Adrenocortical carcinoma with contralateral renal metastases and tumor thrombus: A case report

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ABSTRACT

Adrenocortical carcinoma (ACC) is a rare aggressive malignancy. ACC with renal vein or inferior vena cava (IVC) thrombus is very rare. ACC with contralateral renal metastasis with renal vein thrombus has never been reported. Here we report first such case in the literature where a 40-year-old male presented with right flank pain and weight loss. Definitive preoperative diagnosis failed to be established. Intraoperatively, there was right adrenal mass with left renal vein thrombus invading its wall and extending upto IVC. Right adrenalectomy with left radical nephrectomy with thrombectomy was done. On cut specimen, there was a small mass lesion in the left kidney (upper pole). The diagnosis of ACC with left renal metastasis and renal vein tumor thrombus was confirmed by pathological and immune-histochemical examination. We faced various perioperative challenges in our case. Care must be taken in preoperative diagnostics, intraoperative planning, and postoperative management as ACC may present with contralateral renal metastasis and tumor thrombus.

Keywords: *Adrenocortical carcinoma, Contralateral renal metastasis, Renal vein thrombus, Tumor thrombus.*

Adrenocortical carcinoma (ACC) is a rare aggressive malignancy.ACC with renal vein or inferior venacava (IVC) thrombus is very rare. In literature search upto 2015, Ayati et al found only 44 cases of ACC with tumor thrombus extending to the IVC [1]. ACC with contralateral renal metastasis with renal vein thrombus has never been reported. Here we report first such case with peri-operative challenges.

CASE REPORT

A 40-year-old male presented with complaints of right flank pain with weight loss. The patient did not give any history of such in the past. On evaluation, the vitals were stable.The patient was found to be having large right adrenal mass with IVC (Level II) and left renal vein thrombus (Fig. 1a, 1b and 1c). The patient had multiple lung metastases also and the tumor was non-functional. Morning cortisol level was 12 micrograms per deciliter, morning plasma adrenocorticotropic hormone (ACTH) level was 15 picograms per milliliter and 24-hour urinary catecholamines and metanephrines were within normal limits.

Preoperatively, the patient had lower respiratory tract infection, so, he was started on antibiotics and patient was put onanticoagulant medication (low molecular weight heparin) in view of suspected bland left renal vein thrombus and to reduce thrombus propagation. He was planned for the right adrenalectomy with thrombectomy. Color Doppler was done in the morning of operation; it showed left renal vein thrombus just reaching into IVC.

The patient was operated in a supine position with chevron incision. Kocherization was done and adrenal mass (15x14 cms) was dissected from the right kidney and IVC. Infrarenal IVC, right renal vessels, left renal artery and suprarenal IVC control was taken and clamped. IVC and left renal vein venotomy were done; there was thrombus in the left renal vein just extending upto IVC. Left renal vein thrombus was invading its wall and reaching into the renal sinus. Thrombectomy was not feasible

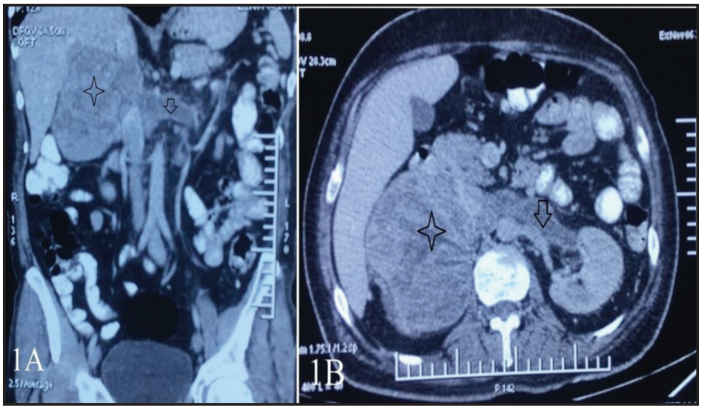

Figure 1: 1a - CT scan coronal section showing Right adrenal mass (marked as star) with IVC and left renal vein thrombus (marked as arrow); 1b - CT scan axial section showing Right adrenal mass (marked as star) with IVC and left renal vein thrombus (marked as arrow)

