Editorial

Hepatic epithelioid hemangioendothelioma: is it actually "indolent"?

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Epithelioid hemangioendothelioma is a rare vascular tumor that was first described by Dail and Liebow involving the lung (1). It can arise in the liver, lung, and bone and has generally been thought to be an indolent lesion (2,3). Hepatic epithelioid hemangioendothelioma (HEHE), was first described by Ishak *et al.* in a case series (1). HEHE can involve the vasculature and extrahepatic involvement can be seen in 36.6% of patients (4). The etiology is unclear but there are reported associations with oral contraceptive use, alcohol consumption, liver trauma, sarcoidosis, Crohn's disease, viral hepatitis, and vinyl chloride or asbestos exposure (4-7). Diagnosis incudes characteristic findings of target like lesion on magnetic resonance imaging (MRI) (8) and infiltrative epithelioid cell growth with Factor VIII Ag, CD34 and CD31 staining positive on biopsy (9). Treatment options include surgical resection, liver transplantation, chemotherapy and radiotherapy (4).

In their recently published report, Dr. Ribeiro presented a case of rapidly progressing HEHE with delayed diagnosis (10). The authors used volumetric data from MRI showing a tumor percentage growth from 9% to 70% of liver, and a tumor growth of 964% over two years. The report is important in several aspects: it quantified the coalescence of nodules resulting in giant mass over time, as well as spreading to other organs, countering the preconception that HEHE is a slow-growing tumor, and tumor cells with transcription factor binding to IGHM enhancer 3 (TFE3) immunoreactivity indicating it as a case of recently described Yes1 associated transcriptional regulator (YAP1)-TFE3 fusion. The report also has important implications in terms of therapy: this patient underwent radiotherapy and sorafenib as surgery was not an option in multiorgan disease in the patient's country.

In terms of therapy options, surgical management is preferred when possible and it is associated with better survival (11). Liver resection is often the first choice for solitary tumors, however, due to the multifocal nature and presence of extrahepatic lesions, liver transplant has often been used. Two European series have reported liver transplantation for HEHE with rates of 5–10 years overall survival of 80.8–83% and 74–77.1% respectively (12,13). A third large retrospective series reported data from the United Network for Organ Sharing (UNOS) and reported a 5-year overall survival of 64% after liver transplantation for HEHE (14). In general, the rate of HEHE recurrence post liver transplant is of approximately 23.7% to 32% (12-14). The 5-year survival is significantly lower with chemotherapy (30%), or no treatment (4.5%) (4).

Dr. Ribeiro's report of rapid growing HEHE highlights the importance of early recognition of HEHE and referral for treatment, including surgery or chemotherapy and radiation. Further studies may define subtypes of HEHE with different growth patterns which can help guide prognosis and treatment options.

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