

CASE REPORT

Radionuclide venography for the evaluation of collateral venous supply in inferior vena cava thrombosis before chemotherapy in a rare adrenal cortical carcinoma

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Abstract

Adrenocortical gland carcinoma (ACC) is a rare tumour with an incidence of about one case per million population. Silent ACC are difficult to diagnose as they are asymptomatic until development of mass effects or other related symptoms. We present a case of a silent ACC in a female who was being planned for platinum-based chemotherapy. CT scan showed partial thrombosis of IVC confirmed by Doppler ultrasound. Radionuclide venography (RNV) was used to confirm inferior vena cava (IVC) flow. Blood flow in the IVC was seen to be reduced; however, there were well developed superficial collateral venous channels in the patient. This case shows that RNV is an effective tool for pre-chemotherapy assessment of venous blood flow, which may help in planning on the type of chemotherapy.

Key words: *Radionuclide venography, adrenocortical carcinoma, venous thrombosis*

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Introduction

Adrenocortical gland carcinoma (ACC) is a rare tumour with an incidence of about one case per million population [1]. ACC shows a bimodal peak: first peak in the fourth and fifth decades and the second in the first decade of life. About 60% of ACC are functional carcinomas that secrete hormones and present with clinical features like Cushing's syndrome due to cortisone, virilizing tumour due to androgens, or feminising tumour due to oestrogens. [2] The overall 5-year survival rate ranges from 16% to 38% depending upon stage of presentation. Recurrence, even after seemingly complete resection, is common, occurring in 23% to 85% of patients [3]. Death usually occurs in the first 2 years.

Case report

A 54-year-old female (Figure 1) presented in the OPD with complaints of pain in the abdomen particularly in the right side of the abdomen together with right lumbar area pain. There was a history of dilatation of the superficial veins for the last 3 months. US showed a right lumbar region mass located just below the liver. Chest x -ray of the patient showing metastatic deposit in the right lower

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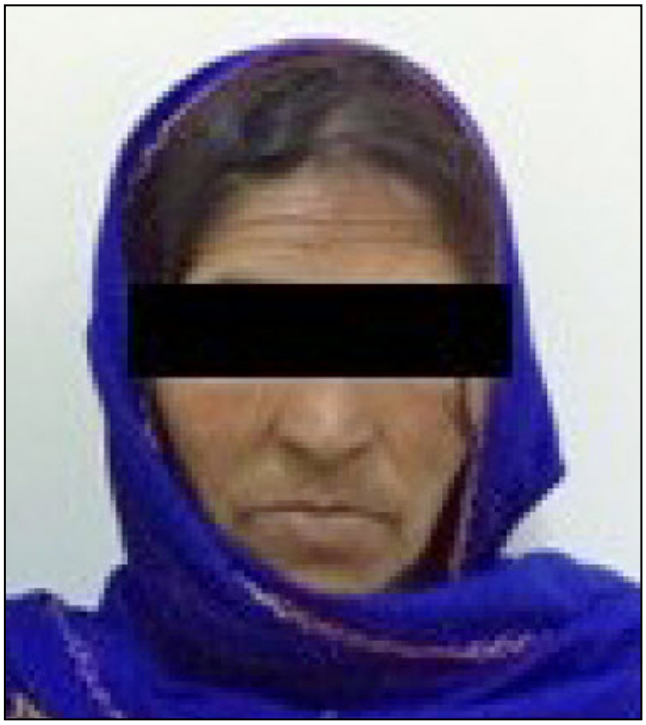

Figure 1 *Female patient with normal facial features (negative Cushing's features)*

