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Case report

Epithelioid Hemangioendothelioma a Rare Entity Cause of Chronic Abdominal Pain: Case Report

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Abstract

Epithelioid hemangioendothelioma is a rare entity with clinical, histological, and evolutionary features that are intermediate between hemangiomas and angiosarcomas; clinically features are generally unremarkable with a good general condition among patients. Histology remains the key for the diagnosis and the conservative treatment is the adequate option. We report the case of a 63 years old female, presented with chronic intermittent, atypical abdominal pain, unique atypical liver nodule with a histology compatible with an EHE and 1 year follow up without recurrence.

Keywords: ***Epithelioid hemangioendothelioma, chronic abdominal pain, liver nodule, Immunohistochemistry,***

Introduction

Epithelioid hemangioendothelioma (EHE) is a rare recently described vascular endothelial neoplasm considered to be with an intermediate malignancy occurring primarily in bone, soft tissue, lung, and liver. The tumor was first described by first described by Weiss and Enzinger in 1982 [1]. In the current classification of the World Health Organization, EHE are classified as locally aggressive neoplasm with potential local recurrence and metastatic state [2]. In this case report we describe a case of liver EHE revealed by chronic abdominal pain in a 63 years old female.

Case report

Patient information

A 63-year-old patient, who's known to be diabetic on metformin and hypertensive on ARB II, who had undergone cholecystectomy 16 years previously, was admitted for exploration of chronic intermittent, atypical abdominal pain in the right hypochondrium. No other functional signs were reported by the patient, especially no vomit, no jaundice, no transit disorders, digestive hemorrhage, or any other associated extra-digestive signs and no alteration of the general state.

Clinical findings

The clinical examination was unremarkable except for an abdominal tenderness in the right hypochondrium without palpable masses. Biological workup showed a hemoglobin at 12.9 g/dl, white blood cells at 7,570/uL, platelet count at 201,000/uL, PCR negative at 3.32 mg/L, tumor markers negative, alpha-feto-protein at 2, CA19-9 at 1. 8, CA125 at 9.9, carcinoembryonic antigen at 2.8, with a normal hepatic workup, negative hepatitis B and C serologies, a lipid workup, triglyceride at 1.29, HDL at 0.53, LDL at 1.22, total cholesterol at 2.01, fasting blood glucose at 1.14.

Diagnostic assessment

An abdominal ultrasound was performed showing a steatotic liver, with doubt about the presence of a suspicious heterogeneous hypoechoic, lesion of segment III which leaded to performing a magnetic resonance imaging that showed a suspicious lesion of segment III measuring 22-23 mm of the liver whose vascular kinetics (spontaneously hyperdense with heterogeneous enhancement at portal and late time), this lesion is surrounded by a peripheral halo in T1 hypo-signal, in T2 iso- signal and enhanced in late time made us suspect a HCC on healthy liver? (**Figure 1**) Or a fibro lamellar carcinoma? A lookup for primary malignancy was performed, including gastroscopy, colonoscopy, endo-vaginal ultrasound. All of these tests were negative.

An echo-guided liver biopsy was performed, showing a papillary epithelial neoplasia on a background of chronic liver disease. With immunohistochemistry, an intense and diffuse expression of tumor cells of papillary epithelial neoplasia of anti CK7, CK19 antibodies evoking a morphological and immunohistochemical aspect of a papillary intraepithelial neoplasia of biliary type (BILIN1) without sign of malignancy on the analyzed material.

Therapeutic intervention

The decision was to perform an exploratory laparotomy, which revealed a segment III liver nodule without peritoneal carcinosis; left hepatectomy was performed removing the tumor segment and anatomopathological examination with a complementary immuno-histochemical showed a moderate positivity for CD31 and a diffuse positivity for CD34 (**Figure 2**) which is in favor of a hepatic epithelioid hemangioendothelioma. The extension CT scan ruled out secondary localization. Post-operative follow-up was simple. And patient is under annual checkup with no recurrence at 1 year.

Follow up and outcomes: the patient was followed up at 1 year and is doing well with no recurrence.

