Case Report

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Unilateral adrenal metastases as an unusual primary presentation of hepatocellular carcinoma: a case report and literature review

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Introduction and importance: Adrenal metastases can rarely present as a solitary clinical manifestation among cases with underlying hepatocellular carcinoma (HCC).

Case presentation: The authors present the case of a 53-year-old male with chronic liver disease due to chronic hepatitis C who presented with left flank pain. Imaging revealed a left-sided suprarenal mass. Following multidisciplinary assessment, the patient underwent left-sided nephrectomy and adrenalectomy, whereas histopathological correlation revealed microscopic foci of metastatic HCC in the resected gland. Postoperative abdominal imaging then revealed multifocal dysplastic lesions scattered through both the hepatic lobes. Subsequently, systemic treatment was initiated with sorafenib.

Clinical discussion: These types of adrenal metastasis from the liver are extremely uncommon and need detailed evaluation of the liver and other potential metastatic sites. The choice of treatment will be indicated according to the type and site of the tumor.

Conclusion: This case highlights the significance of thorough evaluation and individualized management in HCC-associated adrenal metastasis.

Keywords: adrenal gland, adrenalectomy, hepatocellular cancer, metastasis, multidisciplinary approach

Introduction

Hepatocellular carcinoma (HCC) contributes to a substantial burden of cancer-related mortality in the underdeveloped world[1]. Although HCC can metastasize to wide-ranging sites, including abdominal lymph nodes, lungs, bones, and adrenal glands, it is highly uncommon to discover metastatic deposits as the primary clinical presentation among cases of HCC. At the time of diagnosis, adrenal metastasis can be reportedly found in up to 11% of patients with HCC[2]. This case report is per CARE guidelines[3].

Case presentation

A 53-year-old male with a known case of chronic liver disease with a background of previously treated chronic hepatitis C presented to the Urology outpatient unit with the complaint of gradually worsening left flank pain for two months, which was mild to moderate, continuous, dull in character, non-radiating and not associated with food intake. There was no effect of any position or postural change, and no diurnal variation was present. The patient had no complaints of fever, nausea, vomiting, changes in bowel movements, hematochezia, hematuria, burning micturition, or lower urinary tract symptoms. On examination, a middle-aged male of average build and height was lying on the couch; vitals were stable, including blood sugar levels, and no orthostatic hypotension was present. Abdominal examination revealed a left lumbar mass, measuring ~10×8 cm in size, non-tender, firm in consistency, palpable bilaterally, renal punch was negative, and no other viscera was palpable. The rest of the systemic examination was unremarkable. All baselines were normal, including liver function tests, renal function tests, and serum electrolytes. Urine routine examination was unremarkable. Due to a positive history of renal stone disease, the patient underwent CT urography outside the hospital

HIGHLIGHTS

- We describe the case of adrenal metastasis as the primary clinical manifestation of hepatocellular carcinoma (HCC).
- This presentation is very rare and difficult to diagnose.
- A multidisciplinary approach led to a left-sided nephrectomy and adrenalectomy.
- Histopathology and immunochemical studies confirmed the diagnosis.
- There are no definite guidelines regarding Adrenal metastases from HCC, therefore it should be managed individually with a multidisciplinary team.

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setting, which revealed an incidental finding of a left-sided suprarenal mass measuring 13.2 × 10.6 × 12.5 cm.

Later, CT abdomen with adrenal protocol showed a left adrenal lesion measuring 12.6 × 11 × 13.4 cm (AP × TR × CC), which has a relative and absolute washout of 50% each. Nodular liver surface with recanalized umbilical vein, a few epigastric, and left upper quadrant collaterals.

Further workup per protocol of adrenal incidentaloma was done, including normal serum cortisol and overnight dexamethasone suppression test, serum aldosterone and renin levels, and aldosterone/renin ratio returned unremarkable. Normal urinary-free metanephrines ruled out Pheochromocytoma.

Following the initial workup, the case was discussed in a multidisciplinary team meeting and planned to undergo a left adrenalectomy. During the procedure, the plane between the left kidney and the adrenal gland was noted to be highly vascular. At the same time, the tumor was also adherent to the kidney at both the superior and inferior poles as shown in Fig. 1. Following the successful intervention, histopathological analysis was compatible with a diagnosis of benign adrenal parenchyma with microscopic foci of metastatic hepatocellular carcinoma. The tumor was positive for the following immunohistochemical markers: Hep-Par1, Arginase, and CK.

