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Adrenal Cortical Adenoma Developed in Adrenohepatic Fusion, a Mimicry of Hepatocellular Carcinoma – A Case Report –

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Adrenohepatic fusion is the union of the liver and adrenal gland with close intermingling of their respective parenchymal cells. Adrenal cortical adenoma arising in adrenohepatic fusion tissue is extremely rare, although adrenohepatic fusion itself is relatively common. Here we report a case of a 59-year-old man with a mass in the right lobe of his liver. The mass showed slight hyperattenuation during arterial phase and hypoattenuation during portal phase on dynamic computed tomography with contrast enhancement. On pathology, the mass consisted of round to polygonal cells with clear microvesicular or eosinophilic cytoplasm, arranged in nests or in a trabecular pattern. The tumor cells were positive for inhibin and melan-A, but negative for Hep Par-1. In the periphery of the mass, adrenohepatic fusion was identified between the liver and adrenal gland, and was simultaneously resected with the mass. We report this rare case, and discuss its clinical implications, especially the differential diagnosis with hepatocellular carcinoma.

Key Words: Adrenocortical adenoma; Carcinoma, hepatocellular; Fusion, adrenohepatic

Adrenohepatic fusion is characterized by the presence of a fragmented capsule or complete absence of capsular elements, allowing admixture of the parenchyma of the liver and adrenal gland.[1] The pathogenesis of adrenohepatic fusion could be either a developmental defect in formation of the periadrenal capsule,[2] or an acquired capsular defect from unknown causes. This is not an uncommon anatomic condition according to a large autopsy study.[3] However, an adrenal cortical adenoma in adrenohepatic fusion tissue has been encountered rarely and there are only a few reports that describe its clinicopathologic features.[4] Awareness of intrahepatic adrenocortical adenoma is important because radiologically and pathologically, it mimics hepatocellular carcinoma. Here we report a case of intrahepatic adrenal cortical adenoma arising in adrenohepatic fusion tissue, and we discuss its clinical implications.

CASE REPORT

A 59-year-old man was referred to our institute due to a hepatic mass discovered by computed tomography (CT) at an outside hospital during his regular medical check-up. He was previously healthy without any symptoms. Laboratory investigations were unremarkable. Hepatitis B virus antigen and anti-hepatitis C virus antibody were all negative. The alpha-fetoprotein level (3.9 ng/mL) was within normal limits (normal value < 20 ng/mL). Serum hormone levels were not checked because he had no hormone-related symptoms. Transabdominal ultrasonography revealed a bulging, low echoic mass at the posterior segment of the right hepatic lobe. On abdominal multiphasic dynamic CT with contrast enhancement, the mass showed slight hyperattenuation during arterial phase (Fig. 1A) and early washout during portal phase (Fig. 1B). Based on this dynamic enhancement pattern, hepatocellular carcinoma was the primary suspect. Ultrasonography-guided needle biopsy of the mass followed. Polygonal cells with a clear microvesicular cytoplasm and a trabecular growth pattern suggested the diagnosis of a clear cell variant of hepatocellular carcinoma.

The patient underwent right posterior segmentectomy of the liver. During the operation, the right adrenal gland was found to be adherent to the mass and the adjacent liver. Therefore, a part of the right adrenal gland was excised with the hepatic segment because it could not be separated from the liver by blunt dissection. The resected hepatic segment exhibited a well-de-

