CASE REPORT

Radiologically occult hepatocellular carcinoma in a cirrhotic liver presenting with bilateral adrenal metastases

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SUMMARY

Although it is common to have extra-hepatic metastasis of hepatocellular carcinoma (HCC) at the time of presentation, it is extremely rare to have extra-hepatic metastatic HCC without a detectable primary in the liver. We report a unique case in which a patient presented with bilateral large adrenal masses which were subsequently proven to be metastases from HCC. However, there was no tumour seen in the liver on imaging.

KEY WORDS:

Hepatocellular carcinoma (HCC); Extra-hepatic metastasis of HCC; Adrenal metastasis of HCC

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world.1 Although it is common to have extra-hepatic metastasis of HCC at the time of presentation, it is extremely rare to have extra-hepatic metastatic HCC without a detectable primary in the liver.2 We report a unique case in which a patient presented with bilateral large adrenal masses which were subsequently proven to be metastases from HCC. However, there was no tumour seen in the liver on imaging.

CASE REPORT

A 32-year-old Chinese man presented to the emergency department with acute abdominal pain, acute hematemesis and melena. He complained of weight loss and increasing abdominal bloating for 4 months. This patient had a history of childhood acute lymphoblastic leukaemia (ALL) which was successfully treated 20 years ago with no further relapse. On clinical examination, he had a palpable upper abdominal mass, mild jaundice, and ascites. Blood investigations showed haemoglobin 6.2 g/dl [13.5–18.0], bilirubin 2.3 mg/dl [<1.5], alkaline phosphatase (ALP) 173 U/L [39–117], aspartate transferase (AST) 196 U/L [<38], alanine transferase (ALT) 79 U/L [<41], albumin 3.0 g/dl [3.4–5.1], and prothrombin time (PT) 14.2 sec [9.5–14.0]. Hepatitis B surface antigen was reactive.

He was resuscitated with fluids and packed cell transfusion. Emergency esophagogastroduodenoscopy (OGD) showed bleeding esophageal and gastric varices which were treated with sclerotherapy.

Since patient was a hepatitis B carrier, CT scan of the abdomen, which comprises evaluation of the liver in pre-contrast, arterial, porto-venous, and delayed phases, was performed. A simultaneous acquisition of the CT thorax, abdomen and pelvis in porto-venous phases was also done.

The CT study revealed bilateral, large, well-defined, soft tissue density adrenal masses. These masses showed heterogeneous enhancement and no internal fat density or calcification was seen. The right adrenal mass measured 10 x 7 cm and the left adrenal mass was 14 x 12 cm. The left adrenal mass was seen extending across the midline and invading into the inferior vena cava. Extensive pulmonary arterial emboli in bilateral lobar and segmental pulmonary arteries and multiple consolidations in both lungs were seen. The liver appeared shrunken and showed irregular nodular contour with significant atrophy of the left lobe and hypertrophy of the caudate lobe, compatible with cirrhosis of liver. A few scattered 2 to 3 mm size midly hyperdense nodules were seen on non-enhanced CT, compatible with regenerative nodules. There was no enhancing mass in the arterial phase or focal contrast washout in the venous phase or pseudo-capsule formation on the delayed phase was seen to suggest HCC.

Biochemical investigations revealed elevated 24-hour urine norepinephrine and normetanephrine levels 580 nmol/day [89–473] and 4098 nmol/day [600–1900], respectively. Although serum potassium level was 3.3 mmol/L, plasma aldosterone concentration was normal 162.1 pmol/L [97.3–834.0] and aldosterone/renin ratio was 3.36. Basal serum cortisol level was not elevated. Serum chromogranin A (CgA) level was markedly raised at >600 µg/L [0–100].

After achieving adequate alpha-adrenergic blockade with phenoxybenzamine, CT-guided biopsy of the right sided adrenal mass was performed to obtain tissue diagnosis.