Ultrasound imaging did not reveal any focal intrahepatic lesion to localize the primary tumor. Postoperative magnetic resonance imaging liver protocol demonstrated wavy margins favoring chronic liver disease. Multiple (more than 10) T1 hyperintense lesions are seen scattered in both lobes of the liver, demonstrating post-contrast enhancement without washout in the delayed phase or diffusion restriction on DWI/ADC images representing dysplastic/regenerating nodules as shown in Figure 2. Despite normal alpha-fetoprotein (AFP) levels, PIVKA-II levels were substantially elevated to 1170 ng/ml. The patient was subsequently discussed with the Hepatology and Oncology team and treatment options were discussed with the patient and because of the unavailability of other latest treatment options he was initiated on lenvatinib (discontinued because of intolerance) and then sorafenib 200 mg once daily for HCC. At 3-month follow-up, the patient was surviving well, sorafenib was discontinued due to thrombocytopenia. Now the patient is on palliative care with no ongoing treatment for primary disease.

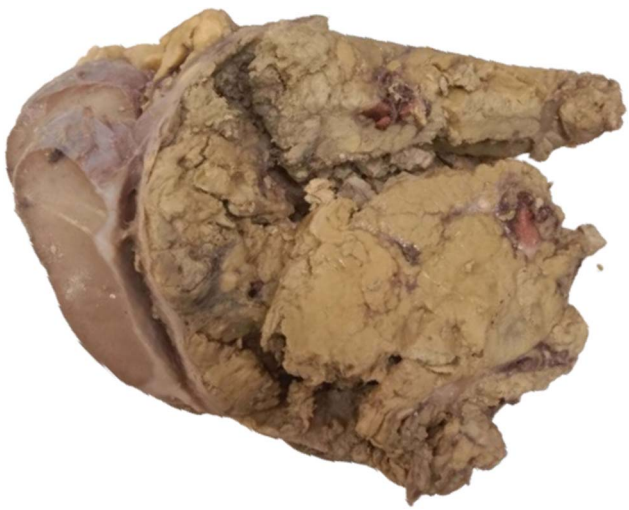

Figure 1. Gross specimen of resected adrenal mass (right) adherent to kidney (left).

