CASE REPORT

Adrenocortical Carcinoma with Renal Vein Tumor Thrombus Extension

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INTRODUCTION

Adrenocortical carcinoma (ACC) is a rare malignancy with an incidence rate of 0.5-1 per million per year. [(1)] Tumor thrombus in this setting has been described but it represents an exceedingly rare surgical entity. However in one retrospective ACC series was reported in 25% of cases.[(1)] Similar to other ACC tumors, up to 50% of tumors with thrombus extension are functional at diagnosis.[(2)] Non-functional tumors are diagnosed due to mass effect or incidentally. Depending on the tumor thrombus level, patients can present with varicocele,[(3)] lower limb edema[(1)] or pulmonary embolus.[(1)] Apart from extension to renal vein and vena cava, extension to right atrium, splenic vein,[(4)] hepatic vein[(5)] and invasion into vena cava[(6)] have also been reported. Herein we report a case of ACC with left renal vein thrombosis in a male patient.

CASE REPORT

A 60-year-old man presented with a 3 month history of left hemi-scrotal pain. The patient did not report any urinary or systemic symptoms. Physical examination was unremarkable. Scrotal ultrasonography (US) was normal. Abdominal US demonstrated normal kidneys and a 10.7 × 8.5 cm heterogeneous mass in the upper pole of the left kidney. Color Doppler US identified left adrenal vein thrombosis with extension into the left renal vein. Laboratory examinations including CBC (hemoglobin 15.7 g/dL), liver function tests (aspartate transaminase16 U/L, alanine aminotransferase 26 U/L, alkaline phosphatase 133 U/L, total bilirubin 0.43 mg/dL), serum creatinine (1.1 mg/dL) and electrolytes (Na 143 mmol/L, K 3.9 mmol/L), and 24-hour urine collection (vanillylmandelic acid 1.5 mg/day, cortisol 15 µ/day) were within the normal ranges. Computed tomography (CT) scan with contrast (**Figure 1a, 1b**) confirmed the US findings. It demonstrated a 10 cm heterogeneous mass with Hounsfield (HU) density of 30 on non-contrast imaging. The tumor had washout of < 50% with attenuation of > 30 HU, 15 minutes after contrast media injection (**Figure 1c, 1d, 1e**). Tumor thrombus was seen extending into the left renal vein on the CT scan images. Chest CT was not suggestive of metastatic disease. After counseling, our patient elected to undergo adrenalectomy using the flank approach. Intra-operatively a large adrenal mass with adhesion to the upper pole of left kidney along with adrenal vein thrombosis was observed (**Figure 2a**). The tumor thrombus extended into the renal vein and inferior vena cava junction. Adrenalectomy with en bloc radical nephrectomy and adrenal vein tumor thrombus excision was performed (**Figure 2b**). The estimated blood loss was 700 mL and the patient required two units of intra-operative blood transfusion. No post-operative

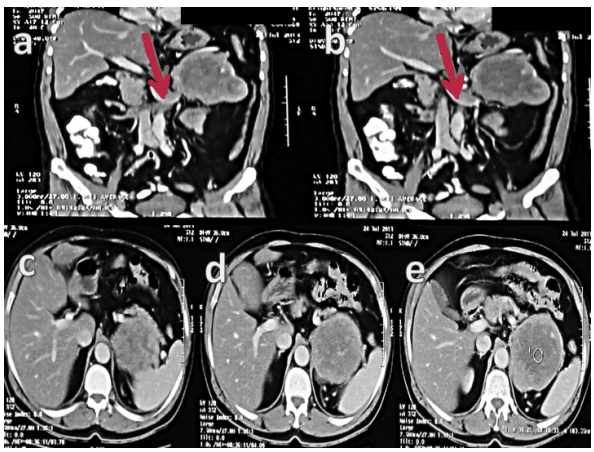

Figure 1. (a and b) Computed tomography scan with coronal view. Arrows demonstrate tumor thrombus extension into the left renal vein; **(c, d and e)** computed tomography with axial view demonstrating large heterogeneous adrenal lesion.

