<u>Revisor A</u>

The authors present a clinical case of hepatic angiosarcom in a young female with an initial imagiologic diagnosis of hemangioma. Our case is an example of the pitfalls of the differential diagnosis of focal hepatic lesions.

Imaging findings are not well described in the manuscript (in which CT imagiologic findings was the diagnosis of hemangioma based?) and probably an MRI might have helped in the differential diagnosis. An ultrasound revealed a heterogeneous, bulky and hyperechoic mass, 13.5 cm wide, in the right lobe of the liver, described as a hemangioma, with no signs of steatosis or chronic liver disease. An abdominal CT-scan was performed to further assess this lesion (figures 1 and 2).

One month later, due to worsening abdominal pain, another CT-scan was performed and the same nodular lesion was identified, 20 cm, and considered a hepatic hemangioma (figure 3).

We can speculate if a Magnetic Resonance Imaging (MRI) could have been useful. If angiosarcoma was suspected in an MRI, she could have been diagnosed with metastatic disease (or not), knowing now that they were there two months later, and the patient wouldn't have been submitted to surgery.

Revisor D Eliminado: described. Alterado Eliminado: . H. Alterado Eliminado: this. Alterado Eliminado: descreveu. Alterado Eliminado: um. Alterado Eliminado: descreveu. Alterado Eliminado: lesões hepáticas e ósseas metastáticas. Alterado Eliminado: , tendo sido sujeita. Alterado Eliminado: e. Alterado Eliminado: em. Alterado Eliminado: diagnosticar. Alterado Eliminado: um. Alterado Eliminado: nos. Alterado Eliminado: à. Alterado Eliminado: irressecabilidade. Alterado Eliminado: and. Alterado

Eliminado: carried out. Alterado Eliminado: with. Alterado Eliminado: our. Alterado Eliminado: Tipically. Alterado

<u>Revisor E</u>

O inicio do abstrat não reflete a conclusão sendo a descrição sumaria do caso clínico. Hemangiomas are usually diagnosed based on ecographic findings. The presence of symptoms, rapid growth or atipical imagiological findings should make us consider other diagnoses including malignant tumors such as angiosarcomas.

Deve ser focado mais as dificuldades de diagnóstico com exames efectuados pois é isso que se pretende no titulo. This case shows how difficult it is to diagnose hepatic angiosarcoma relying only on imaging findings. Two CT-scans were performed and none suggested this diagnosis.

Na descrição das toxicidades estão referidos os graus à exceção da neuropatia a acrescentar. . Toxicities included grade 2 alopecia and anaemia, grade 1 neutropenia and grade 1 neuropathy.

Uma nota quanto a frase " powerful analgesic medication" – alterado para opioid analgesic medication

Valorizados os achados imagiológicos, nomeadamente se foi realizado contraste IV e em que fase foram realizadas as leituras pois tem implicação na acuidade diagnóstica por imagem. An abdominal triphasic CT-scan with contrast injection was performed to further assess this lesion, with arterial, portal and late phases (figures 1 and 2).

Inicia com referencia a idade, e esta não está referida no background, o que seria importante referir ... are more frequent in male patients between 50 and 70 years old and risk factors may include chemical carcinogens ...

podendo ser encurtada a frase seguinte de não exposição a carcinogéneos dado já ter sido referido no background e não ser importante para o objetivo do texto proposto. Hepatic angiosarcoma can be associated to chemical carcinogens and anabolic steroids^{1,6 8}, but our patient had no suspicious exposure.

" is not recomended" em substituição de " is not an option" - alterado

Revisor F

Commented [j1]: To the angiosarcoma or the lumbar vertebrae ? To the lumbar region

Commented [j2]: TC: alterado

Commented [j3]: PET-CT: alterado

Commented [j4]: A quê? Antálgica, dirigida à região lombar

Commented [j5]: ,vinyl chloride and ... Alterado

Commented [j6]: Neverthless, it's the most common malignant mesenchymal tumour of the liver. Other diseases related to angiosarcomas are Nevertheless, it's the most common malignant mesenchymal tumour of the liver, found more frequently than fibrosarcoma, malignant fibrohistiocytoma and leyomiosarcoma.

Commented [j7]: Of months (6 months without treatment)

Commented [j8]: If adequate hepatic reserve and limited to one lobe. Alterado

Commented [j9]: It can't be performed in metastatic disease. Alterado

Commented [j10]: Irradiation ? antalgic position ? describe the tenderness more specifically. without irradiation or antalgic position, and partial relief with nonsteroidal anti-inflammatory drugs

Commented [j11]: Why wasn't an MRI considered by the surgeon ? or if it was why wasn't it performed ? We can speculate if a Magnetic Resonance Imaging (MRI) could have been useful. If angiosarcoma was suspected in an MRI, she could have been diagnosed with metastatic disease (or not), knowing now that they were there two months later, and the patient wouldn't have been submitted to surgery.

Commented [j12]: Characterize the histology of the specimen. The surgical specimen showed a hepatic angiosarcoma with free surgical margins, consisting of hepatic pleomorphic cells, with more than 20 atypical mitosis, positivity to CD31 and CD34 and negativity to HMB 45 and pancytokeratins AE1/AE3.

Commented [j13]: Peridiocity?? Every 3 weeks

Commented [j14]: Were bisphosphonates, calcium +and vitamin D started or not ? and why? Yes, she started bisphosphonates, calcium and vitamin D

Commented [j15]: ..rare form of hepatic cancer. Alterado

Commented [j16]: an. Alterado

Commented [j17]: wouldn't. Alterado

Commented [j18]: REFRASE: as she could have been diagnosed at that time with metastatic disease or not, knowing now that they were there two months later. If angiosarcoma was suspected in an MRI, she could have been diagnosed with metastatic disease (or not), knowing now that they were there two months later, and the patient wouldn't have been submitted to surgery

Commented [j19]: By percutaneous biopsies only 25% of correct diagnosis are obtained and 5% die after. Misdiagnosis by fine-needle aspiration biopsy may occur due to the heterogeneity of malignant vascular tumours and the presence of necrotic zones, leading to high rate of inconclusive histological/cytological results. According to some authors, *this* should not be used due to the risk of bleeding and biopsy-induced metastases^{2,10,11}. Open liver biopsies or laparoscopy may be more accurate and safe². However, in case series, percutaneous biopsy was described as a safe procedure ⁹. Therefore, the role of histological sampling for angiosarcoma is still controversial.