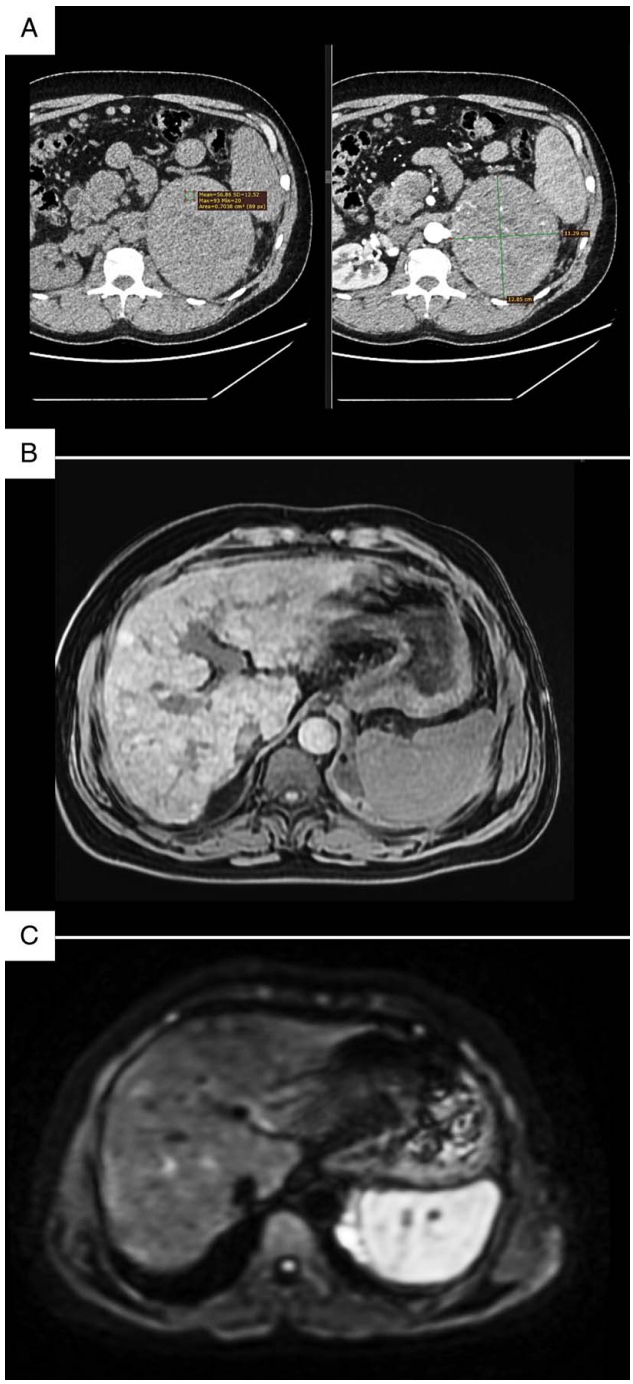

Figure 2. (A) Pre-contrast and arterial phase showing size, density and washout characteristics of adrenal lesion. (B) MRI showing multiple liver lesions hyperintense on T1. (C) Diffusion-weighted imaging showing no diffusion restriction.

Discussion

Owing to the vast complex vascular supply of liver parenchyma, hepatic tumor cells can directly invade the portosystemic circulation and form secondaries at distant sites. Isolated HCC-related

Table 1

Literature review of different cases having adrenal metastasis from HCC

References	Main presentation at diagnosis	Time of diagnosis of adrenals mass with respect to HCC presentation	Nature of adrenal mass (hormone sensitive/ silent tumor)	Site of adrenal mass (unilateral /bilateral)	AFP levels at the time of adrenal mass diagnosis (IU/ml)	Immunochemical markers of adrenal mass	Main management plan	Outcome
Paganetti *et al.*[16]	Previous hx of HCC in segment 7 and 8 then recurrence in 3,4a,4b,5, later patient developed lesion on left adrenal	After HCC presentation	Silent tumor	Left adrenal mass	Normal	NA	Bi-segmentectomy for segment 7, 8 and then TACE for 3,4a,4b,5	Patient recovered well from surgery but didn't agree for transplant
Ueda *et al.*[17]	Previous hx of lung cancer, now presented with mass in Segment 4 and then left adrenal mass after 3 months	After HCC presentation	Silent tumor	Left adrenal mass	6.9	Hepatocyte-paraffin-1 (+)	Surgery and Trans-arterial Chemoembolization for HCC and later TACE left adrenal metastases	Patient died after one month
Zeineddine *et al.*[18]	Hx of Cirrhosis due to Hepatitis C, Posterior subcapsular mass in Segment 6 underwent transplant, after 5 years patient had adrenal mass.	After HCC presentation	Silent tumor	Right adrenal mass	13.8	Arginase-1 (+), Glypican-3 (+), and GepPar-1 (+)	Initially liver transplant was done for liver mass and later SBRT for adrenal mass	Patient continue to do well and currently on cyclosporine
Wei *et al.*[12]	Hx of unchanged liver mass and then right adrenal mass adherent to renal hilum with a thrombus of the inferior vena cava	After HCC presentation	Silent tumor	Right adrenal mass	1.87	NA	Right adrenalectomy. radical nephrectomy and IVC reconstruction for adrenal mass	Enhancing soft tissue within the surgical bed on 10th month MRI
Kwak *et al.*[19]	Asymptomatic, routine workup showed in Segment 7 liver mass and then after 2 years nodule on adrenal gland was noted.	After HCC presentation	Silent tumor	Left adrenal mass	Zero	NA	Partial hepatectomy with cholecystectomy for HCC and left adrenalectomy for adrenal mass	No recurrence was noted after 21 months
Rodríguez *et al.*[20]	Hx of transplant due to cirrhosis, after 10 years a nodule in Segment 6 and left-sided adrenal mass was noted.	With HCC presentation	Silent tumor	Left adrenal mass	111.89	Hep Par-1 (+), cytoplasmic TTF-1 (+), CAM 5.2 (+), CD10 (+)	Liver transplant was done for liver mass and left adrenalectomy for adrenal mass	Total remission
Igarashi *et al.*[21]	HCC in Segment 8 and then right adrenal gland tumor with inferior vena cava tumor thrombus after 1 year	After HCC presentation	Silent tumor	Right adrenal mass	56.8	Glypican-3 (+), TERT (+), CTNNB1 (+), TP53 (+), ARID2 (+)	Partial hepatectomy, right adrenalectomy, and IVC tumor thrombectomy	Future imaging showed multiple recurrences and patient died after 8 months
Nugroho *et al.*[22]	Hx of jaundice and abdominal pain, then diagnosed with lesions in hepatic duct and Segment 4, adrenal mass was diagnosed on follow-up CT	After HCC presentation	Silent tumor	Right adrenal mass	4950	glypican-3 (+), hepatocytes (+)	S4 segmentectomy and hepaticojejunostomy for liver mass and right adrenalectomy for adrenal mass	Recurrence in Segment 7 after 1 years
Tsalis *et al.*[11]	Retroperitoneal tumor originating from left adrenal mass and HCC was diagnosed 7 months later	Before HCC presentation	Silent tumor	Left adrenal mass	75.6	NA	Left adrenalectomy for adrenal mass and later trans-arterial embolization (TACE) for HCC	Patient died after 3 months

