

# Adrenocortical Tumor Presenting As Hemoperitonium - A Rare Case

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**Abstract:** Adrenocortical carcinomas are rare malignancies, which can present with diverse clinical manifestations. They can be functional, i.e., hormone secreting tumors or non-functional. In cases of hormone-secreting tumors, the hormone in excess determines the diagnostic clinical presentation. On the other hand, biologically inert tumors are diagnosed either due to their mass effect or as incidental findings. A very few present as a result of their potentially life-threatening complications. We present here a case of a 28-year-old female patient who underwent emergency laparotomy due to signs of acute abdomen and concomitant cardiovascular collapse caused by a spontaneously ruptured left adrenocortical carcinoma. The patient was operated for that and left adrenalectomy with splenectomy was performed where the tumor was removed in toto.

## 1. Introduction

Adrenal cortical carcinoma is an aggressive endocrine malignancy, though rare with an estimated incidence of 0.5 and 2 cases per million and accounting for about 0.05% to 0.2% of all malignancies.<sup>(1,2)</sup> they show bimodal distribution with majority of cases presenting between 4<sup>th</sup> and 5<sup>th</sup> decade of life and few cases before first decade of life. They can be either hormone secreting functional tumors or incidentally diagnosed non functional tumors. The latter present due to their mass effects or extremely devastating complications.

Prompt evaluation by biochemical and imaging studies establishes the diagnosis. Surgery remains the main stay of treatment in most of the cases. Use of chemotherapy is under study for recurrent cases. Radiotherapy is reserved for few recurrent and non operable malignancies. Acc carries poor prognosis with a five year survival rate less than 38%.

## 2. Case Report

A 28 years old female presented to the Emergency Room with features of acute abdomen and cardiovascular collapse. Patient was immediately resuscitated and haemodynamically stabilized. FAST was performed which revealed haemoperitonium and suspected splenic hematoma approximately measuring 10 X 10 cm. There was no history of trauma and serum Beta HCG levels were normal ruling out any ruptured ectopic pregnancy. Emergency Explorative laparotomy was performed in view of haemoperitonium. The blood was evacuated and abdominal organs were examined. Intra operatively, liver, spleen and mesentery were normal and ooze was noted from retroperitoneum into the abdomen. Bleeding was controlled and patient stabilized. There was a mass identified in the left supra renal region intra-operatively. On table biopsies were obtained and sent for histopathological examination. Abdomen was closed over external drains with mass left in situ and patient shifted to ICU. Immediate post-operative period was uneventful. (Fig 2)



Figure 1: Port wine stain



Figure 2: Intra operative specimen

Post-operatively CT scan was done. It revealed a left adrenal mass measuring 11 X 8 Cm. Meanwhile, histopathology revealed it to be adrenocortical tumor. To differentiate from functional and non functional tumors, blood investigations were sent. Serum levels of adrenal androgen hormones, cortisol and mineralocorticoids were in normal limits. 24 hours urine VMA levels were sent to rule out pheochromocytoma and turned out normal. The patient was taken up for second surgery where left adrenalectomy and splenectomy was performed.(Fig 3a and 3b)

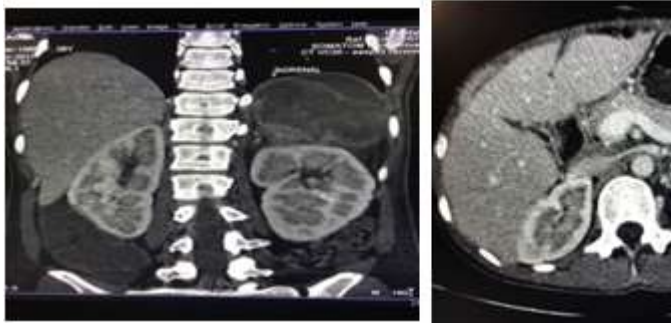


Figure 3a and 3b: CT Abdomen

Incidentally, patient has a port wine stain over the right side of the face. However, CT brain was normal with no neurological deficits clinically. (Fig 1)

