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Case Report

Adrenocortical Carcinoma With Renal Vein Thrombus Extended to Inferior Vena Cava: A Case Report

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Adrenocortical carcinoma (ACC) is a rare aggressive tumor. Renal vein and inferior vena cava (IVC) thrombi have been found as uncommon presentations of ACC; however, the implementation of comprehensive therapy has remained controversial in such cases. We report a case of a 46-year-old woman with a large ACC associated with the invasion of tumor to IVC confirmed by imaging and immunohistochemistry examinations. The patient was treated successfully using aggressive surgery, including adrenalectomy and thrombectomy adjunct to an adrenocorticolytic agent. However, she died of metastasis complications at 3-month follow-up period. ACC is a rare malignancy, mostly presenting in advanced stages with poor prognosis. Implementing aggressive surgical therapy might be effective for the management of such cases; however, the short survival duration in our case underscores the need for defining the precise therapy of metastatic ACC associated with venous invasion.

Key words: Adrenocortical carcinoma – Inferior vena cava thrombus – Distant metastasis – Adrenalectomy

Adrenocortical carcinoma (ACC) is a rare aggressive malignancy and naturally has a poor prognosis. The annual incidence of ACC has been reported as approximately 1 to 2 per million among the US population.[1] Patients with active endocrine adrenal tumors are often diagnosed with Cushing's syndrome associated with virilizing features; however, patients with nonfunctional tumors may present with symptoms consistent with a mass-occupying lesion such as abdominal or flank pain.[2]

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Surgery has long been considered as the only curative therapy, in which the overall 5-year survival of patients undergoing a complete resection has been found to be approximately 32% to 48%.[3] Although renal vein and inferior vena cava (IVC) involvements are common problems in renal cell carcinoma, those are uncommon presentations of ACC and make surgery difficult. The involvement of IVC is a main obstacle to surgical therapy in patients with ACC.[4] Herein, we report a case of a large ACC tumor associated with thrombus extension to both the renal vein and IVC, which was treated using aggressive surgery and resulted in short-term survival. This report assesses the previously reported ACC cases with venous thrombosis extending to IVC.

Case Report

A 46-year-old woman presented to our hospital with a complaint of left flank pain of 5-month duration. She had a history of hepatobiliary carcinoma in her mother diagnosed 20 years ago as well as a history of cerebral glioblastoma in her brother detected 2 years ago. Physical examination revealed a hard mass in the left upper quadrant of her abdomen. Routine laboratory tests were in normal limits except for liver function tests, which showed in the upper limit of normal values, including alanine transaminase and aspartate aminotransferase tests, 65 and 74 U/L, respectively. Ultrasound investigation showed a huge mass in the upper pole of her left kidney associated with multiple liver metastases consistent with the primary diagnosis of metastatic renal cell carcinoma or adrenal tumor. The imaging of her abdomen by computed tomography (CT) scan showed a large retroperitoneal mass in the upper pole of the left kidney displacing her left kidney downwards. The functional tests of the adrenal gland were in normal range, as well. Magnetic resonance imaging (MRI) showed a solid mass lesion ($12 \times 12 \times 10$ cm) associated with heterogeneous signal intensity and enhancement after contrast injection at the left side of the abdominal cavity, which seemed to originate from the upper pole of the left kidney with pressure effect resulting in a downward displacement of the kidney along with multiple liver and lung metastases (Fig. 1). Thereafter, a CT-guided abdominal mass biopsy was also performed, and the diagnosis of ACC was consequently confirmed on the basis of pathology and immunohistochemistry examinations. The immunohistochemistry test was positive for Melan-A, vimentin, Ki67 20%, and synaptophysin, and also showed negative results for endomysial antibody, creatine kinase, HepPar, calretinin, and chromogranin.

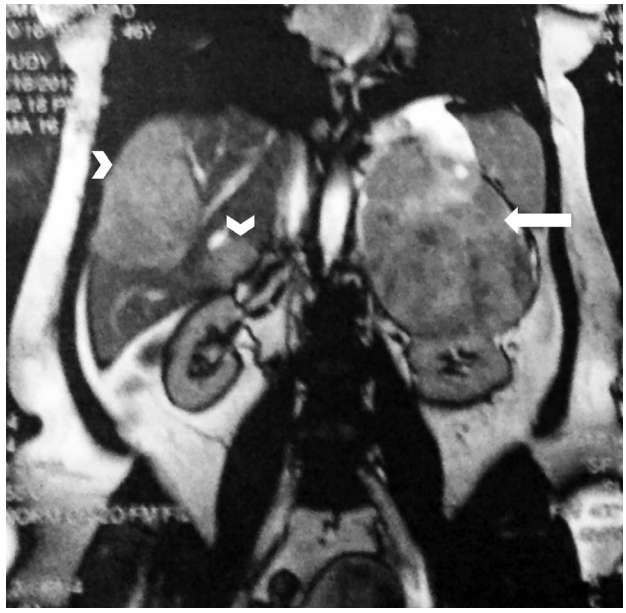

Fig. 1 MRI showing adrenal tumor (arrow) and liver metastasis (arrowheads).

