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CONTRAST-ENHANCED CT AND ANGIOGRAPHIC FINDINGS IN HEPATIC PERIVASCULAR EPITHELIOID CELL TUMOR

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We report a case of hepatic perivascular epithelioid cell tumor (PEComa) in a woman who was not a carrier of viral hepatitis and had a normal alpha-fetoprotein (AFP) level. CT scan showed a well-enhanced mass in the arterial-phase followed by early washout in the portal venous-phase in the lateral segment of the liver. Angiography revealed a hypervascular tumor in the liver with rapid washout of the contrast. If a hepatic tumor is found in a female patient with normal AFP level who is not a carrier of hepatitis and is free of alcoholic liver cirrhosis, tissue biopsy should precede treatment to avoid misdiagnosis of liver PEComa as hepatocellular carcinoma.

Key-word: Liver neoplasms, angiography.

Perivascular epithelioid cell tumors (PEComas) belong to a family of mesenchymal neoplasms that include angiomyolipoma, clear-cell "sugar" tumors of the lung and other organs, lymphangiomyomatosis, and a rare group of morphologically and immunophenotypically similar lesions that may affect soft tissues, viscera, and bones (1-3). Perivascular epithelioid cells were named by Bonetti et al. (4) to describe the epithelioid cells found in these neoplasms. PEComas, which are immunoreactive with melanocytic markers, have been reported to occur at almost all body sites, and have an epithelioid appearance, clear-acidophilic cytoplasm, and perivascular distribution. The uterus is the most prevalent reported site of involvement. Primary hepatic PEComas are extremely rare, and only 12 cases have been reported before (5-15), most being monotypic or epithelioid angiomyolipomas. Most cases of PEComa are benign, but two cases of metastatic PEComa have been reported. PEComas of the liver have been misdiagnosed by imaging as focal nodular hyperplasia, adenoma, or hepatocellular carcinoma. No angiographic findings of PEComas have been previously reported.

We report a case of PEComa of the liver diagnosed by 'early washout' of the lesions on computed tomography (CT) and angiographic scans.

Case report

A 51-year-old woman with a history of ovarian cancer received an oophorectomy 34 years earlier and wedge resection for a gastric tumor (intramuscular gastrointestinal stromal tumor [GIST] with submucosal leiomyoma) 3 years earlier. The patient had no history of tuberous sclerosis. She had poor appetite, with body weight loss of 6 kg in 1 month. Abdominal ultrasound showed a mixed-echoic mass in the left lobe of the liver. CT scan of the abdomen showed a 9-cm well-defined heterogeneously enhancing mass lesion in segments 2 and 3 of the liver. The mass was enhanced in the hepatic arterial-phase scan with early washout in the portal venous-phase scan (Fig. 1). The level of the alpha-fetoprotein tumor marker was 2.29 (normal range: 0-20 ng/ml). Angiography revealed a hypervascular tumor stained in the lateral segment of the liver and rapid washout of the tumor (Fig. 2). The tumor displaced the left gastric artery and compressed the stomach. Hepatocellular carcinoma (HCC) was diagnosed and treated with surgery. At surgery, a well-encapsulated elastic-to-firm tumor measuring $9.0 \times 8.8 \times 5.8$ cm was found in the left hepatic lobe, and hepatic S2 and S3 bisegmentectomy was performed. On histological examination, central necrosis was found in the part of the capsule showing low density on the CT scan. The parenchymal tumor resembled a PEComa, and histological examination of tumor sections revealed numerous tortuous vessels with radiating sheets, nests, and fascicles of epithelioid and spindle cells displaying clear to granular eosinophilic cytoplasm, round to oval nuclei, prominent nucleoli, and 1-2 mitotic figures per 10 high-power fields. Focal multinucleated giant cells and cytologic atypia were observed (Fig. 3). The tumor cells were diffusely positive for HMB-45, vimentin, and smooth muscle actin; focally positive for S-100 protein, and negative for cytokeratin, desmin, CD21, CD117, and CD34, immunohistochemically confirming the diagnosis of hepatic PEComa (4). The patient had no tumor recurrence at her 9-month follow-up visit.