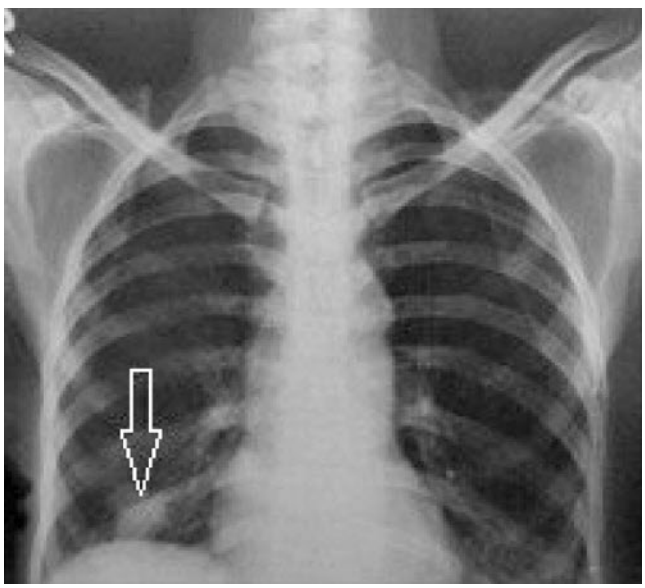

Figure 2 *Chest x -ray of patient showing metastatic deposits in right lower zone*

zone consistent with metastatic focus (Figure 2). All biochemical investigations were within normal limits with normal serum glucose at 2.5 mmol (Reference: 3.9-6.9 mmol/L), serum cortisol at 8 mcg/dl (Reference: 6-23 mcg/dl), and 24-hour urine vanillylmandelic acid (VMA) at 2.0 mg/24hr (Reference: <6.0 mg/24 hr). During surgery, complete excision of tumour was performed. CT scan abdomen and pelvis showed a large tumour involving the upper pole of the right kidney (Figure 3A). Post-operative CT scan (Figure 3B) showed residual lymphadenopathy in porta hepatis and para-aortic regions as well as, along with partial thrombosis of inferior vena cava caudal to the liver. As the patient was being planned for cisplatin-based chemotherapy, which needs aqequate hydration as per protocol Doppler US was done to evaluate the flow in IVC so as to avoid any fluid overload or ascites (Figure 4).

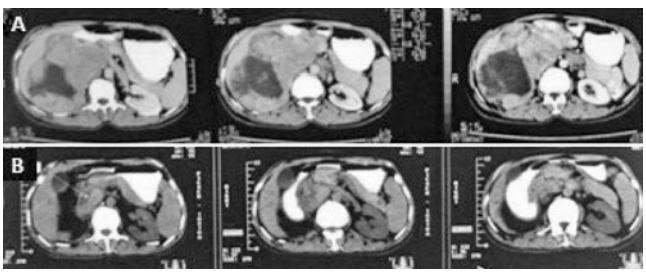

Figure 3 *(A) Preoperative CT scan of right sided adrenocortical carcinoma at the level of LV2/3. Necrotic right adrenal mass attached to the liver and the second portion of the duodenum with displacement of the right kidney and IVC. (B) Postoperative CT scan of adrenocortical carcinoma (tumour removed)*

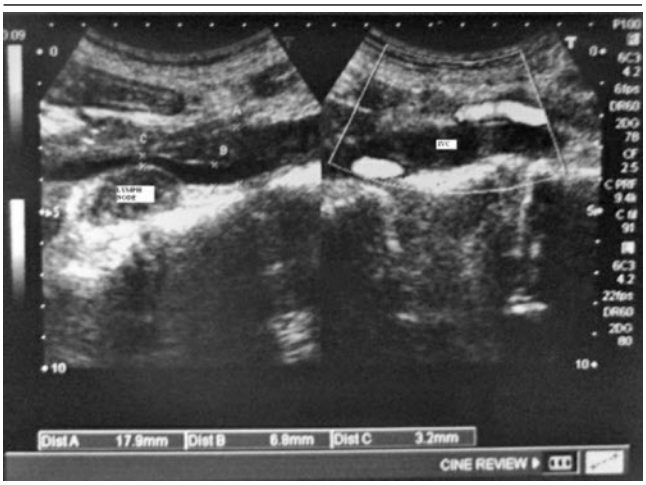

Figure 4 *Post-operative Doppler US scan of adrenocortical carcinoma showing partial blockade of Inferior vena cava with significant collateral flow (arrow) and lymphadenopathy*

