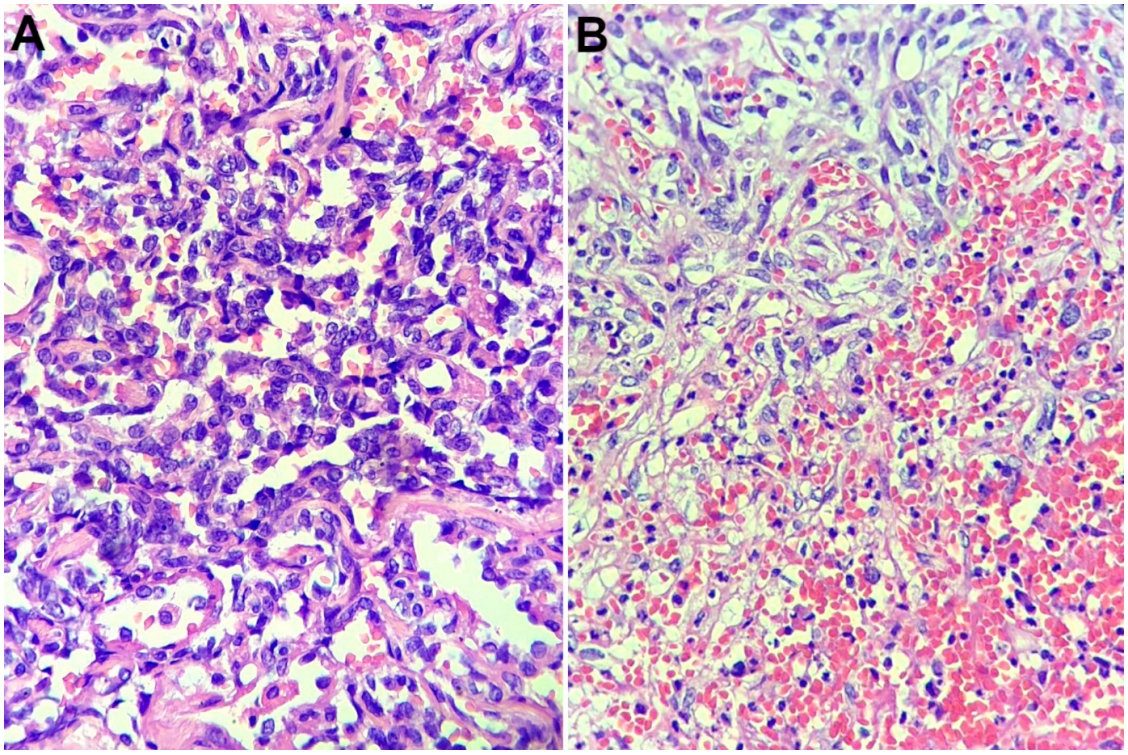

Figure 4. Histology. A: Lung biopsy sample: communicating vascular channels, lined by atypical endothelial cells, containing red blood cells. B: Omentum biopsy sample: formation of cavity filled with blood and ruptured abnormal vascular channels within the tissue

DISCUSSION

In this report, we present a case of idiopathic hepatic angiosarcoma diagnosed in the event of a spontaneous hemoperitoneum that lead to hemorrhagic shock. The patient's presentation at the emergency room suggested several possible causes, leading to a comprehensive initial evaluation. Posterior investigation was greatly guided by the finding of a hepatic mass on ultrasound and occurrence of intraabdominal bleeding, which pointed a direction towards the most likely diagnosis.

Spontaneous hemoperitoneum is the clinical entity in which there is blood within the peritoneal cavity from a non-traumatic and non-iatrogenic cause[1,2]. Symptoms can be non-specific although abdominal pain is frequently reported. Benign and malignant hepatic conditions can cause hemorrhage, with hepatic adenomas being the most frequent benign neoplasms and hepatocellular carcinoma the most frequent malignant neoplasm associated. Malignant disease more often causes liver rupture, with HCC accounting for the majority of cases and metastatic disease for less than 2% of cases[1].