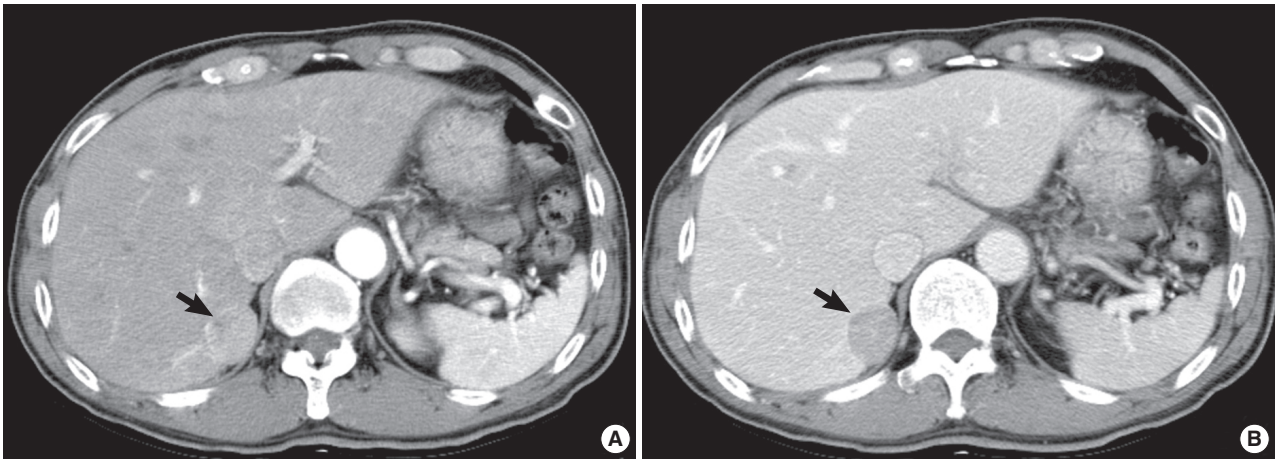

Fig. 1. Abdominal multiphasic dynamic computed tomography with contrast enhancement. (A) The mass (arrow) shows slight hyperattenuation during arterial phase, and (B) hypoattenuation during portal phase.

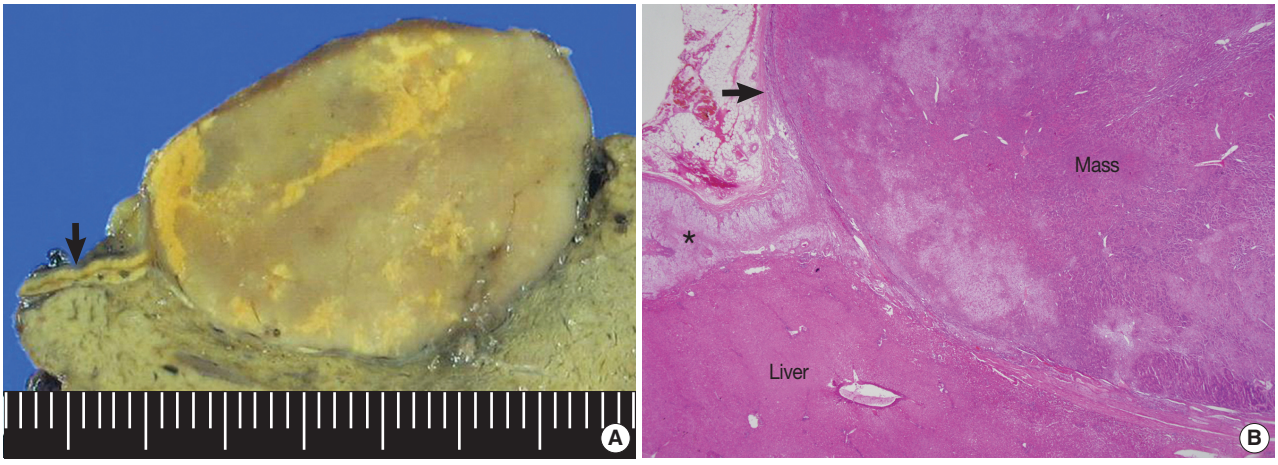

Fig. 2. (A) Photograph of the gross anatomy of a resected liver. A well-defined round protruding mass (3.0×3.0×2.5 cm) shows yellowish gray and solid cut surface with golden yellow areas. Note that a part the adrenal gland is attached to the mass (arrow). (B) Photomicrograph of the mass. The mass is well-demarcated and bulging contoured. The Gleason's capsule overlying the mass is continuously covering the adrenal gland (arrow). Note the adrenal gland (asterisk).

marcated round protruding mass measuring 3.0×3.0×2.5 cm (Fig. 2A). The cut surface of the mass was yellowish gray, solid and firm with golden yellow areas. Neither hemorrhage nor necrosis was identified. A part of the adrenal gland was invaginated into the liver and attached to the mass. The hepatic capsule overlying the mass was continuously covering the adrenal gland (Fig. 2B).