Discussion

The clinical presentation of hepatic PEComa has no specificity. The symptoms and signs are similar to those of other tumors arising from the liver. Generally, indigestion, loss of appetite, nausea, body weight loss, and intermittent colic pain can occur, and on physical examination tenderness to palpation and liver enlargement may be observed. These tumors have occurred in female patients aged from 13 to 70 years (median age: 55) (5-15). Of the reported 12 cases (5-15), 6 cases occurred in the left lobe (7-9, 11, 14, 15), 4 in the right lobe (5, 6, 10, 12), 1 in the caudate lobe (7), and 1 in the ligamentum teres (13). Tumor sizes ranged between 1.5 and 20 cm. Four patients had normal levels of serum AFP and were negative for hepatitis B surface antigen and anti-hepatitis C virus antigen (6, 10, 12, 15); reports of the other 8 cases did not mention this. Two patients had a history of melanoma (13, 14), and 1 had a history of GIST (8). Four had no history of tuberous sclerosis.

Our patient had a history of GIST in the stomach 3 years prior to diagnosis of PEComa in the liver. Carlos et al. (8) reported a case of PEComa coexisting with GIST. Loss of heterozygosity (LOH) in chromosome 16p (harboring the TSC2 locus) has been detected in some PEComas, but it has not been investigated in GISTs (1, 3). Based on this finding, we conclude that the coexistence of these two lesions in our case is a coincidence.

PEComas are characterized by their perivascular location, often with a radial arrangement of cells around the vascular lumen. Typically, the cells in PEComas are mainly epithelioid in the immediate perivas-

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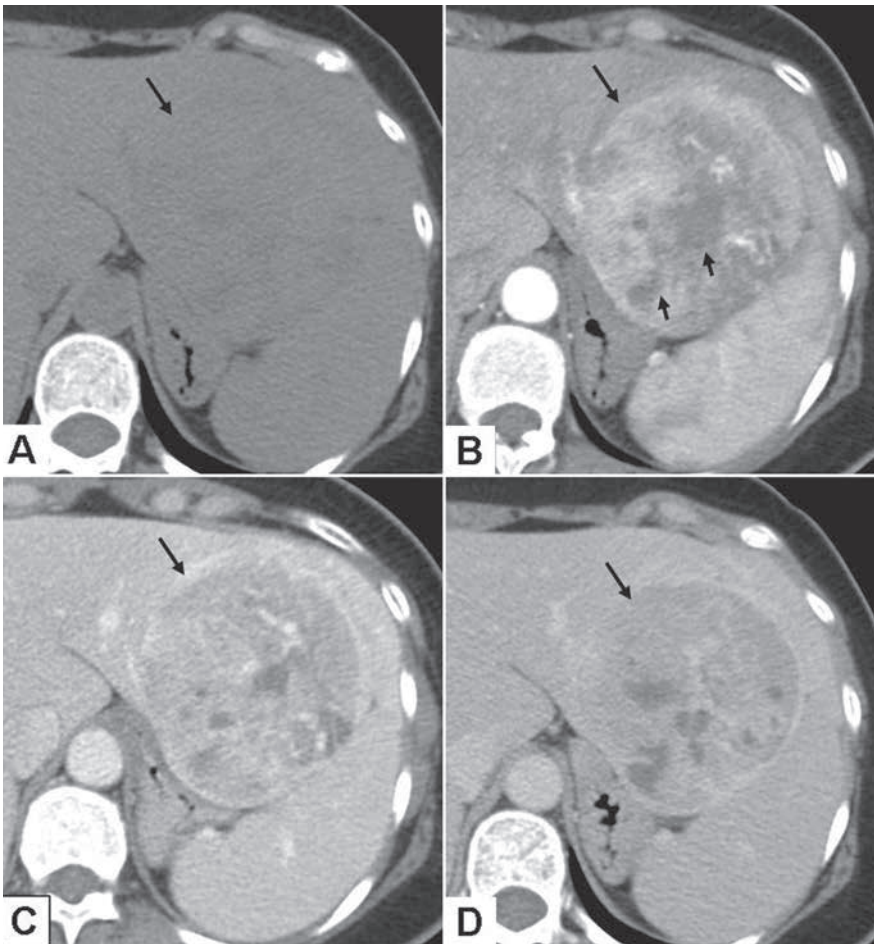

Fig. 1. — Dynamic three-phase CT scan of the liver. (A) Non-contrast image showing a isodense mass (arrow) in the left lobe of the liver. (B) Arterial phase showing encapsulated mass (arrow) with heterogeneous enhancement and central necrosis (small arrows). (C) Fast washout of the tumor mass (arrow) in the portal venous phase. (D) Delayed phase showing an isodense area of the mass (arrow).

cular location and mainly spindle shaped resembling smooth muscle cells away from vessels. PEComas are characteristically positive for melanocytic markers, such as HMB-45, Melan-A, smooth muscle actin, and muscle-specific actin; less often positive for desmin, CD117, and S100, and usually negative for cytokeratin (4).