Rupture of a hepatic angiosarcoma leading to hemoperitoneum is a possible clinical manifestation of this malignancy, which happens in about 17-27% of cases[3]. Angiosarcomas are a subtype of soft-tissue sarcoma, originated from endothelial cells of blood and lymphatic vessels, that represent about 2% of soft tissue sarcomas, and 2% of all primary liver tumors[4,5]. It is the third most common primary malignancy of the liver in adults and the first of mesenchymal origin. Hepatic angiosarcomas occur more often in the sixth and seventh decades of life and is 4 times more frequent in men than in women[6]. Metastasis occur more often in the lungs, through hematogenous dissemination, but can also appear in the bones and soft-tissue structures[5]. Etiology is idiopathic in the majority of cases, although some risk factors have been established. Environmental exposure to chemicals such as thorotrast, polyvinyl chloride and arsenic powder has been largely implicated in the development of this malignancy[3,5,7]. Clinical manifestations are varied. The most common presenting symptoms are upper abdominal pain, abdominal swelling, weight loss and nausea.[6] Physical examination signs frequently reported are hepatomegaly, ascites and jaundice[7,8].

In the case we reported, the patient's laboratory exams featured a normocytic/normochromic anemia with decreased serum iron and transferrin saturation and elevated ferritin, highly suggestive of chronic disease anemia. Moreover, she presented markedly elevated thrombin time and INR, and decreased prothrombin activity, which reflects dysfunction of the extrinsic pathway of coagulation. In this context, it could be due to a hepatic disease coagulopathy, in which synthesis of clotting factors is reduced or occurs abnormally leading to impairment of coagulation. Hepatic angiosarcoma has been linked to clotting abnormalities

and thrombocytopenia predisposing to hemorrhages in other studies, sometimes correlated with anemia and hemoperitoneum[3,8,9]. Disseminated intravascular coagulopathy is a possible but rare manifestation that has been reported in about 5% of cases[7,10].

Decreased albumin has also been linked to this malignancy and reflects impaired synthetic function.[7] It is important to consider that other factors can alter serum albumin such as nutritional status and catabolism, while prothrombin time can be altered in vitamin K deficiency, warfarin anticoagulation and consumptive coagulopathy.

Regarding the assessment of hepatocellular injury, biliary tract and excretory function, the patient presented unaltered AST and ALT, total and direct bilirubin within normal ranges, markedly elevated GGT and borderline alkaline phosphatase. These findings were, therefore, limited to identify the predominant pattern of liver abnormality. Elevated GGT has been reported in hepatic angiosarcoma and, in this scenario, could be caused by the expansive lesion. Laboratory results in hepatic angiosarcoma are often non-specific, but moderately elevated AST and ALT, elevated alkaline phosphatase and thrombocytopenia are frequently reported in studies. Tumor markers are most commonly negative or only mildly elevated, similarly to our case, in which CEA, AFP, CA 19-9, CA 15-3, CA 125 were all within normal ranges[3,7,8]. The primary purpose of these markers is to raise suspicion of HCC, metastatic disease and other malignancies, with AFP being the most helpful marker to evaluate HCC[6]. Viral hepatitis was evaluated in our case by ordering Anti-HBs, HBsAg and Anti-HCV. The results suggested previous vaccination for hepatitis B and negative serology for acute hepatitis B and C. Total Anti-HBc and Anti-HBc IgM would be useful in this scenario to exclude previous acute hepatitis B.

Imaging studies are useful to support clinical investigation, especially regarding the differential diagnosis of solid liver lesions. In our case, the liver lesion presented poorly defined masses of heterogeneous echogenicity on ultrasound. It was hypo or isodense compared to the parenchyma on non-enhanced CT and on contrast-enhanced CT it showed heterogeneous pattern of enhancement during arterial and portal venous phase, with areas suggestive of necrosis and hemorrhage. The main hypothesis suggested by these findings was of atypical hemangioma.