Microscopically, the tumor consisted of nests or trabeculae interrupted by fine sinusoidal capillary networks. The tumor cells were round to polygonal and had clear microvesicular cytoplasm with distinct cell membranes and round to ovoid nuclei. More compact areas consisting of smaller cells with eosinophilic granular cytoplasm were also found (Fig. 3A). Instances of cellular atypia were few and mitotic figures were not identified. The diagnosis of adrenal cortical adenoma was rendered based on the histologic findings and was supported by positive immunostaining for inhibin alpha (1:50, R1, Serotec, Oxford, UK) (Fig. 3B) and melan-A (1:50, A103, Novo, Newcastle, UK) (Fig. 3C) and negative immunostaining for Hep Par 1 (1:200, OCH1E5, Dako, Glostrup, Denmark). The adrenal gland and the liver were separated by a thin fibrous capsule over most of their apposed surfaces. However, multiple foci of the defect were identified in the capsule through which the parenchymal cells of the two organs had direct contact with each other (Fig. 4). This finding was consistent with adrenohepatic fusion.

A follow-up CT a month postoperatively demonstrated an

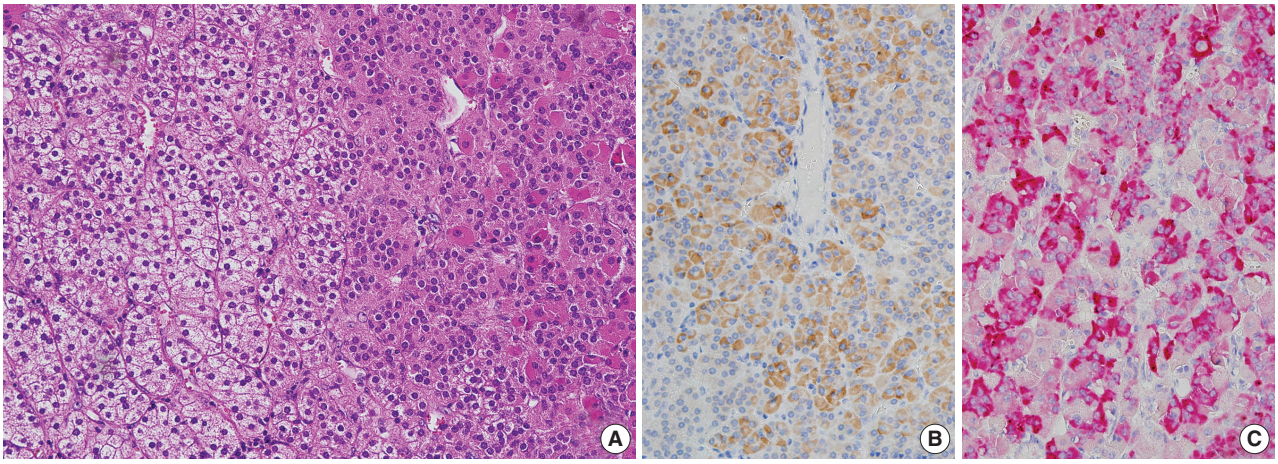

Fig. 3. (A) The tumor consists of cell nests or trabeculae with fine capillary networks. The cells have clear microvesicular (left half) or eosinophilic (right half) cytoplasm and uniform round nuclei without atypia. (B) The tumor cells show cytoplasmic positivity for inhibin and (C) melan-A.