Histopathology revealed polygonal cells with vesicular nuclei showing prominent eosinophilic nucleoli. There was significant cellular pleomorphism and frequent (3-4/hpf) mitotic activity. There were large areas of necrosis and vascular invasion. Immuno Histochemistry showed inhibin-positive, chromogranin and synaptophysin-negative and Ki67-33%. (Fig 4a,4b and 4c)

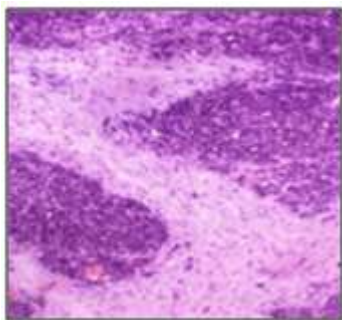


Figure 4a: Histopathology

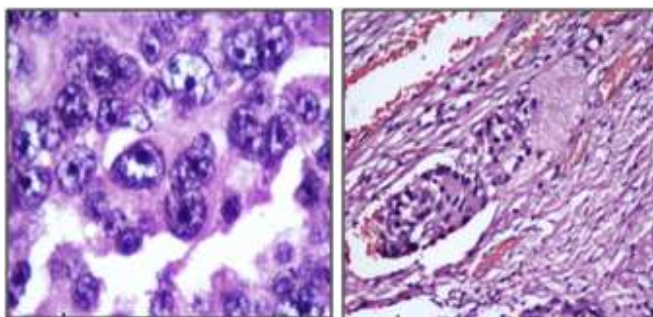


Figure 4b and 4c: Immunohistochemistry

### 3. Discussion

Adrenal cortical carcinoma is an aggressive endocrine malignancy, though rare with an estimated incidence of 0.5 and 2 cases per million and accounting for about 0.05% to 0.2% of all malignancies.<sup>(1,2)</sup> the mean age of diagnosis is fourth to fifth decade of life. However a second peak is noted in paediatric population between birth and ten years.<sup>(3)</sup> There is a slight female predominance in gender distribution with female to male ratio of 1.2 to 1.5:1.

Adrenal cortex neoplasm may be categorized into functioning and nonfunctioning tumors. About 24% to 79% of ACC are functional, and the vast majority of them present with symptoms related to excess corticosteroids, presenting as Cushing syndrome (30% to 40%)<sup>(4)</sup>, followed by virilisation (10% to 15%), and feminization (3% to 5%) due to elevated androgens. Majority of them show an overlap of these hormones, presenting as so-called mixed Cushing syndrome (12% to 18%). Adrenocortical carcinoma presenting as Conn's syndrome due to excessive mineralocorticoid, Aldosterone is rare, less than 1%.<sup>(5)</sup>

The clinical presentation varies from symptoms related to excess hormone production, abdominal symptoms due to mass effect, constitutional symptoms or discovered incidentally during an abdominal imaging investigation performed for an irrelevant to the tumor indication.<sup>(6)</sup> Nonfunctional adrenocortical carcinomas are associated with nonspecific symptoms such as nausea, vomiting, back pain, abdominal discomfort, or an ill defined sense of abdominal fullness, possibly due to mass effects of tumour enlargement on adjacent structures<sup>(6)</sup> and a very few present with anorexia, weight loss and fever.<sup>(7)</sup> However the tumour presenting with signs of acute abdomen is an extremely rare presentation of adrenocortical carcinoma.

Due to the rarity of incidence, European Network for the Study of Adrenal Tumors (NSAT), founded in 2002, proposed standard diagnostic procedures in 2006. Initially, hypercortisolism is ruled out by 24-hour urinary free cortisol and serum cortisol levels, late-night salivary cortisol, low- and high-dose dexamethasone suppression test, and basal corticotropin levels. Serum testosterone testing, serum adrenal androgens, including dehydroepiandrosterone (DHEA) and DHEA-sulfate, as well as 24-hour urinary 17 ketosteroids and 17 hydroxycorticosteroids is done for patients with virilization syndrome suspicious for androgen excess. On the other hand patients with feminization syndrome should undergo plasma estradiol and plasma estrone for confirmation. Plasma aldosterone and renin activity levels are done in patients with suspected excess mineralocorticoids.