Hemangiomas usually present on ultrasound as well defined hyperechogenic nodules that could be hypoechogenic in the center due to fibrosis, necrosis or calcification. On non-enhanced CT, usual presentation is of a nodular homogeneous lesion, hypodense compared to the normal parenchyma. After administration of contrast, the lesion shows peripheral centripetal enhancement, with attenuation coefficient similar to the aorta. Delayed scans show density of the lesion similar or superior to the liver parenchyma. Atypical hemangiomas may show other patterns such as delayed enhancement and central enhancement without centripetal fill-in. Furthermore, presence of intralesional hemorrhage, fibrosis and necrosis could lead to a heterogeneous pattern on imaging studies that confuse diagnosis. Differential diagnosis is made with other solid liver lesions like adenomas, that could present heterogenous arterial enhancement with areas of hemorrhage and calcification in atypical cases, and hepatic angiosarcoma[11].

Regarding hepatic angiosarcoma, ultrasound image can show single or multiple lesions with heterogeneous echogenicity due to necrosis and hemorrhage.[3] On non-enhanced CT, the lesions can either be multiple or singular and may be predominantly hypodense with hyperdense spots due to recent hemorrhage. Hypodense areas may occur as a result of necrosis and old hemorrhage. After administration of contrast, the lesions show a heterogeneous pattern of enhancement, with spots of density superior to the liver parenchyma but inferior to the aorta. Enhancement develops progressively on delayed scans, with some areas remaining hypodense due to fibrosis or necrosis[11,12].

Biopsy and histopathologic analysis are paramount to establish definitive diagnosis. Clinical correlation to the findings is essential to the pathologist. In this case, for instance, the presence of pulmonary nodules and a history suggestive of rapid tumor growth were responsible for the suspicion of angiosarcoma. Although intraoperative biopsy was performed opportunely during an emergency laparotomy, the quality of the fragments obtained was suboptimal, due to the context, and clinical correlation was impaired because the biopsy was performed before the case could be properly discussed. Thus, a review of the initial analysis was necessary, which could have been prevented by performing planned surgical biopsy and correlation to clinical history. Percutaneous biopsy is not recommended because of the vascular nature of the tumor and the possibility of hemorrhage[4,7].

Macroscopically, hepatic angiosarcomas usually involve both lobes of the liver and more frequently presents as a large dominant mass but could also present as multiple nodules or diffuse micronodular infiltration. Histological evaluation may show highly atypical pleomorphic sinusoidal endothelial cells with hyperchromatic nuclei, which line blood spaces and grow in a confluent infiltrative manner along sinusoids and other vascular channels. Endothelial cells often present a spindle or polygonal morphology. Solid areas resembling fibrosarcoma may be seen, as well as numerous mitotic figures. Areas of infarct, atrophy, fibrosis and calcification are frequent[4,13].

Immunohistochemistry allows diagnostic confirmation by studying expression of specific molecular markers. CD31, CD34 and factor VIII-related antigen are markers expressed in endothelial cells that have been used to confirm the vascular nature of the tumor. Recently, ERG, a transcription factor expressed in endothelial cells, was

reported to be superior in diagnosis of angiosarcoma than other markers[13]. However, up to this point, no markers were associated with prediction of prognosis[4,8].

There are few studies reporting survival rates of hepatic angiosarcoma. A review of the literature from 1979 indicated that only 3% of patients with primary hepatic angiosarcoma survive longer than 2 years, with a median survival of 6 months, without treatment[7]. Complete surgical resection is considered to be the only definitive treatment that can improve survival.[8] Still, like our case, most cases present multifocal lesions and are unresectable at diagnosis. In these patients, palliative chemotherapy could be an option and several treatment modalities have been reported, with no established chemotherapy regimen. Primary hepatic angiosarcoma is reported as a radioresistant and radiotherapy is usually not indicated[3,14]. Liver transplantation is contraindicated due to the high recurrence rates. Rupture of hepatic angiosarcoma has a devastating prognosis despite surgery or arterial embolization. As seen in our case, tumor dissemination and peritoneal angiosarcomatosis cannot be managed effectively through surgery and can induce massive blood loss[15].