Hematoxylin and eosin-stained sections of the right adrenal tumour showed a lesioncomposed of nests and islands of tumour cells with eosinophilic cytoplasm and moderate to severe nuclear pleomorphism (figure 2A and 2B). Tumour giant cells were present. Numerous mitotic figures were seen.No stromal desmoplasia or lymphovascular emboli were observed. Immunohistochemistry was performed and the tumour cells were diffusely and strongly positive for Hepar-1 which is a marker for HCC (figure 2C). They were negative for adrenocortical markers (leucocyte common antigen, Melan-

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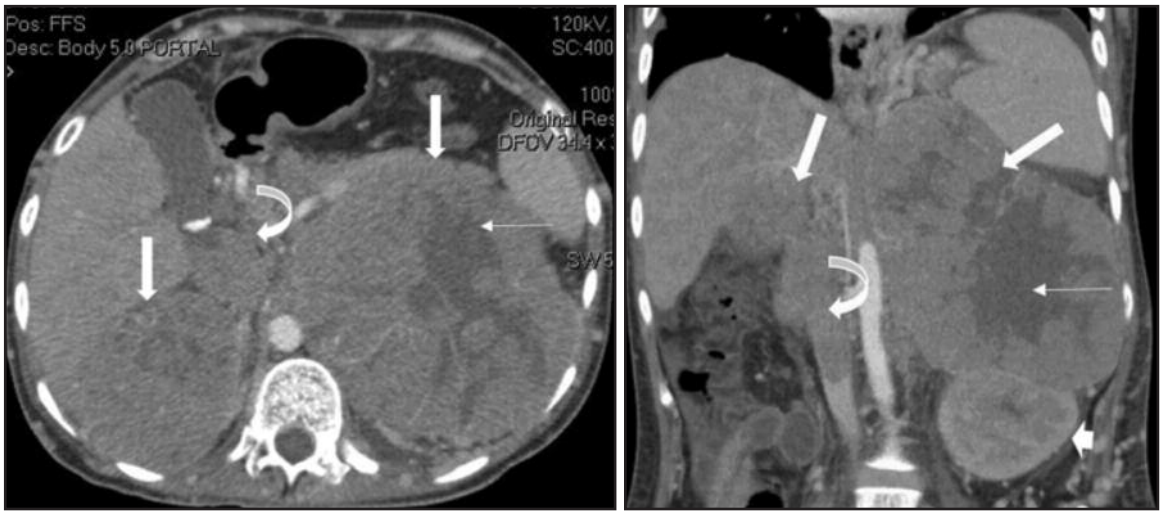

Fig. 1A &B: Contrast enhanced axial CT image at the level of adrenal glands shows, large, well defined, heterogeneously enhancing, solid masses in bilateral adrenal glands (arrows). Ill-defined hypo enhancing area is seen in the left adrenal mass (thin arrow) suggestive of tumour necrosis. The inferior vena cava is filled with enhancing soft tissue which is suggestive of tumour thrombus (curved arrow). Left kidney is displaced by the left adrenal mass (short arrow in figure 1-B).