Of the 12 reported cases (5-15), abdominal ultrasonographic findings varied from hypoechoic to hyperechoic in 5 cases of PEComa (6, 7, 13-15). CT scans in 5 cases revealed a well-demarcated mass, without fatty density; only 1 case had peripheral calcification. Of these 5 cases, 3 cases showed early enhancement and early washout pattern and were misdiagnosed as HCC. The tumors have also been misdiagnosed as focal nodular hyperplasia, adenoma, or hepatocellular carcinoma (7, 11, 12, 15).

MRI in the 5 cases of PEComa revealed heterogeneous or homogeneous low signal on T1-weighted images, heterogeneous or homogeneous high signal on T2-weighted images, and no notable signal drop on T1-weighted fat suppression images (6, 7, 11, 14, 15). The MRI in 2 of the 5 cases showed homogeneous contrast enhancement in the arterial phase and rapid washout in the venous phase (6, 7). The MRI in one case showed homogeneous enhancement in the arterial and venous phases (14). No contrast was administered in two cases (11, 15). Ji et al. reported an enhancement pattern (related to tumor hypervascularity with central punctiform or filiform vessels) that was characteristic of PEComas and different from that of other hepatic tumors. The enhancement pattern can be divided into two types: lesions with abundant central vessels showing rapidly decreased enhancement; and lesions with small or no vessels demonstrating prolonged enhancement in the portal venous/delayed phase (16). Our angiographic images of PEComa revealed abundant central vessels and rapid washout in the delayed phase, which was compatible with the enhancement pattern seen in CT scan images.

The PEComas in these 12 cases had no fat component, hemorrhage, cystic component, or central scarring on CT or MRI. Necrosis was present in large but not small PEComas.

In 4 cases, the diagnosis of PEComa was biopsy proven, and complications were not mentioned. The resections of these 12 tumors ranged from tumorectomy to hemihepatectomy (5-15). In most cases, PEComas are benign, and patients have good postoperative prognosis and no recurrence after several months of follow-up. However, in 2 of the 12 cases, the PEComas metastasized (5, 10). Thus, PEComa is potentially malignant, and surgery is required when biopsy-proven PEComa is diagnosed.

Folpe and colleagues (3) suggested diagnostic criteria for malignant PEComa, including a size greater than 8.0 cm, mitotic count of more than 1 per 50 high-power fields, and necrosis; a division into benign, uncertain malignant potential, and malignant categories has been based on the presence of none, 1, 2, or 3 of these criteria, respectively. Infiltrative growth or edges, marked hypercellularity, and marked nuclear pleomorphism/atypia may be secondary features suggesting aggressive behavior or malignancy.

According to the American Association for the Study of Liver Diseases, HCC can be diagnosed by imaging studies and AFP elevation without confirmation by biopsy. Therefore, most centers rely on imaging studies (CT, MRI, and angiography) instead of biopsy for the diagnosis of HCC, but nonhistologic (imaging) criteria are not standardized. Consequently, PEComa may be misdiagnosed as HCC and mistakenly treated with transcatheter arterial chemoembolization.

In summary, if a hepatic tumor is found in a female patient who is a non-HBV and non-HCV carrier with normal AFP level and no alcoholic liver cirrhosis, tissue biopsy should be done before treatment so that PEComa in the liver is not misdiagnosed as HCC and then treated with transcatheter arterial chemoembolization.