Doppler study showed dampened blood flow in IVC with good collateral vessel flow as shown in Figure 4. To confirm the IVC thrombosis, we performed ascending radionuclide venography without tourniquet using 370 MBq of Tc-99m pertechnetate. Injection was administered in a right foot vein as shown in Figure 5. ADAC® gamma camera with a large field-of-view covering the region from mid thighs upwards (rectangular region in schematic of Figure 5) was used to image RNV. Normal path of pertechnetate is straight through the femoral vein into the external iliac vein and then from IVC (Figure 5, right panel) to the heart. The scan showed significant collateral flow through the anterior superficial abdominal veins likely inferior-epigastric veins (D) into thoraco-epigastric veins (E) as marked in Figure 5 (left & middle panels).

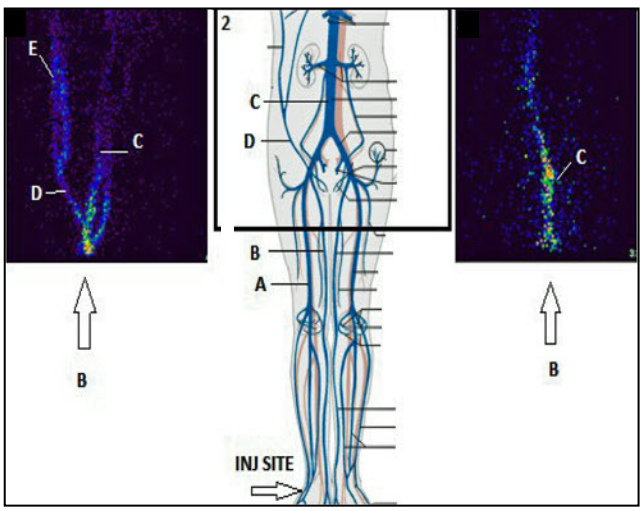

Figure 5 *Post-operative radionuclide venography (RNV) of IVC of adrenocortical carcinoma showing: (right panel) partial flow towards partially obstructed IVC and very good collateral flow (labelled as "D and E") in the superficial abdomino-thoracic veins; (middle panel) normal venous drainage of lower limbs into IVC and collaterals (rectanglular box demarcating the gamma camera field-of-view for RNV; (right panel) showing normal RNV in a subject with normal inferior vena cava (Note that the blood from femoral vein freely drains into abdominal part of IVC (labelled as "C"), with no collateral flow seen.*

Histopathology showed high nuclear pleomorphism with bizarre nuclei and mitotic activity as shown in Figure 6. Weiss criteria for assessment of prognosis of ACC were used (Table 1). High mitotic rate along with venous and capsular invasion of tumor predicts that ACC in this patient would have poor prognosis. Patient already had lung metastases (Stage IV disease) which also confer to bad prognosis. However patient was promptly put on chemotherapy and despite of metastatic lung disease patient tolerated chemotherapy very well.

Table 1 *Weiss criteria for assessing the prognosis*

Criteria	Histopathology
Nuclear grade	III
Mitotic rate > 2/50/HPF	Seen
Atypical Mitosis	Present
>1/3rd diffuse pattern	Present
Necrosis	Present
Venous invasion	Seen
Sinusoidal invasion	Seen
Capsular invasion	Seen

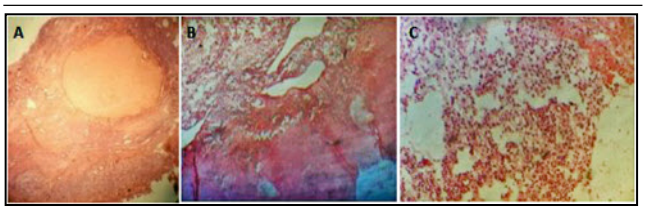

Figure 6 *Tumour showing vascular invasion and mitotic activity (H and E, ×200)*

The patient underwent complete surgical resection of the tumour. The gross specimen consisted of a centrally necrotic, peripherally viable appearing, heterogeneous gray to pink-yellow friable suprarenal mass, 17×8×10 cm, 1350 grams, completely effacing the adrenal gland. Pancreas and kidney were adherent to the tumour but otherwise uninvolved by tumour. Spleen and colon were also uninvolved by tumour. Microscopic examination shows hyper chromatic bizarre nuclei (Figure 6). Prominent nucleoli were seen along with vascular invasion of the tumour cells.