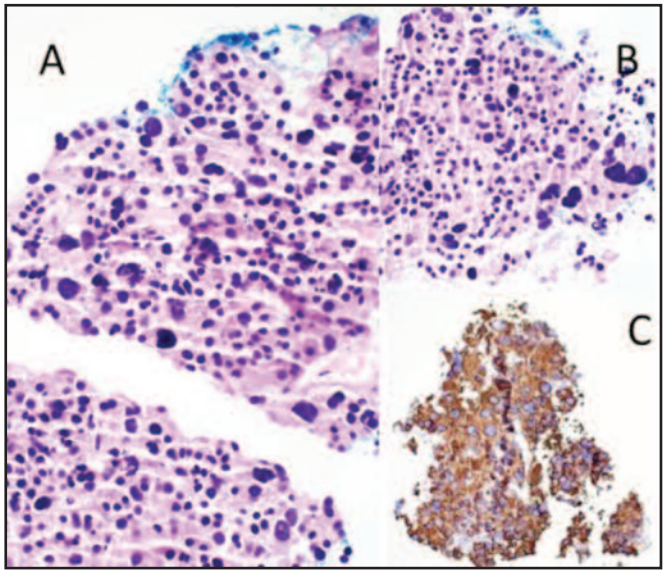

Fig. 2A &B: Hematoxylin and eosin-stained photomicrograph (magnification x400) of lesion with mitotic figure and nuclear pleomorphism (Figure 2-A); Hematoxylin and eosin-stained photomicrograph (magnification x400) of lesion with tumor giant cells (figure 2-B); Hepar-1 immunohistochemical staining showing strong diffuse staining. (magnification x200) (Figure 2-C).

A, and inhibin), glycophorin-A, CD61, and S100 protein. Neuroendocrine markers like synaptophysin and chromogranin were negative. Based on histopathology, the right adrenal mass was diagnosed to be metastatic HCC. Alpha-fetoprotein (AFP) level was found to be 33,127.0 ng/mL [up to 15.0], confirming the diagnosis of HCC.

The patient's family opted for best supportive care and the patient eventually succumbed to his disease two months after presentation.

DISCUSSION

Hepatocellular carcinoma (HCC) is one of the common malignancies in the world with an estimated annual incidence of 0.5 to 1 million.[1] Peak age incidence of HCC is between 50 and 70 years, with a male to female ratio of 4:1.[1] Cirrhosis, especially secondary to chronic hepatitis B and C infection, is a major risk factor for the development of HCC.[2] Extra-hepatic metastatic HCC is commonly seen at the time of presentation and its incidence is reported to be 37% in one series.[2] The commonest extra-hepatic metastatic location are lungs (55%), lymph nodes (53%), bone (28%), and adrenal glands (11%).[1] It is extremely rare to find extra-hepatic metastatic HCC without a radiologically detectable primary tumour in the liver. Only a few cases of osseous and pulmonary metastatic HCC[3,4] and one case of adrenal metastatic HCC [5] with occult primary have previously been reported. Having said this, the non-detectability of the HCC in our case was established on the basis of the CT diagnostic criteria which are most widely used in daily practice. It should be born in mind that the detection of a diffuse or minute HCC in the background of cirrhosis is extremely difficult on CT and MRI as both modalities have several limitations. In spite of several guidelines, the various diagnostic criteria, be it for CT or MRI or angiography, do not comprehensively address the full spectrum of lesions and pseudolesions, from benign to malignant, encountered in the cirrhotic liver. However, the detailed discussion on the limits and diagnostic performance of various modalities in detection of HCC is beyond the scope of this article. According to some authors, the occurrence of metaststic HCC with no detectable primary in liver may represent spontaneous regression of the primary tumour.

Metastasis is the most frequent cause of bilateral adrenal masses. Differential diagnoses include bilateral pheochromocytomas, bilateral adrenocortical carcinomas, and lymphoma.

Optimal management of incidentally discovered adrenal masses is not well established. Every patient with an incidentally discovered adrenal nodule should be investigated with imaging and/or biopsy to exclude malignancy. However, surgical removal of adrenal tumour of size greater than 6 cm is advocated as they are associated with high incidence of malignancy.

With thorough pre-procedural planning including review of imaging and laboratory data, careful intra-procedural monitoring and availability of adrenergic blockade and/or anesthesia assistance, imaged-guided biopsy of an adrenal mass can be performed safely.

In our patient, CT-guided biopsy was performed. Histopathology and immunohistochemistry showed that the right adrenal lesion was metastatic HCC. Unlike our case, the diagnosis of adrenal metastatic HCC with occult primary reported by Tsalis *et al.* was made only after surgical resection.[5]

CONCLUSION

Bilateral large adrenal masses can be a primary presentation of HCC in spite of no radiologically detectable HCC in the liver. Though unusual, it should always be considered in a patient with risk factors for HCC like hepatitis B or C infection. Recognising this presentation early is important as it usually has a grave prognosis.

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