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Metastatic Testicular Germ Cell Tumor or a Chemoresponsive Liver Hemangioma?

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ABSTRACT

Testicular germ cell tumors are the most common solid organ malignancy in young adult men. The presence of non-pulmonary visceral metastasis is an independent factor that places such patients into the higher risk group. Hepatic hemangiomas are the most common tumors of the liver and are entirely benign. Overlap between these entities may occur, particularly when metastases are hypervascular.

We describe a case of a 27-year-old man with a testicular germ cell tumor and a nodule in the right hepatic lobe suggestive of hemangioma. After three cycles of chemotherapy, a size reduction in the hepatic nodule was confirmed, and this lesion was removed. Pathology revealed a fibrosing hemangioma.

In this case report, the authors discuss the possible mechanisms for the hemangioma chemotherapy response.

Keywords: germ cell tumor, chemoresponsive, liver hemangioma

INTRODUCTION

Testicular germ cell tumors are the most common solid organ malignancy in young adult men. Of testicular tumors, 40% are seminomas and 60% non-seminomas.[1] Non-seminoma is the more clinically aggressive tumor. The presence of non-pulmonary visceral metastasis is an independent factor that places such patients into the higher risk group.[2] Management of patients with non-pulmonary visceral metastasis from non-seminoma includes full schedule chemotherapy with bleomycin, etoposide, and cisplatin (BEP) for four cycles (standard), given as 5-day schedule, and resection of any residual radiographic abnormality if technically feasible.[1]

Hepatic hemangiomas are the most common tumors of the liver and are entirely benign.[3] Treatment is unnecessary unless their expansion causes symptoms. Liver metastases and hemangiomas may be distinguished with imaging modalities, including magnetic resonance imaging (MRI), on the basis of lesion morphology and T2 measurements.[4] However, overlap between these entities may occur, particularly when metastases are hypervascular.[5]

CASE REPORT

A 27-year-old man detected a mass in testicular auto-examination. Ultrasound confirmed testicular mass was suspicious for malignancy. Alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) levels were 33 ng/mL and 16 mIU/mL, respectively. Thoracic, abdominal, and pelvic computed tomography (CT) showed two micronodules (5 mm) in the anterior segment of the left lung lobe and a 27-mm nodule in the right hepatic lobe suggestive of hemangioma, hypothesis that was corroborated by MRI (**Figure 1**).

The patient was submitted to radical orchiectomy. Pathology revealed a 3-cm germ cell tumor with teratocarcinoma and embrionary carcinoma components (**Figure 2**). After orchiectomy, an elevation of tumor markers was registered (AFP: 428.2 µg/dL, HCG: 46.7 U/L), and the patient received primary chemotherapy. Because hepatic lesion was assumed a hemangioma, the tumor was classified as IS, and three cycles of BEP were given. With chemotherapy, the tumor markers normalized, as expected. The reevaluation CT scan showed a size reduction of the hepatic nodule (from 27 to 18 mm) (**Figure 3**). With these unexpected findings, the multidisciplinary group decision was to perform hepatic lesion excision. Pathology revealed a fibrosing hemangioma (**Figure 4**).

DISCUSSION

This clinical case presented a diagnosis and decision-making challenge. Even though the hepatic lesion had a low pretest probability of being malignant, if this lesion did represent metastatic disease, the treatment plan and prognosis would be different. The shrinking of the hepatic lesion raised the possibility for the lesion to be metastatic.

Hepatic hemangioma is the most common liver tumor. Hemangiomas are often solitary, but multiple lesions may be present in both the right and left lobes of the liver in up to 40% of the patients.[6] The point prevalence of hepatic hemangiomas may reach 20%.[7] This observation is confirmed by the increasing recognition of hemangiomas in asymptomatic patients undergoing radiologic imaging tests of the abdomen for other reasons. However, hepatic hemangioma can be confirmed in more than 90% of patients by a CT scan

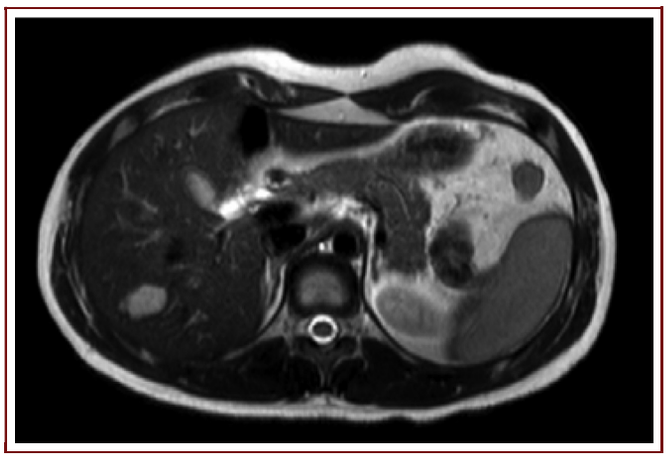

Figure 1. Hepatic MRI: hepatic lesion with hypersinal in T2 ponderation, corresponding to a provable fibrosing hemangioma.