After the completion of all diagnostic examinations, given the efficacy of surgical therapies to improve survival even in metastatic ACC cases,[5] a laparotomy was performed with chevron incision. During the operation, we noticed a hypervascular mass in the upper pole of the left kidney with renal hilum involvement along with a venous thrombus extending to both the left renal vein and IVC. Consequently, we completed surgery, performing adrenalectomy, left nephrectomy, para-aortic lymphadenectomy, and thrombectomy using the temporary ligation of both proximal and distal parts of IVC thrombus. The pathology report of the liver biopsy revealed an ACC, 16.5-cm in size, associated with multifocal vascular invasion, extensive necrosis, invasion to perirenal fat and renal hilum veins, and metastasis to hilar lymph nodes and the liver. The patient was referred to an oncologist to undergo chemotherapy with a regimen of Mitotane, as an adrenocorticolytic agent. However, she died of metastasis complication and diagnosing at advanced stages after 3-month follow-up.

Discussion

ACC is a rare and typically aggressive tumor, in which approximately 60% of cases present with the symptoms and signs of adrenal steroid hormone elevation that are similar to our case and are associated with female predominance (female to male ratio, 2.5).[6] Some cases have previously been reported; therefore we conducted a MEDLINE literature search over a 32-year period and found 44 cases of ACC with tumor thrombus extending to the IVC.[1–4,7–20] There were 18 nonfunctioning tumors and 26 functioning tumors, predominantly right-sided (32 right-sides versus 12 left-sides) and measuring 18 to 255 mm (median, 110 mm). Fifteen patients (34.1%) presented with distant metastases. Half of the cases were men with a median age of 51 years (range, 1–84 years). Clinical manifestations in functional tumors consisted of virilizing,[10] heterosexual pseudoprecocious puberty,[11] and Cushing's syndrome[3]; and in nonfunctional tumors, comprised flank mass,[1] varicocele,[2] hemoptysis,[12] and dyspnea.[14] The upper limit of thrombus extension was infrahepatic IVC in 22 cases, retrohepatic IVC in 7 cases, and suprahepatic IVC in 16 cases, including 12 with extension into the right atrium. In addition, median survival duration has been reported to be 8 months (range, 2–61 months).

Although invasive surgery is the only therapeutic option, Kim *et al* reported a case of a large ACC with thrombus extension to the right atrium in which, despite the patient's refusal to undergo surgery, the tumor regressed spontaneously during follow-up.[14] Some investigations found that the survival and quality of life of such cases improved after radical surgery.[19,20] In fact, in metastatic cases, even after radical surgery, 5-year survival has been shown to be 24%[13]; in another report, 5-year survival has been 7%, although in this case, surgery improved survival.[5] According to our literature review, the median survival for metastatic and nonmetastatic cases was 8 months, and given the 3-month survival in our case and those of previously reported cases, it seems that we need further large-scale study.

Regarding the management of atrial thrombus, several reports have suggested that the complete surgical removal of primary tumor with cavoatrial mass using cardiopulmonary bypass is the treatment of choice.[3] Similarly, in the cases we found in MEDLINE, 12 patients had been diagnosed with atrial thrombus, and most of them had successfully undergone cardiopulmonary bypass surgery. No clinical trial has been performed comparing the difference between other modalities such as interventional procedures with open heart surgery.

ACC is often diagnosed after a great delay in an advanced stage, as shown in the present case. The only potential curative treatment for ACC has been postulated to be repeated surgical resection,[15] which is technically possible in most patients. The most important predictor of survival in patients with adrenal cancer is the adequacy of resection. In a case series of ACC with thrombus, all patients underwent complete resection of venous thrombus and had 5-year survival rates ranging from 32% to 48%, while the median survival was less than 1 year in patients undergoing incomplete excision. Other treatment options include Mitotane, adjuvant chemotherapy, and palliative irradiation.[9] The treatment of advanced ACC cases basically consists of surgical resection and Mitotane- or Cisplatin-based chemotherapy.[21] Some studies investigating the Mitotane alone in metastatic, unresectable, or incomplete resection cases have demonstrated a response rate of 19% to 33% associated with 9-month survival in largest study.[22–24] In the previously reported cases, as stated in this report, postoperative Mitotane was administered in 29 patients. Given these findings and the short survival of our case, it seems that the aggressive surgery associated with adjuvant chemotherapy may not be considered as the treatment of choice for such cases, although it may be associated with increasing the survival rate.

In conclusion, ACC is a rare malignancy mostly presenting in advanced stages with poor prognosis. Our findings demonstrate that the aggressive surgical treatment might be effective for the management of ACC cases associated with thrombus extension to the IVC. Yet, the short survival duration in our case underscores the need for a large-scale clinical trial to find the precise therapy for metastatic ACC cases associated with venous invasion.

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