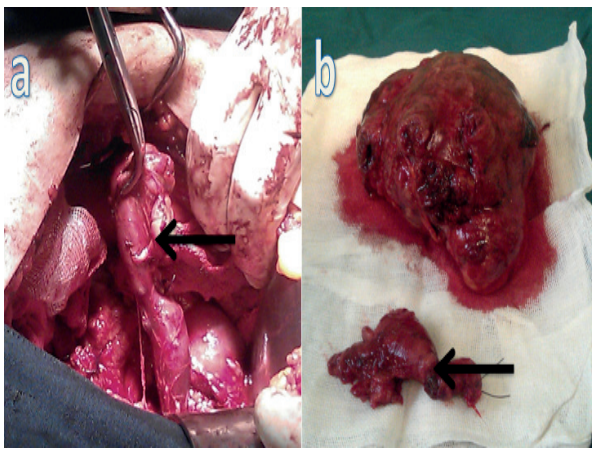

Figure 2. (a) Intra-operative image demonstrating the left renal vein filled with the tumor thrombus; **(b)** gross pathology, the tumor thrombus within the renal vein is isolated after en bloc removal.

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complications occurred. The histopathology confirmed ACC with tumor thrombosis of the left adrenal vein. On histopathology assessment the tumor had 7 out of 9 criteria of Weiss scoring for ACC.[7] These included high Fuhrman nuclear grade (3/4), mitotic counts > 5/50 per high power field, less than 25% clear cells composing tumoral cells, diffuse architecture in more than 1/3 of tumor, presence of necrosis, venous invasion and invasion of sinusoid structure. There was no evidence of renal involvement, and surgical margins were negative (pT3). The patient received adjuvant chemotherapy (mitotane 4g/day) post operatively and currently remains on this treatment. At the follow up time of 5 months, the patient remains free of local/systemic recurrence.

DISCUSSION

ACC is a rare malignancy and ACC with tumor thrombus extension is a rare presentation of this malignancy. Depending on the extent of the tumor thrombus, patients can present with a variety of sign and symptoms.[3-6] After initial office assessment, laboratory assessment should include comprehensive endocrine evaluation. Acquisition of CT scan of chest and abdomen (adrenal protocol with delayed contrast media washout phase) is universal to all ACC staging. With regards to the tumor thrombus, magnetic resonance imaging (MRI) is a better modality for assessing the extent of the thrombus extension.[8] Further imaging (bone scan, head CT) is performed according to degree of clinical suspicion. Complete surgical resection with a negative margin (R0 resection) is the only curative option for localized disease.[9] On retrospective review of 275 patients with ACC undergoing primary tumor resection, R0 resection was associated with 25% reduction of local recurrence (Hazard ratio 0.74).[2] Presence of the tumor thrombus adds to the complexity of the surgery. The level of the tumor thrombus is an important factor for determining the surgical approach and type of incision. Although laparoscopic adrenalectomy in the setting of ACC with tumor thrombus has been described,[10] an open approach remains the gold standard surgical modality. Depending on the extent of the tumor thrombus, open surgery can be performed via flank, subcostal, chevron or thoracoabdominal approach. The principle of surgery is early proximal and distal vascular control followed by tumor thrombectomy. Where the inferior vena cava wall is invaded by the tumor, if R0 resection is possible complete excision and reconstruction of the cava should be performed. For the tumors extending into the atrium, cardiopulmonary bypass and cardiothoracic surgical assistance is necessary. Kidney sparing surgery should be performed where possible but one must have a low threshold for en bloc nephrectomy if renal invasion is suspected. There are no explicit recommendations to differentiate benign and malignant adrenocortical tumors. A few systems incorporating histological criteria have been proposed. The most frequently cited is the Weiss criteria revised by Aubert.[7] Our case satisfied 7 out of the 9 criteria, which is beyond the threshold of 3 suggestive of malignant tumor behavior. It is noteworthy to mention that the morphological criteria for diagnosis of benign and malignant adrenocortical tumors are different between adult and pediatric populations.[11] Furthermore in both populations, when adrenocortical tumors are composed exclusively or predominantly of oncocytes (oncocytic adrenocortical neoplasms) morphological criteria for predicting clinical behavior are different from those applied in tumors with non-oncocyte morphology and Lin-Weiss-Bisceglia score system is more appropriate.[12]
The decision for administration of adjuvant therapy is made based on the tumor stage, resection status and the presence of Ki-67 proliferation marker.[13] Adjuvant therapy with mitotane has been shown to prolong overall survival and disease free survival.[14,15] Close follow-up with 3 monthly CT scan imaging of the chest and the abdomen for the first 2 years is of importance, as the risk of recurrence remains high.