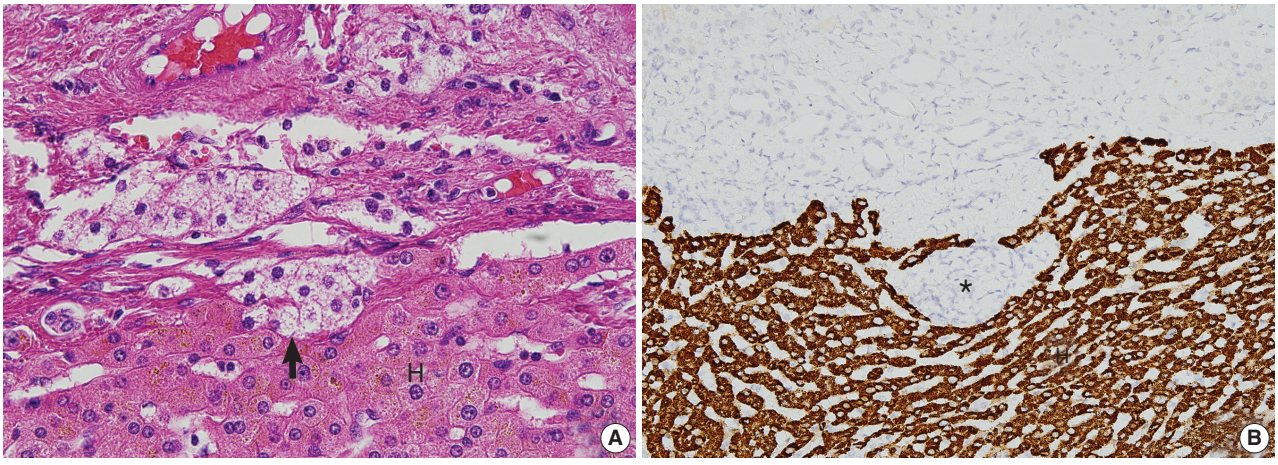

Fig. 4. The site of adrenohepatic fusion. (A) The adrenal cortical cells (arrow) have direct contact with hepatocytes (H) at the site of adrenohepatic fusion. (B) Hep Par 1 staining highlights the admixture of hepatocyte (H) and adrenal cortical cells (asterisk).

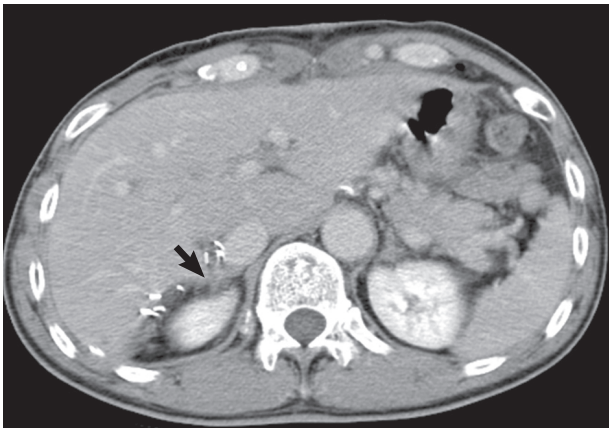

Fig. 5. Postoperative abdominal contrast-enhanced computed tomography. An incompletely remaining adrenal gland (arrow) is in the hepatic segmentectomy site.

incompletely removed right adrenal gland at the site of the hepatic segmentectomy (Fig. 5). We reviewed the situation on a preoperative CT and confirmed that the location of the adrenal gland remaining postoperatively was the same as that of the preoperative normal right adrenal gland that had adhered to the mass.

During a one and a half-year postoperative period, there were no remarkable complications or signs of tumor recurrence.