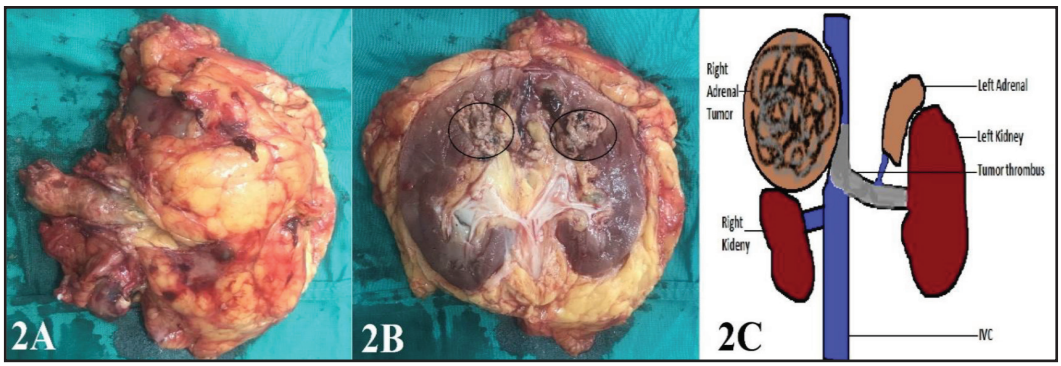

Figure 2: (2a) Specimen of right adrenal mass and left kidney with renal vein thrombus. (2b) Cut open specimen of left kidney showing upper polar mass (encircled). (2c) Diagrammatic representation (postoperative) of the right adrenal mass with IVC and left renal vein thrombus

so, right adrenalectomy with left radical nephrectomy was done. On cut specimen, there was a mass lesion (2x2 centimeters) in the left kidney (Fig. 2a, 2b and 2c). On histopathological examination, the diagnosis of ACC with left renal metastasis and renal vein tumor thrombus was made and it was confirmed by immunohistochemical (IHC) examination using IHC markers Vimentin, Melan A and Ki67. (Fig. 3a, 3b, 3c and 3d).

Postoperatively, the patient was shifted in stable condition to an intensive care unit for monitoring. Approximately after 6 hours, he developed persistent hypotension despite adequate resuscitation and inotropes. The endocrine opinion was sought and they advised serum cortisol levels and hydrocortisone infusion. Serum cortisol levels were low. The patient stabilized and hydrocortisone was tapered off gradually over 5 days. At one month follow-up, the patient is stable, wound is healthy and there is no adrenal insufficiency. The patient is planned for mitotane-based chemotherapy.

DISCUSSION

Most of ACC which are non-functional are difficult to diagnose [2]. Majority of patients present with tumor-related symptoms

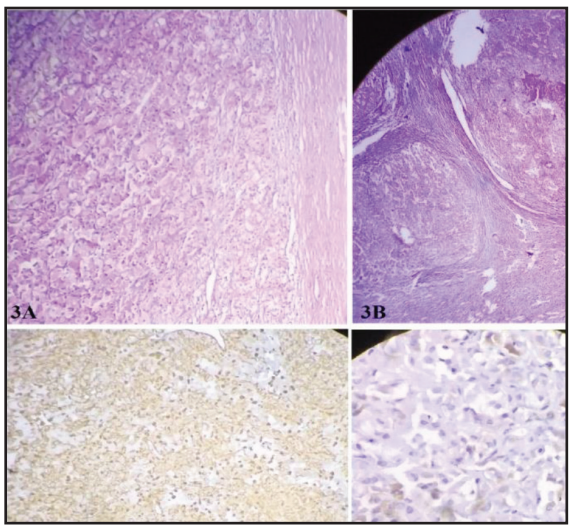

Figure 3: (3A) Hematoxylin-eosin stain showing adrenocortical carcinoma. (3B) H-E stain of renal mass. (3C)ACC metastasis with positive immunostaining pattern for Vimentin, (3D) ACC metastasis with positive immunostaining pattern for Melan A.

which can be secondary to local or systemic disease burden or hypersecretion of adrenal hormones,which is found in 50%-79% of adults and 90% of pediatric ACCs [3]. Hypercortisolism is the most common presentation of patients presenting with hormone excess (50%–80% of hormone-secreting ACCs) followed by adrenal androgens. Concurrent androgen and cortisol production is evident in roughly half of all ACC patients with hormone excess. Autonomous aldosterone secretion is rarely seen in ACC [4].

