Case Report
A rare case of hepatoid adenocarcinoma of the adrenal gland

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Abstract: Hepatoid adenocarcinoma (HAC) is a rare type of extrahepatic adenocarcinoma, with morphological characteristics identical to hepatocellular carcinoma (HCC). HAC is difficult to accurately diagnose because of its clinical similarity to HCC. The diagnosis is always achieved by pathological examination after the surgery. This case report describes a sixty-year-old male patient who was referred to the Shandong Provincial Hospital due to right abdominal discomfort. The computed tomography showed a cystic solid mass in the adrenal region. The patient was operated with the diagnosis of adrenal tumor. The pathological examination following surgery showed right adrenal HAC. Furthermore, the tumor cells were immunohistochemically positive for Heppar1+, Glapican3+ and CK+. The histological features together with the immunohistochemical findings confirmed the diagnosis of a rare case of HAC of the adrenal gland.

Keywords: Hepatoid adenocarcinoma, adrenal gland, immunohistochemical finding, AFP

Introduction
Hepatoid adenocarcinoma (HAC) of the adrenal gland is a particular type of adrenal tumor with adenoid and hepatocyte differentiation. In 1985, a alpha-fetoprotein-producing gastric adenocarcinoma with hepatocyte characteristics was reported by Ishikura et al [1]. HACs have been reported in the stomach, duodenum, colon, gallbladder, pancreas, lung, urinary bladder, and adrenal gland [1-9]. HAC is reported to occur with lymph node and liver metastasis and exhibits poorer prognosis than common carcinoma [10]. We report a case of a sixty-year-old male patient with right abdominal discomfort. Ultrasound and computed tomography (CT) showed a cystic solid mass in the right adrenal gland region with no other pathology finding. Our patient is still surviving (after 30 months).

Case presentation
A sixty-year-old man presented with right abdominal pain for two days prior to admission. Ultrasound showed a cystic solid mass with low density and enhancement under abdominal CT in the right adrenal gland region (Figure 1A, 1B).

The imaging specialists considered the mass as pheochromocytoma. There was no other pathology detected in ultrasound and CT. Gastrointestinal barium examination from esophagus to duodenum only found gastritis. AFP was 6.39 ng/ml, aldosterone was 257.20 pg/ml, and cortisol was 748.50 nmol/L. The patient was operated with the diagnosis of adrenal tumor. There was a 5×7 cm mass adhering to the right kidney, liver and vena cava. The mass was cut and sent for biopsy, which showed right adrenal HAC (metastatic carcinoma by paramount consideration), with immunohistochemical stains Heppar1+, Glapican3+, CD34+, CK+, AFP-, α-inhibin-, CgA- and CEA- (Figure 2). Ki-67 proliferation index was 30%. We also used arginase-1 to verify hepatoid differentiation. The patient is still surviving, with no recurrence seen in follow-up visit (from 2013-05-21) (Figure 3).

Discussion
Hepatoid adenocarcinoma (HAC) is an aggressive and highly malignant tumor with adenoid
A rare case of extrahepatic hepatoid adenocarcinoma

Figure 1. There were a cystic solid mass in the right adrenal gland region. The cystic solid part was low in density and the solid part was mild enhanced after contrast-media injection.

Figure 2. The histopathological findings of the tumor. A. The overall view (HE ×200) suggested hepatocellular carcinoma. We can see thick trabecular structure in the view. B. We can see the adenoid-differential cell. C. We can see positive immuno-histochemical stains which suggesting the hepatocellular differentiation under 400 times: arginase1+ (picture above left), Heppar1+ (picture above right), GPC3+ (picture blow left), CD34+ (picture blow right, CD34 is positive in sinus endothelial cells). D. The tumor cells didn’t produce AFP, AFP- (picture above left). The negative stains such as α inhibin- (picture above right) and CgA- (picture blow left) help us to exclude pheochromocytoma or adrenocortical adenoma. The CK+ shows that the tumor cells may be bipotential cells.
A rare case of extrahepatic hepatoid adenocarcinoma