CONCLUSION

Hepatic angiosarcoma is a rare malignancy that consists in a diagnostic challenge that requires transdisciplinary medical evaluation. The non-specific presentation and differential diagnosis with other hepatic neoplasms demands comprehensive understanding of the manifestations of hepatic diseases and a high level of suspicion. Blood tests may show altered hepatic function and imaging studies provide characterization of the neoplasm but diagnosis is only established definitively by surgical biopsy and pathologic analysis. Angiosarcoma is an aggressive tumor and complete surgical resection is the most effective treatment when possible, with palliative chemotherapy being a prominent option for those not eligible for surgery. Further research is required, particularly to improve management and survival of these patients. Studying such cases allows the future professionals to learn from every manifestation, contributes to continued education and motivates medical research in areas that could significantly improve patient care.

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REFERENCES

1. Lucey BC, Varghese JC, Anderson SW, Soto JA. Spontaneous hemoperitoneum : a bloody mess. Emerg Radiol. 2007;14:65-75. doi: 10.1007/s10140-007-0594-0.
2. Furlan A, Fakhran S, Federle MP. Spontaneous abdominal hemorrhage: causes, CT findings and clinical implications. Am J Roentgenol. 2009;193:1077-87. doi: 10.2214/AJR.08.2231.
3. Molina E, Hernandez A. Clinical manifestations of primary hepatic angiosarcoma. Dig Dis Sci. 2003;48(4):677-82. doi: 10.1023/A:1022868221670.
4. Chaudhary P, Bhadana U, Singh RAK, Ahuja A. Primary hepatic angiosarcoma. Eur J Surg Oncol. 2015:1-7. doi: 10.1016/j.ejso.2015.04.022
5. Young RJ, Brown NJ, Reed MW, Hughes D, Woll PJ. Review Angiosarcoma. Lancet Oncol. 2010;11:983-91. doi: 10.1016/S1470-2045(10)70023-1.
6. Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease - 2 Volume Set: Pathophysiology, diagnosis, management. 10th ed. Local: Saunders; 2015.
7. 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. Med Balt. 1979;58(1):48-64.
8. Zhu Y, Chen Y, Matro E, et al. Primary hepatic angiosarcoma : A report of two cases and literature review. World J Gastroenterol. 2015;21(19):6088-96. doi: 10.3748/wjg.v21.i19.6088.
9. Lee S, Song C, Gi Y, et al. Hepatic angiosarcoma manifested as recurrent hemoperitoneum. World J Gastroenterol. 2008;14(18):2935-8. doi: http://dx.doi.org/10.3748/wjg.14.2935.
10. Mazharuddin S, Podduturi V, Guileyardo JM, Cooper B. Hepatic angiosarcoma associated with disseminated intravascular coagulation. Baylor Univ Med Cent Proc. 2015;28(1):54-6.
11. Rocha, Antônio José da; Silva CIS, D'ippolito G. Gastrointestinal - Série CBR - Colégio Brasileiro de Radiologia e Diagnóstico Por Imagem. Rio de Janeiro: Elsevier; 2011.
12. Bruegel M, Muenzel D, Waldt S, Specht K, Rummeny EJ. Hepatic angiosarcoma: cross-sectional imaging findings in seven patients with emphasis on dynamic contrast-enhanced and diffusion-weighted MRI. Abdom Imaging. 2013;38(4):745-54. doi: 10.1007/s00261-012-9967-2.
13. Wang Z, Yuan J, Chen W, et al. Transcription factor ERG is a specific and sensitive diagnostic marker for hepatic angiosarcoma. World J Gastroenterol. 2014;20(13):3672-9. doi: 10.3748/wjg.v20.i13.3672.
14. Kim HR, Rha SY, Cheon SH, Roh JK, Park YN, Yoo NC. Clinical features and treatment outcomes of advanced stage primary hepatic angiosarcoma. Ann Oncol. 2009;20(4):780-7. doi: 10.1093/annonc/mdn702.
15. Leowardi C, Hormann Y, Hinz U, et al. Ruptured angiosarcoma of the liver treated by emergency catheter-directed embolization. World J Gastroenterol. 2006;12(5):804-8.

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