In metastatic ACC, multimodal therapy is often required. Debulking surgery should be considered in patients with the oligometastatic disease if > 80 % disease burden can be removed [5]. Althoughdebulking surgery may not improve survival, it may alleviate tumor-related side effects and enhance response to adjuvant therapies.In this patient, we considered debulking surgery as the patient had a resectable primary disease with IVC and opposite renal vein thrombus, which needed immediate surgical intervention. Adjuvant mitotane based chemotherapy was planned.

Recently, 304 patients were included in the First International Randomized trial in Locally Advanced and metastatic Adrenocortical Carcinoma treatment (FIRM-ACT) trial which compared the response of mitotane with etoposide-cisplatin-doxorubicin (M-EDP)and mitotane-streptozotocin (M-Sz) as a first-line or second-line treatment.Overall survival was similar between the groups,but M-EDP was associated with better progression-free survival and objective response rate compared to M-Sz (5.0 vs. 2.1 months, 23.2 vs. 9.2%, respectively) [6]. Based on this trial, M-EDP can be considered the first line regimen for patients requiring systemic therapy.

Preoperatively, the patient was diagnosed to be having large right adrenal mass with IVC and left renal vein thrombus. But, during the operation he was found to be having left renal metastasis also. This could be explained as contrast-enhanced computed tomography scan of the abdomen was done one and a half months before surgery. During this period the renal mass might have increased in size. Many aggressive ACCs may grow quickly and involvement of adjacent structures may change, so, the imaging should be obtained as close as possible to the anticipated date of surgery [7]. In view of existing lower respiratory tract infection, we could not proceed for the surgery

till it improved.So, meanwhile anticoagulants were started to reduce chances of thrombus propagation and further occlusion of left renal vein lumen. Anticoagulant therapy reduces thrombus propagation but does not produce clot lysis, thus risking post-thrombotic syndrome [8]. Level of tumor thrombus and vascularity of the left kidney was confirmed on Color Doppler before taking the patient to the operation room, as any change in renal vascularity or thrombus level would have changed the surgical planning.During operation, IVC and renal vessels control were taken to limit blood loss and to avoid migration of any tumor thrombus emboli. Venotomy and thrombectomy were not feasible as tumor thrombus was invading the vein wall. So, the decision of left radical nephrectomy was made. On cut specimen, there was a small mass at the upper pole of left kidney. Metastasis to left kidney with renal vein and IVC tumor thrombus can be explained by either of the two mechanisms. First, retrograde metastasis, the tumor might have spread to the left kidney via IVC and left renal vein tumor thrombus after the direct involvement of the IVC by ACC. Second, anterograde metastasis, direct hematogenous metastasis to the left kidney from ACC leading to the left renal vein and IVC thrombus. Implementing aggressive surgical therapy might be effective for the management of such cases [9], as the most important predictor of survival in patients with adrenal cancer is the adequacy of resection. In a case seriesof six patients by Figueroa et al, the patients of ACC with thrombus had 5-year survival rates ranging from 32% to 48% if it was completely resected, while the median survival was less than 1 year in patients undergoing incomplete excision [10].

The left renal upper polar tumor was confirmed to be ACC metastasis on histopathological and immunohistochemical examination. Ascertaining the possibility of ACC metastasis to an organ is sometimes difficult. Especially it was imperative in our case to differentiate ACC metastasis from renal cell carcinoma. In such instances, a battery of immunostains which are expressed in most ACCs can provide evidence of adrenocortical differentiation [11], including Vimentin [12], MelanA (Mart1) [13] and Synaptophysin [14]. Approximately after six hours of the operation, our patient developed refractory hypotension. All the possible causes of postoperative hypotension were examined and ruled out. After endocrinology opinion injection hydrocortisone infusion was started in view of hypocortisolism. Ligation of the left adrenal vein during nephrectomy with contralateral adrenalectomy might have resulted in temporary post-operative hypotension due to hypocortisolism.

To the best of our knowledge, this is the first report of ACC with contralateral renal metastasis and tumor thrombus.

CONCLUSION

We faced various perioperative challenges. Care must be taken in preoperative diagnostics, intraoperative planning, and postoperative management as ACC with contralateral renal metastasis and tumor thrombus is possible.

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