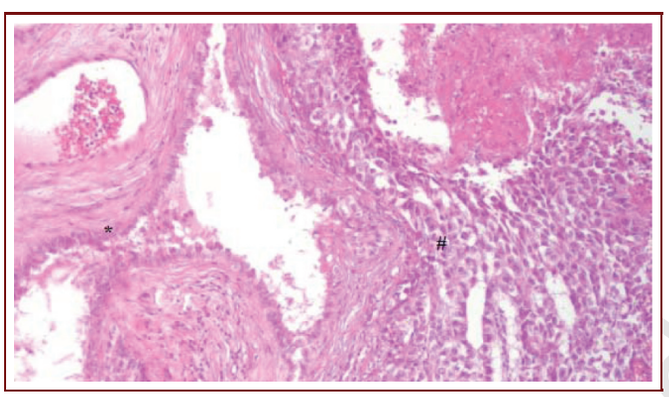

Figure 2. Germ cell tumor: teratoma (*) and embrionary carcinoma components (#).

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or an MRI.[8] Other studies showed that the diagnosis of hepatic hemangioma remained dubious in nearly 10% of the patients using three different imaging modalities (including ultrasound, CT, MRI, scintigraphy, and angiography).[9] Microscopically, the tumor is composed of cavernous vascular spaces of varying sizes lined by a single layer of flat endothelium and filled with blood. The vascular compartments are separated by thin fibrous septae and may contain thrombi.[10] The etiology of hepatic hemangiomas is

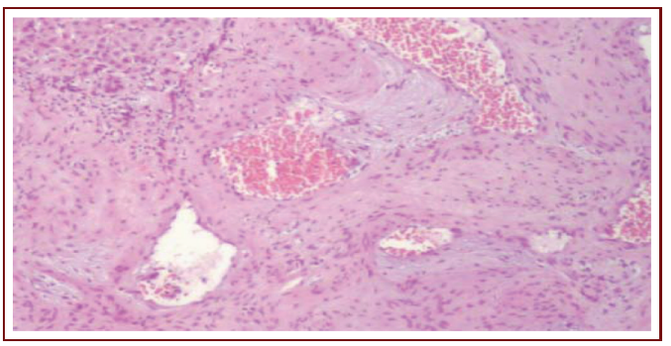

Figure 4. Fibrosing hepatic hemangioma.

incompletely understood. They are considered to be vascular malformations of congenital origin that enlarge by ectasia rather than by hyperplasia or hypertrophy. Hormonal influence over tumor growth is suggested by enlargement during pregnancy and estrogen and progesterone therapy and regression after withdrawal of therapy.[8,11–13] Vascular endothelial growth factor (VEGF) is recognized as an essential regulator of normal and abnormal blood vessel growth.[14] It is postulated that higher expression of VEGF and angiopoietins leads to increased angiogenic activity in cavernous hemangioma endothelial cells.[15] Stromal cells cultured from surgically removed life-threatening hemangiomas released an endothelial cell mitogen in vitro that was indistinguishable from VEGF, and systemic injections of neutralizing anti-VEGF antibodies inhibited the angiogenic response in nude mice grafted with neonatal hemangioma cells.[16] Bevacizumab is a recombinant monoclonal antibody against VEGF and has been shown to be effective in the hemangioma size reduction.[15] Another case report, very similar to ours, reported a patient with testis cancer with a hepatic hemangioma that responded partially to systemic chemotherapy.[17] Our hypothesis is that the decreased size of the hemangioma in our patient could have been a result of chemotherapy, perhaps through antiangiogenic mechanisms.[18]

CONCLUSION

Our case report shows that, in the absence of definitive imaging criteria, a chemotherapy-induced response of hemangioma can mimic a chemotherapy response of metastatic

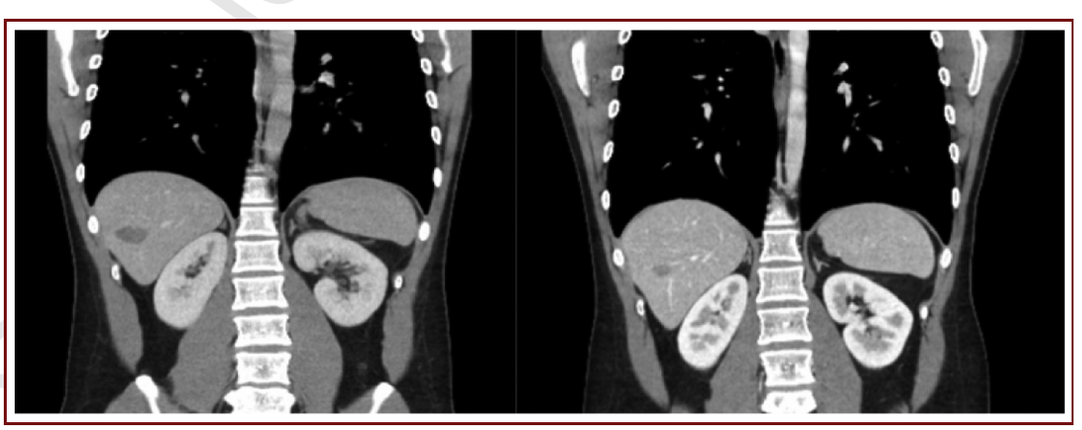

Figure 3. Downsizing of hepatic lesion during chemotherapy, from 27 mm (left image) to 18 mm (right image).

disease. Differentiating these two entities solely on clinical grounds can become a huge challenge, if not impossible.

3 Disclosure: The authors declare no conflict of interest.

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