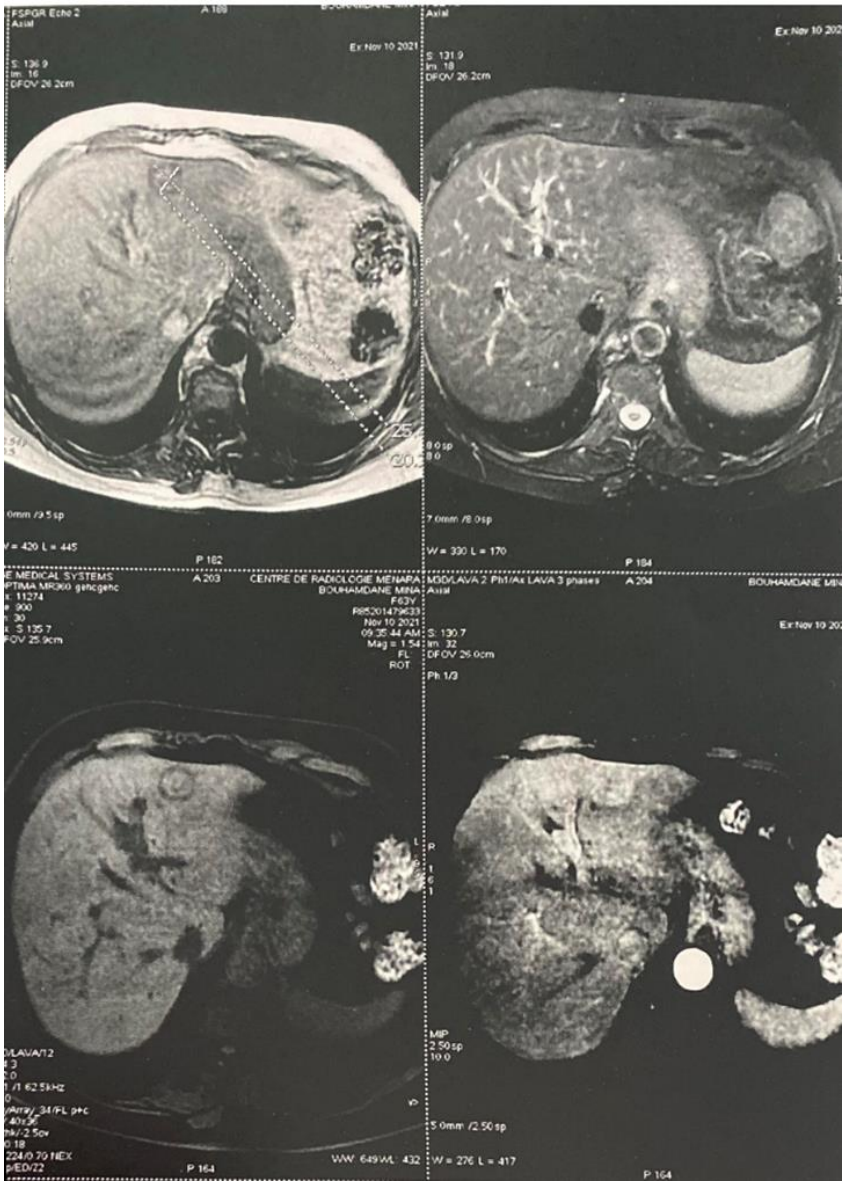

Figure 1: Liver MRI showing an Iso-signal aspect of the segment III nodule and a late filling of the lesion with a multicentric target appearance and a hypointense peripheral halo.

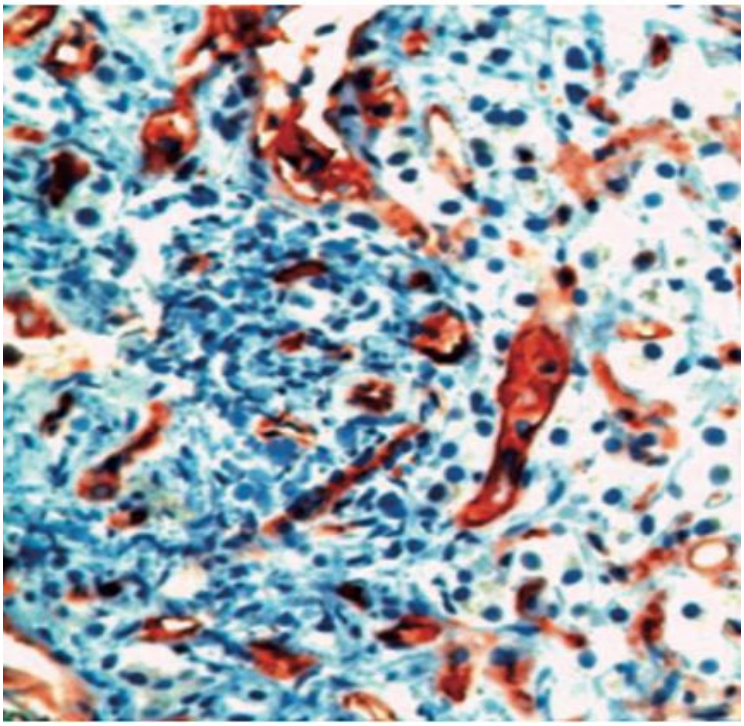

Figure 2: IHC showing a positivity of anti CD34

Discussion

Epithelioid hemangioendothelioma is a rare entity classified as a heterogeneous group of vascular tumors with clinical, histological, and evolutionary features that are intermediate between hemangiomas and angiosarcomas; they are therefore "borderline" tumors [3]. It was first described by Dail and Liebow in 1975. In 1982, Weiss and Enzinger defined the term epithelioid hemangioendothelioma, the current name, for a vascular soft tissue tumor with a histology mimicking a carcinoma but a clinic intermediate between benign hemangioma and highly aggressive angiosarcoma [4-6]. Epidemiologically, EHE is more common in women and the mean age of discovery is 45 years [7,8]; and is most often found in bones, lungs, liver, brain, heart or retroperitoneum. Oral contraception and vinyl chlorure exporure are some risk factors that has been incriminated [7,9].