CONCLUSION

ACC is a rare condition and tumor thrombus represents a relatively uncommon presentation for this condition and where suspected needs to be further studied during the pre-operative work up. Complete resection with negative margins represents the best chance of cure for the patient. Adjuvant chemotherapy can be considered depending on final histopathology assessment and has been shown to improve survival.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Chiche L, Dousset B, Kieffer E, Chapuis Y. Adrenocortical carcinoma extending into the inferior vena cava: presentation of a 15-patient series and review of the literature. Surgery. 2006;139:15-27.
2. Ayala-Ramirez M, Jasim S, Feng L, et al. Adrenocortical carcinoma: clinical outcomes and prognosis of 330 patients at a tertiary care center. Eur J Endocrinol. 2013;169:891-9.
3. Cheungpasitporn W, Horne JM, Howarth CB. Adrenocortical carcinoma presenting as varicocele and renal vein thrombosis: a case report. J Med Case Rep. 2011;5:337.
4. Stein JP, Selby RR, Cote RJ, Hopkins B, Figueroa AJ, Skinner DG. Adrenal cortical carcinoma associated with a splenic vein tumor thrombus. Scand J Urol Nephrol. 1998;32:140-2.
5. Reyes MA, Ciancio G, Singal R, Manoharan M. Adrenocortical carcinoma with tumor thrombus in the right hepatic vein. Int J Urol. 2006;13:1233-5.
6. Yavascaoglu I, Yilmaz M, Kordan Y. Cardiac and caval invasion of left adrenocortical carcinoma. Urol Int. 2008;81:244-6.
7. Aubert S, Wacrenier A, Leroy X, et al. Weiss system revisited: a clinicopathologic and immunohistochemical study of 49 adrenocortical tumors. Am J Surg Pathol. 2002;26:1612-9.
8. Mueller-Lisse UG, Mueller-Lisse UL, Meindl T, et al. Staging of renal cell carcinoma. Euro Radiol. 2007;17:2268-77.
9. Fassnacht M, Libe R, Kroiss M, Allolio B. Adrenocortical carcinoma: a clinician's update. Nat Rev Endocrinol. 2011;7:323-35.

10. Kim JH, Ng CS, Ramani AP, et al. Laparoscopic radical adrenalectomy with adrenal vein tumor thrombectomy: technical considerations. J Urol. 2004;171:1223-6.
11. Magro G, Esposito G, Cecchetto G, et al. Pediatric adrenocortical tumors: morphological diagnostic criteria and immunohistochemical expression of matrix metalloproteinase type 2 and human leucocyte-associated antigen (HLA) class II antigens. Results from the Italian Pediatric Rare Tumor (TREP) Study project. Hum Pathol. 2012;43:31-9.
12. Wong DD, Spagnolo DV, Bisceglia M, Havlat M, McCallum D, Platten MA. Oncocytic adrenocortical neoplasms--a clinicopathologic study of 13 new cases emphasizing the importance of their recognition. Hum Pathol. 2011;42:489-99.
13. Berruti A, Fassnacht M, Baudin E, et al. Adjuvant therapy in patients with adrenocortical carcinoma: a position of an international panel. J Clin Oncol. 2010;28:e401-2.
14. Menaa F, Menaa B. Development of mitotane lipid nanocarriers and enantiomers: two-in-one solution to efficiently treat adreno-cortical carcinoma. Curr Med Chem. 2012;19:5854-62.
15. Terzolo M, Angeli A, Fassnacht M, et al. Adjuvant mitotane treatment for adrenocortical carcinoma. N Engl J Med. 2007;356:2372-80.