A case of recurrent hepatic haemangioendothelioma

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ABSTRACT

Hepatic haemangioendothelioma is a rare (1:1,000,000) mesenchymal tumour of the liver of vascular origin. Metastatic malignancies, other primary liver tumours and cholangiocarcinomas all have significantly worse prognoses and may mimic hepatic haemangioendothelioma. Hence, careful pathological assessment with appropriate tumour markers and immunohistochemistry are essential. We present a rare case of recurrence of hepatic haemangioendothelioma after 10 years post-hemihepatectomy. Surgical approaches include liver resection, liver transplantation and ablative techniques with chemotherapy and radiotherapy reserved for patients where a surgical approach is not possible. Hepatic haemangioendothelioma has an unpredictable course that is generally indolent and it is associated with a significantly better long-term survival. Consequently, it is important that these tumours are recognised and the approach to the diagnosis should be methodical. Owing to the protracted course of the disease, a prolonged duration of surveillance and an aggressive approach towards disease recurrence are essential for long-term survival.

KEYWORDS

Liver – Haemangioendothelioma – Hepatic – Recurrent

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Background

Hepatic haemangioendothelioma (HHE) is a rare (1:1,000,000) mesenchymal tumour of the liver of vascular origin.¹ It was first described by Weiss and Enzinger in 1982 as a primary soft tissue tumour that is intermediate-grade, with a clinical course between that of a benign haemangioma and a highly-malignant angiosarcoma.² When epithelioid-type cells are present, these are further classified into hepatic epithelioid haemangioendotheliomas (HEH). Pathologically, prior to their recognition, they were also often misdiagnosed as metastatic carcinoma because they often present as multiple nodules with a solid growth pattern and variable radiological features. Following their description however, it was appreciated that they were a different entity with a lack of pleomorphism, mitotic activity and the presence of focal vascular channels on histology.²

Case history

A 50-year-old woman presented with right-sided abdominal pain and diarrhoea. She previously had a left hemihepatectomy and resection of segment six of the liver, with histopathology confirming HEH with clear margins (Figures 1 and 2).

Her original presentation in 2009 followed a computed tomography (CT) urogram for follow-up of a renal cyst that had been drained. The urologist in charge of her care referred her to the liver service in the belief that this was a metastatic disease, which was the conclusion from the radiologist based on the multiple nodules on the CT. Magnetic resonance imaging demonstrated multiple abnormal areas in the liver with additional bilateral lung nodules.

In view of the lack of an obvious primary site, a laparoscopy was performed which demonstrated no abnormality other than the liver lesions that were biopsied. The biopsies demonstrated complete loss of the normal liver architecture and residual islands of hepatocytes demonstrating variable degrees of ballooning with portal tracts and the remaining interstitium markedly expanded by an insidious infiltrate of pleomorphic epithelioid and spindle cells. The morphological features and the subsequent positive staining for the endothelial marker CD31 confirmed a diagnosis of epithelioid haemangioendothelioma.

The patient subsequently went on to have a liver resection (left hemihepatectomy and segment six) and eight weeks later, she underwent bilateral lung resections (video-assisted thoracoscopic surgery). Subsequent surveillance for the next 10 years showed no evidence of recurrence until the most recent surveillance imaging revealed recurrence at

the hepatic resection margins (Fig 3). This was resected again with a R0 margin and the patient recovered uneventfully. This case highlights a long duration to recurrence and overall survival. A prolonged surveillance is recommended as the natural history of the disease is unpredictable.

Discussion

HEH is more common in women, with a mean age of 41.7 years (range 40–65 years).^{2,5} Although the incidence of HHE is lower than angiosarcoma, it has a higher prevalence in the population owing to its indolent nature.¹ Metastatic malignancies, other primary liver tumours or cholangiocarcinomas all have significantly worse prognoses and may mimic HHE therefore, careful pathological assessment with appropriate tumour markers and immunohistochemistry are essential. The importance of recognising these tumours relates to their overall survival of 55%, which is significantly better than other hepatic malignancies.⁵

The symptoms of HHE can range from nonspecific abdominal discomfort to overt liver failure, with commonly described symptoms as right upper-quadrant pain, hepatomegaly and weight loss.⁴ Some patients may even present with Budd–Chiari syndrome when there is the involvement of the major hepatic veins. Although HEH has been described as a low-grade tumour, there is a high rate of regional and distant metastases; 87% of patients presented with bilobar and multifocal disease and 37% of patients were observed to have extrahepatic involvement.⁴ In contrast to many other types of primary liver tumour,

HEH does not arise on a background of chronic liver disease.

Cross-sectional imaging features of HEH may show predominantly peripheral hypodense discrete nodules or multiple lesions that may become confluent. Lesions typically have a hypovascular core, while the periphery of these tumours enhances with intravenous contrast. The definitive diagnosis is based on positive immunohistochemical

Figure 2 Portal venous phase computed tomography showing separate nodules in the left lobe, again in a peripheral location

Figure 1 Portal venous phase computed tomography showing peripheral hypoechoic lesions in the inferior right lobe. The lobulated appearance is probably due to separate lesions that have coalesced.

Figure 3 Venous phase magnetic resonance image. Anterior peripheral lesion consistent with recurrence, adjacent to the previous resection margin.

staining for factor VIII-related antigen (FVIII-RAg) and specific endothelial markers, such as CD-31 and CD-34.^{1,5}

Owing to the rarity and the variable clinical course of these tumours, there is currently no consensus on the treatment of HHE other than, as for all sarcomas, surgical resection is preferred where possible. Surgical approaches include liver resection, liver transplantation and ablative techniques with chemotherapy and radiotherapy reserved for patients where a surgical approach is not possible. The mode of treatment is decided mostly based on the presence or absence of extrahepatic involvement.

Surgical therapy, including liver resection and liver transplantation, are associated with the best prognosis, with five-year survival rates of 75% and 54.5%, respectively.⁴ However, liver transplantation is the most common treatment modality due to the difficulty of oncological resection as HEH tends to involve the liver in a diffuse manner, with 87% of patients presenting with the involvement of bilateral lobes.⁴ The largest analysis of HEH adult liver recipient cohort clearly confirms that extrahepatic disease localisation is not a contraindication for liver transplantation.⁵ However, the emergence of extrahepatic metastases at the time of diagnosis, presence of tumour necrosis, advanced mitosis grading, and a high Ki-67 proliferation index were unfavourable prognostic factors.⁶

In conclusion, although HHE has an unpredictable course, it is generally indolent and it is associated with a

significantly better long-term survival. Consequently, it is important that these tumours are recognised and the approach to the diagnosis should be methodical when unusual radiological features are present, especially when no primary site can be identified. Owing to the protracted course of the disease, a prolonged duration of surveillance and an aggressive approach towards disease recurrence are essential for long-term survival.

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