The revealing symptoms are highly different and non-specific, most often incidental. Abdominal pain is the most frequent finding, the general condition is usually preserved, but weight loss is noted in 22% of patients [10]. Exceptionally, it may be revealed by a Budd-Chiari syndrome following invasion of the suprahepatic veins, hemoperitoneum, hepatocellular insufficiency or portal hypertension. Biologically, there is no specific marker and liver balance disturbances are inconsistent at the time of diagnosis. Moderate elevation of alkaline phosphatase activity is observed in 54 to 70% of cases, gamma-glutamyl transferases in 16% of cases and transaminases in 10 to 18% of cases. Tumor markers (alpha-fetoprotein, CEA and CA19-9) are consistently absent in serum [10,11].

The literature data regarding the imaging of hepatic EHE are limited, it is usually a single nodular lesion demonstrated in 11% of patients; it seems to represent the early form of HEE, as in our observation, and then the multinodular form. The tumors are calcified in 13% to 20% of cases. A retraction aspect of the liver capsule is observed in 11% to 25% of cases for peripheral lesions [10,12,13]. On ultrasound, epithelioid hemangioendotheliomas are characterized by a multi-heteronodular and heterogeneous hypoechoic appearance [14]. The CT scan shows: initially an hypodense nodular lesions, enhanced in the periphery after injection of contrast; and then a late or diffuse phase, characterized by confluent nodular lesions, large hypodense patches, rather peripheral. The primary differential diagnosis is that of liver metastases [13,14]. On MRI, lesions are homogeneous, with hyposignal in T1 and heterogeneous in T2, enhancement is progressive, centripetal. None of these aspects is specific and the primary differential diagnosis are liver metastasis, hepatic cholangiocarcinomas or atypical angioma. Extrahepatic localizations are frequent (57% of cases) and present in 30% of cases at the time of diagnosis [10]; unlike our case there was no secondary localization.

Histologically, EHE is characterized by spindle-shaped epithelioid cells arranged in nests or cords with intracytoplasmic vacuoles in a myxohyaline stroma. Intracytoplasmic vacuole formation represents the primitive vascular differentiation of endothelial cells.Venous invasion is a constant and characteristic sign. Dissemination of tumor cells occurs along the sinusoids, progressively destroying the hepatic architecture. There is never invasion of the arterial lumen and bile ducts [10]. The immunohistochemical study is essential; it confirms the vascular nature of the tumor which expresses in the core biopsy samples endothelial markers such as factor VIII RAG, vimentin, CD 31 (CD=Cluster of differentiation) and sometimes CD 34, as well as Ulex Europaeus; there is also a significant positivity of the Fli-1 protein for HEE. Epithelial markers are usually negative.

The evolution without treatment is unpredictable and life expectancy can be long.The choice of treatment is discussed on a case-by-case basis, from simple clinico-radiological monitoring, through liver resection and chemotherapy, to possible liver transplantation. Curative surgery is the treatment for liver EHE in case of an isolated, single and accessible lesion, as in our case, simple surgical resection is recommended, even if recurrences after resection are found to be very aggressive. In case of an inoperable or multifocal lesion, careful monitoring can be proposed as a first line treatment. The goal of systemic therapy is palliative aiming to slow the progression of the disease and maintain quality of life. There is no standard systemic treatment. When patients present with clinical signs (deterioration of general condition, fever, hemolytic anemia, coagulation disorders, pleural or peritoneal effusions), systemic treatment should be considered, but there is no consensus on this subject [17]. The survival of patients with HEE is highly variable. Some live for decades without treatment with metastasis and others die within months despite treatment. In the literature, the average survival rate is 64% at 1 year, 38% at 3 years and 25% at 5 years.

Despite various encouraging retrospective observations, there is currently no consensus regarding the treatment of hepatic epithelioid hemangioendothelioma, given the rarity and highly variable evolution of this pathology. Moreover, the location of the disease depends on the appropriate therapy [18].

Conclusion

The diagnosis of HEE should be suspected in front of unique or multiple focal lesions that presents a halo enhancement post-injection. The key to the diagnosis remain histology with Immunohistochemistry which should reveal cells containing factor VIII-associated antigen, and positivity for CD31, CD34wich confirms the vascular origin of the tumor cells. Treatment is essentially surgical and should be as conservative as possible.

Conflicts of interests

The authors declare no conflicts of interest.

Author's contributions

All the authors have read and agreed to the final manuscript.

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