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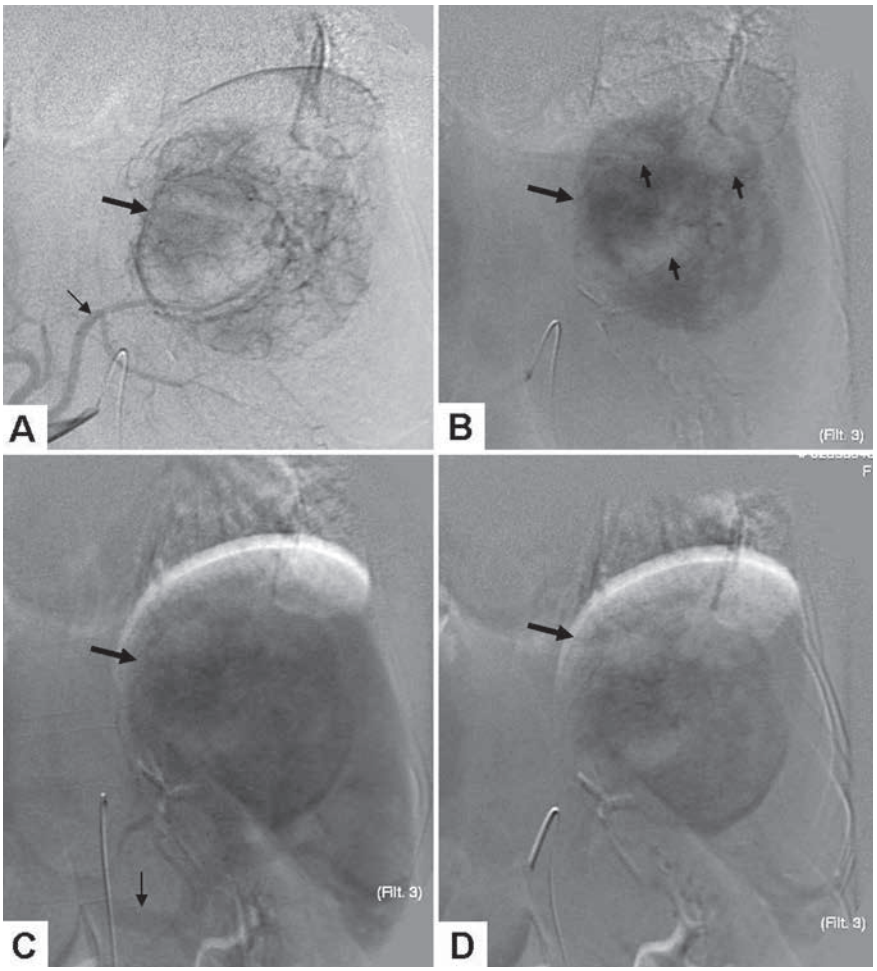

Fig. 2. — Angiography showing a mass in the lateral segment of the left lobe of the liver. (A) Neovascularity (thick arrow) of the left hepatic artery (thin arrow) in the early arterial phase. (B) Tumor stain (arrow) in the late arterial phase. Note that avascular zone represents central necrosis (small arrows). (C) Portal phase showing washout of the tumor stain (arrow). Small arrow indicates the portal vein. (D) No tumor stain in the late venous phase.

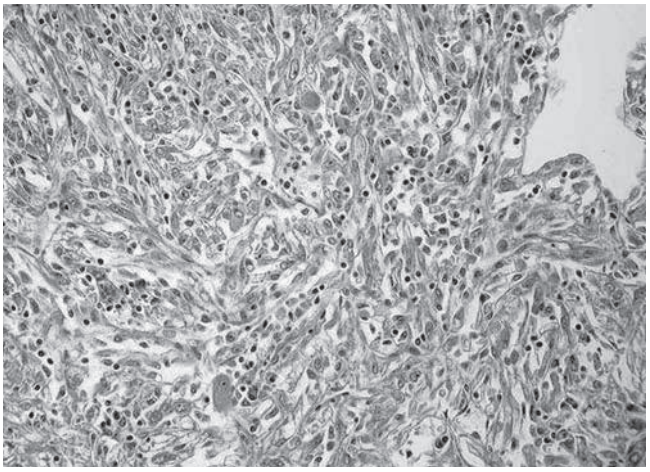

Fig. 3. — Photomicroscopic image shows numerous tortuous vessels with radiating sheets, nests, and fascicles of epithelioid and spindle cells displaying clear to granular eosinophilic cytoplasm, round to oval nuclei, prominent nucleoli and 1 or 2 mitotic figures per 10 high-power fields (H & E).

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