Both MRI and CT have shown to be equally effective in determining tumor size and features suggestive of a malignant adrenocortical tumor.<sup>(8,9,10)</sup> The characteristics suggestive of malignancy are tumor heterogeneity, large tumor size (greater than 6 cm), presence of calcifications, irregular tumor margin, and high CT Hounsfield unit (greater than 10).<sup>(11)</sup>

The incidence of fine needle aspiration cytology (FNAC) has reduced significantly due to well developed imaging modalities and biochemical evaluation apart from being associated with a risk of needle track metastasis. It is avoided in cases suspected of pheochromocytoma due to risk of hypertensive crisis and haemorrhage.<sup>(11)</sup>

Although majority of ACCs are sporadic, specific inherited cancer syndromes like Li-Fraumeni syndrome, multiple endocrine neoplasia type 1 (MEN-1) syndrome, and Gardner syndrome caused by germline mutations in TP53, MEN-1,

and APC genes, respectively,<sup>(12)</sup> have a high frequency of ACC compared to benign adrenocortical adenomas, with some alterations such as loss-of-heterozygosity (LOH) of 11q13, the locus that contains MEN-1, occurring in up to 100% of ACC.<sup>(13)</sup> Among the several diagnostic and prognostic markers identified by Several genome-wide expression studies, helpful in the clinical management of patients with ACC, overexpression of IGF-2 is Common<sup>(14)</sup>. Ki-67/MIB1 has been associated with poor prognosis in several malignant tumors.

Recently, ACC was shown to express the estrogen receptor. In a study, the 5-year survival rate for those with ER-positive tumors was 60% compared to 0% in ER-negative tumors.<sup>(15)</sup>

Weiss et al described the histological criteria to distinguish benign from malignant adrenocortical tumours in 1989 and is widely used.<sup>(16)</sup>

The International Union Against Cancer (UICC) and the World Health Organization (WHO) proposed a new staging system in 2004 mainly based on two well known staging systems, the MacFarlane system or the Sullivan modification of the MacFarlane system to predict outcome and guide treatment strategies.

Surgery is the only curative option hence, it is the mainstay of treatment for ACC. Complete surgical resection is helpful in patients with stage I and II disease and in few patients with stage III. *En bloc* resection for left ACC usually includes distal pancreatectomy, splenectomy, left nephrectomy and sometimes partial gastrectomy or left hemicolectomy. For right sided ACC it may include right hepatic lobectomy, right nephrectomy and thrombus resection in the renal vein and inferior vena cava.

Although the recommended approach is transabdominal, few advocate use of laparoscopic adrenalectomy for localized tumors less than 10 cm without affecting disease-free survival. The tumor spillage or incomplete resection should be avoided, as the local recurrence rate is as high as 60% to 80%.

Mitotane is the only U.S. Food and Drug Administration (FDA) approved chemotherapeutic agent for the treatment of ACC. The rate of tumor regression with mitotane therapy alone ranges between 34% to 61%. The combination of mitotane with etoposide, doxorubicin, and cisplatin showed best response rate as reported by Berruti et al.

Radiotherapy has no role in adrenocortical carcinoma and is reserved for palliation in cases with symptomatic bone metastases. Local tumor bed irradiation has shown to reduce the local recurrence rate.

The prognosis for ACC is poor. The overall five year survival ranges between 16% to 38 %.<sup>(4)</sup>

#### 4. Conclusion

Adrenocortical carcinoma presenting as hemoperitonium is extremely rare. ACC should always be included as

differential diagnosis in cases presenting with spontaneous hemoperitonium.

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