DISCUSSION

According to the descriptions of Schechter,[5] aberrant adrenal tissue is classified into adrenal heterotopia and aberrant adrenal rest. The latter is an accessory adrenal gland associated with a

normal orthotopic adrenal gland on the same side, whereas the heterotopic adrenal gland is the only adrenal gland on that side that is partly or wholly incorporated into contiguous organs such as the kidney or liver. Heterotopic adrenal gland clinging to the liver is further subdivided into adrenohepatic fusion and adrenohepatic adhesion. Histologically, the adhesions have an intact connective tissue septum of variable thickness interposed between the parenchymatous elements of either organ. In adrenohepatic fusion, an intervening connective tissue septum is at least partially lacking.[1,6,7] The pathogenesis of adrenohepatic fusion is not yet clear. The proposed mechanism is a defect or delay in the formation of organ capsules from the periadrenal mesenchymal stroma in during development.[2] In contrast, a higher incidence of adrenohepatic fusion at autopsy in adults than in children suggests that it may be an acquired abnormality.[3] Adrenohepatic fusion has clinical implications in that adrenal metastasis from hepatocelluar carcinoma could be occurring through an adrenohepatic fusion,[8] and heterotopic adrenal tissue might be accidentally removed during hepatectomy for other reasons.

In a large autopsy study, Honma[3] found adrenohepatic fusion in 63 of 636 autopsies (9.9%) indicating that this was a relatively common anatomic condition. However, adrenal cortical adenomas in the liver parenchyma have been rarely encountered. Most of the reported cases were adrenal rest tumors, which means the adrenal cortical tumors originated from accessory adrenal tissue in the liver with intact adrenal glands in their normal position.[9-11] To our knowledge, a single case of adrenal cortical tumor in adrenohepatic fusion tissue has been described in the literature.[4]

By using postoperative follow-up CT, we identified incompletely removed right adrenal gland at the site of the hepatic segmentectomy and confirmed that the location of the remaining adrenal gland was the same as that of the normal right adrenal gland that had adhered to the mass. We failed to identify adrenal gland other than this by preoperative or postoperative abdominal CT, which means this was the orthotopic adrenal gland, not an ectopic gland. Therefore, the possibility of adrenal rest tissue in the liver was excluded. Adhesion between liver and adrenal gland can be an acquired condition resulting from severe inflammation involving the two organs.[6] However, this was not the cause in our case because the patient had no history of inflammatory disease and because there was no histological evidence of previous inflammatory processes such as a healing scar or architectural distortion of the parenchyma. Additionally, intimate intermingling of adrenal cortical cells and hepatocytes was observed, apparently suggesting that our case is a true example of intrahepatic adrenal cortical adenoma developed in adrenohepatic fusion tissue.

Intrahepatic adrenal cortical adenoma can be misdiagnosed as hepatocellular carcinoma, both radiologically[4,8,10] and pathologically.[12] Either tumor may be seen by contrast-enhancement CT as a hypodense mass with hyperattenuation during arterial phase and hypoattenuation during delayed phase.[4,8,10] Careful investigation may reveal incorporation of the right adrenal gland into the liver under the hepatic capsule and absence of a fat plane between liver and adrenal gland, which would be a clue that would make us suspect intrahepatic adrenal cortical adenoma.[4] Pathologically, a needle biopsy specimen of adrenal cortical adenoma could be confused with a clear cell type of hepatocellular carcinoma because of their histologic similarity. The cells of adrenocortical adenoma may be arranged in a cord or trabecular pattern with abundant vasculature and a sinusoidal structure, all of which are characteristics of hepatocellular carcinoma. On the other hand, some hepatocellular carcinomas may consist of cells with clear cytoplasm or microvesicular fatty changes, simulating adrenocortical adenoma. Immunohistochemical staining for each entity, for example, inhibin or melan-A for adrenocortical adenoma and hepatocyte antigen for hepatocellular carcinoma, would be helpful.

In conclusion, if there is a mass in the right posterior hepatic lobe, and if the right adrenal gland is found to have close approximation to a liver mass on an imaging study, biopsy is needed and immunohistochemical staining should be done to investigate the possibility of adrenocortical adenoma before starting aggressive treatment for hepatocellular carcinoma.

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