Discussion

As shown in this case, in cases of suspected IVC thrombosis, Doppler USG and RNV are the best tools for evaluating the venal caval blood flow and the collaterals. Collateral blood flow is a compensation process due to partial thrombosis of IVC over long time. This also confirmed clinical findings as there were well palpable veins along anterolateral aspect of anterior abdominal wall on the right side. This explains that why the patient did not develop ascites. Blood flow through IVC is very critical when starting cisplatin, where hydration is very necessary along with chemotherapy. If there are blood flow abnormalities then cisplatin (CAP regimen) may be skipped and other chemotherapy regimens (FAP regimen) may be considered.

ACC is a rare neoplasm with poor prognosis and with an incidence of one in one million population. There is a slight female predilection (58.6%). In children, the incidence is 0.3/million under 15 years of age. In Southern Brazil, it is 10-15 times higher. ACC occurs with increased frequency in children with Beckwith-Wiedmann syndrome and Li-Fraumani syndrome. However, most of the tumours are sporadic.

ACC is less responsive to radiation therapy as well as chemotherapy in its management. Clinical trials have shown different regimens giving optimal results in terms of tumour response. Mitotane an oral drug have shown encouraging results in neoadjuvant and adjuvant settings along with etoposide, doxorubicin and cisplatin or alone. Mitotane remains the major chemotherapeutic option for the management of ACC because it is a relatively specific adrenocortical cytotoxin. It is used as primary therapy, as adjuvant therapy, and as therapy in recurrent or relapsing disease.[5] Non-affordability issue & freely non-availability of drug refrains the patient to use Mitotane. The patient was started on injectable chemotherapeutic agents including cisplatin, doxorubicin and etoposide regime with doses adjusted according to the body surface area. The affordability of this drug regimen was an important factor together with the fact that the patient had a high mitotic index for disease in the lung, and a high mitosis rate has a potential for good therapeutic response to chemotherapy. As the patient could not afford mitotane, the CAP regimen was considered a good alternative for management of ACC in stage IV disease. However, as the recurrence rate and five year survival are poor therefore further research is required to evaluate the causes and management of such rare tumours.

Mitotane is currently used in treatment of ACC. It apparently causes adrenal inhibition without cellular destruction. The exact mechanism of action is unknown. It inhibits cholesterol side-chain cleavage and 11-beta-oxyhydrase reactions. It also appears to reduce the peripheral metabolism of steroids. Alteration of extra-adrenal metabolism of cortisol reduces measurable 17-hydroxy corticosteroid while stimulating the formation of 6-beta-hydroxy cortisol. Plasma levels of corticosteroids do not fall.

The First International Randomized Trial in Locally Advanced and Metastatic Adreno cortical Carcinoma Treatment (FIRM-ACT) study group reported that first-line therapy patients who received mitotane and etoposide had higher response rates and longer median progression-free survival than patients treated with streptozocin plus mitotane (5 mo vs 2.1 mo, respectively). Toxicity rates for both of the combinations were similar. Overall survival in the entire group was not significantly better; however, the study revealed that for those patients who did not receive alternative second-line therapy, overall survival was better with mitotane plus etoposide.[6]

In cases where mitotane fails, chemotherapeutic regimens containing cisplatin alone or in combination often are used. (Cyclophosphamide, doxorubicin [Adria mycin], and cisplatin [CAP]; 5-fluorouracil, Adriamycin, and cisplatin [FAP]; and cisplatin with etoposide-16 have been tried. Cisplatin also is often used in combination with ongoing mitotane administration.

As our patient was non-affording for Mitotane therefore we put patient on CAP chemotherapy. Overall response to two cycles of CAP was very good and no toxic effects were seen. Response evaluation was done by hematology and biochemistry including TLC, urea, creatinine and radiologically with USG abdomen and pelvis and chest x-ray. Patient is under treatment at our institute and is on chemotherapy with regular follow up.

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