and hepatocyte differentiation. The histogenesis of HAC may be due to hepatoid differentiation of the adenocarcinoma cells as the tumor progresses or from the bipotential cells that differentiate into cells with glandular and hepatoid features [11]. In 1985, Ishikura first showed that HAC was a cancer with hepatocyte characteristics (1). HAC usually occurs in the stomach, but is also found in the duodenum, colon, gallbladder, pancreas, lung, urinary bladder and adrenal gland. HAC has only been reported in case series or single case reports because it is extremely rare. HAC is predominant in males and middle-aged or elderly people. The clinical symptoms of HAC depend on the site of the tumors, and most patients have no specific clinical symptoms. Due to the lack of specific symptoms, HAC usually metastasizes before diagnosis. The most common metastases sites of HAC are liver and lymph nodes [11].

AFP is valuable in the diagnosis of HAC in most cases, since its levels are usually significantly high in the serum and tumor tissue [2, 12]. Postoperative serum AFP level can be used as a predictor for tumor recurrence or metastasis [13]. In our case, the serum AFP was not elevated (6.39 ng/ml), and AFP was negative in the tumor tissue. The patient has shown no recurrence till date (following up for 30 months), suggesting that AFP may play an important role in the invasion and metastasis of HAC.

There are no specific imaging characteristics for diagnosis of HAC. HAC is shown as a sub-stantive or cystic solid mass under ultrasound. On the CT, HAC is usually detected as a hypervascular neoplasm, with an intense arterial uptake followed by “washout” of contrast in the venous phase [12]. The tumor was seen as a low-density cystic solid mass with mild enhancement in our CT image. It is difficult to distinguish HAC from hepatocellular carcinoma (HCC) by these imaging techniques. In our case, we found no mass in the liver or other abdominal viscera in CT or ultrasound. During the operation, we could separate the tumor from surrounding tissues such as liver and right kidney.

A pathological examination is mandatory for definitive diagnosis. HAC is morphologically similar to HCC in histology, and polygonal tumor cells can be found in hematoxylin and eosin stains. Polygonal tumor cells proliferate in both trabecular and glandular structures. The heterologous tumor cells are eosinophilic and arranged in trabeculae or small sheets, which are separated by sinusoidal vessels. But it is difficult to obtain a definite diagnosis of HAC from histological findings. Pathological markers and immunohistochemical (IHC) stains can provide definitive diagnosis for HAC. AFP is very important for the diagnosis of HAC, since it is usually positive in the serum and neoplasm tissue, but HAC of the adrenal gland does not always produce AFP. Arginase-1 and Heppar-1 are specific markers for hepatoid differentiation, and always found to be positive. Although AFP was negative in our pathological section, the HAC could be diagnosed based on its definition [1]. The stains were diffusely positive for arginase-1, Heppar-1, glypican-3 and CD34. The negative staining for CgA, syn, α-inhibin, pCEA, CK19, EMA, HMB-45 and MelanA ruled out the possibility of pheochromocytoma, adrenocortical adenoma and other possible tumors.

Surgery is the only therapeutic approach for HAC. The estimated mean survival time is 12 months [12]. In our case, the patient has been followed-up for about 30 months and no metastasis or recurrence was found. AFP-negative HAC may have a better prognosis than AFP-producing HAC. Chemotherapy and radiotherapy are not sensitive to HAC. No adjuvant procedure is proven to be effective for survival. As HAC is morphologically similar to HCC, the chemotherapy used to treat HCC may be useful for HAC. In our case, the patient refused further treatment after surgery.
A rare case of extrahepatic hepatoid adenocarcinoma

Conclusion

In our case, diagnosis of the HAC was contributed by the immunohistochemistry, and its adrenal origin was confirmed by imaging and tumor location. When a cystic solid mass in the adrenal region is detected by imaging, other pathologies may occur excluding pheochromocytoma or adrenocortical adenoma. Extrahepatic HAC, for example, is a probable diagnosis, which should be considered. The prognosis of AFP-negative HAC is not always poor. In our case, the patient is still surviving (after 30 months).

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Disclosure of conflict of interest

None.

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References