AFP, alpha-fetoprotein; CT, computed tomography; HCC, hepatocellular carcinoma; NA, not applicable; IVC, inferior vena cava; SBRT, stereotactic body radiation therapy.

adrenal metastasis is an extremely uncommon presentation and often warrants a detailed survey of the liver and other potential sites of secondary deposits[4]. Although bilateral adrenal metastases have been associated with primary adrenal insufficiency in 3–8% of cases, our case study, with unilateral metastasis, did not demonstrate any significant hypoadrenalism[5]. Among other factors, the overall choice of treatment modality in adrenal metastases should be governed by the site, size, number of primary and secondary lesions, and the patient's ECOG status.

No consensus exists about the definitive mode of treatment in adrenal metastases, and each case needs to undergo thorough vetting within a multidisciplinary team meeting. Obtaining a needle-guided preoperative histopathological diagnosis can be an effective strategy; nonetheless, tumor size greater than 3–4 cm usually warrants complete resection regardless of the malignant nature of the disease[6,7]. In addition to surgical resection, chemotherapy, and radiotherapy also constitute optional modes of tumor treatment. Transarterial embolization (TAE) has also been used as a potentially effective mode of ablative therapy. In their limited case series, Taniai *et al.*[8] reported favorable outcomes following hepatectomy and adrenal tumor resection, whereas TAE was also successfully implemented in one case with a good prognosis. In combination with TAE, subcutaneous intratumor chemotherapy can be potentially performed for both the hepatic and adrenal tumors simultaneously since one case report suggested complete tumor clearance after this approach[9]. In one study comparing surgical treatment of adrenal metastasis with systemic chemotherapy, it was found that surgical resection of adrenal tumors led to a higher rate of disease-free survival[10].

However, in cases where the primary source of the tumor is unknown or only vaguely evident, surgical resection of the adrenal lesion can be recommended, as demonstrated in the study by Tsalis *et al.*[11]. Comparably, one study failed to localize any primary source of HCC after surgical removal of metastatic adrenal HCC. Moreover, it is also atypical to find normal tumor markers among such cases. Nonetheless, such cases can be started on tyrosine kinase inhibitor therapy[12]. In one extensive study involving 990 hepatectomy and 303 liver transplantation procedures due to underlying HCC, up to 10 (0.8%) patients had concomitant adrenal metastases. For eight patients undergoing adrenalectomy, a mean postoperative survival period of 112 months was recorded. In line with this, Teegen *et al.*[13] have suggested opting for adrenalectomy whenever the primary liver disease is well-controlled and the patient is a potential candidate for surgical intervention. The ultimate prognosis, however, remains debatable as such patients are unlikely to survive without a definitive treatment plan for HCC. Moreover, disease recurrence is a potential possibility, while adrenal metastases may even occur several months following liver transplantation in HCC[14]. One case study saw a 73-year-old patient undergoing bilateral adrenalectomy after initial sessions of hepatic TAE. After a postoperative duration of 9 months, the patient died due to lung metastases. This challenges the clinical efficacy of a commonplace use of surgical intervention for adrenal metastases, which additionally poses the risk of life-long use of adrenocortical hormones[15]. The literature review of different studies having adrenal metastasis is shown in Table 1.

Conclusion

The case report underscores the rare occurrence of HCC presenting with adrenal metastasis. While isolated adrenal metastasis is uncommon, it necessitates a comprehensive assessment of both the primary tumor and potential metastatic sites. Treatment decisions must be individualized by correlating tumor characteristics, the patient's health status, and available therapeutic options.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

R.G.G.: writing—original draft. M.S.: writing—original draft. H.N.: writing—review and editing. S.A.: conceptualization. U.A. R.K.: methodology. A.M.B.: literature review.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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