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Case Report

Adrenocortical carcinoma (rare tumor): a case report and literature review

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ABSTRACT: A 40-year-old male patient presented with complaints of pain in abdomen, anorexia, low-grade fever and significant weight loss of one-month duration. USG and CT abdomen showed a large right adrenal space-occupying lesion with mass effect. The mass was resected but the patient succumbed to the surgery within 24 hours. On histopathological examination and immunohistochemistry a diagnosis of adrenocortical carcinoma (ACC) was made. ACC is a rare endocrine and heterogeneous malignancy with incompletely understood pathogenesis, aggressive course and poor prognosis. Although surgery is the mainstay of treatment in ACC, yet due to late patient presentation with large masses especially in hormonally inactive tumors, many are too late for curative resection, as was this case.

KEY WORDS: ***Adrenal; Adrenocortical carcinoma; Histopathology; Immunohistochemistry***

INTRODUCTION

Adrenocortical carcinomas (ACCs) are highly aggressive uncommon malignancies with a worldwide incidence of about 0.5-2 cases per million populations per year accounting for 0.02-0.2% of all cancer related deaths[1-4].Regardless of the size approximately 1 per 1500 adrenal tumors is malignant[4]. Due to its very low incidence, single institutions report only isolated cases of ACCs while only specialized centres are able to publish larger series over very long time periods[2]. ACCs tend to occur in two major peaks, one small peak in the first decade and a larger peak in the fourth to fifth decades[1,5]. Slight gender predominance is observed with women demonstrating an increased incidence (58.6%) over men (41.4%). This increase in incidence in women could be due to increased cigarette smoking and oral contraceptive use[5]. ACCs are classified as functional or non-functional. Functional tumors produce excess hormones like steroids and present with related symptoms while non-functional tumors present with symptoms related to tumor burden. Approximately 60% of all ACCs are functional. Children and women present more commonly with signs of hormonal excess than men who present with local symptoms due to large tumors and exhibit a rapid downhill course, like the current case[1,6,7].

CASE DETAILS

A 40-year-old male presented with complaints of pain in abdomen, anorexia, low-grade fever and significant weight loss of one-month duration. The patient did not have any other remarkable past or present medical history.

On physical examination the patient had abdominal tenderness over the hypochondriac and the right lumbar areas. Both USG and CT abdomen showed large space occupying lesion in the right lumbar area with mass effect and a small retropancreatic lymph node. The CT showed a nonfilling IVC with contrast. Chest X-ray showed a faint round opacity over the left lung lower zone. Hormonal parameters were normal.

The patient was operated upon and the right adrenal mass along with the right kidney was sent to the pathology department. However, the patient expired within 24 hours of surgery.

Histopathological Examination: On gross examination, the right adrenal mass measured 16.5x11.5x1cm and weighed 1250grams. The external surface of the mass was variegated, tan

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yellow with areas of necrosis, hemorrhage and had infiltrative borders. The cut surface of the mass was solid lobulated, pale yellow to tan with areas of necrosis as seen in **Figure 1**.

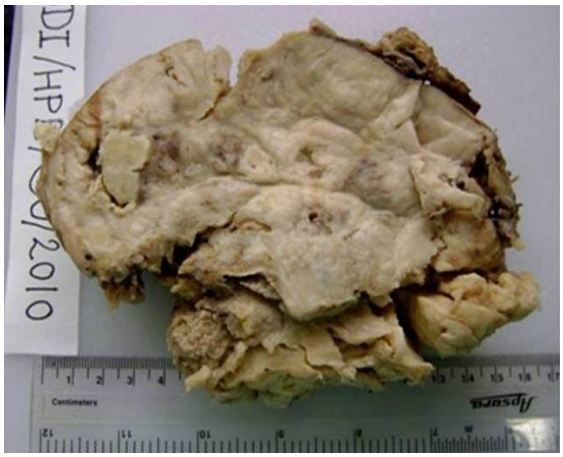

Figure 1: Adrenocortical carcinoma, formalin fixed cut section showing areas of necrosis, lobulations and infiltrative borders.

Both the external and cut surfaces of the right kidney were unremarkable on gross examination. The haematoxylin and eosin stained paraffin sections of the mass on low power showed tumor cells to infiltrate in solid sheets (**Figure 2a)**. On higher power the neoplastic cells were hyperchromatic **(Figure 2b)**, arranged in trabecular pattern **(Figure 2c)** with angioinvasion **(Figure 2d)** and large areas of necrosis **(Figure 2e)**.

They were highly pleomorphic and showed brisk mitoses with some atypical ones **(Figure 3a)**, intranuclear cytoplasmic inclusions **(Figure 3b)** and multiple tumour giant cells **(Figure 3c)**. Random sections from the right kidney were unremarkable on microscopy.

On immunohistochemistry, the sections from the adrenal mass showed diffuse strong positivity for synaptophysin **(Figure 4a)**, focal positivity for inhibin **(Figure 4d)**, negative staining for chromogranin and epithelial membrane antigen (EMA), (**Figure 4b)** and **(Figure 4c)** respectively.

Based on the findings of gross, microscopy and immunohistochemistry, a diagnosis of ACC was made.

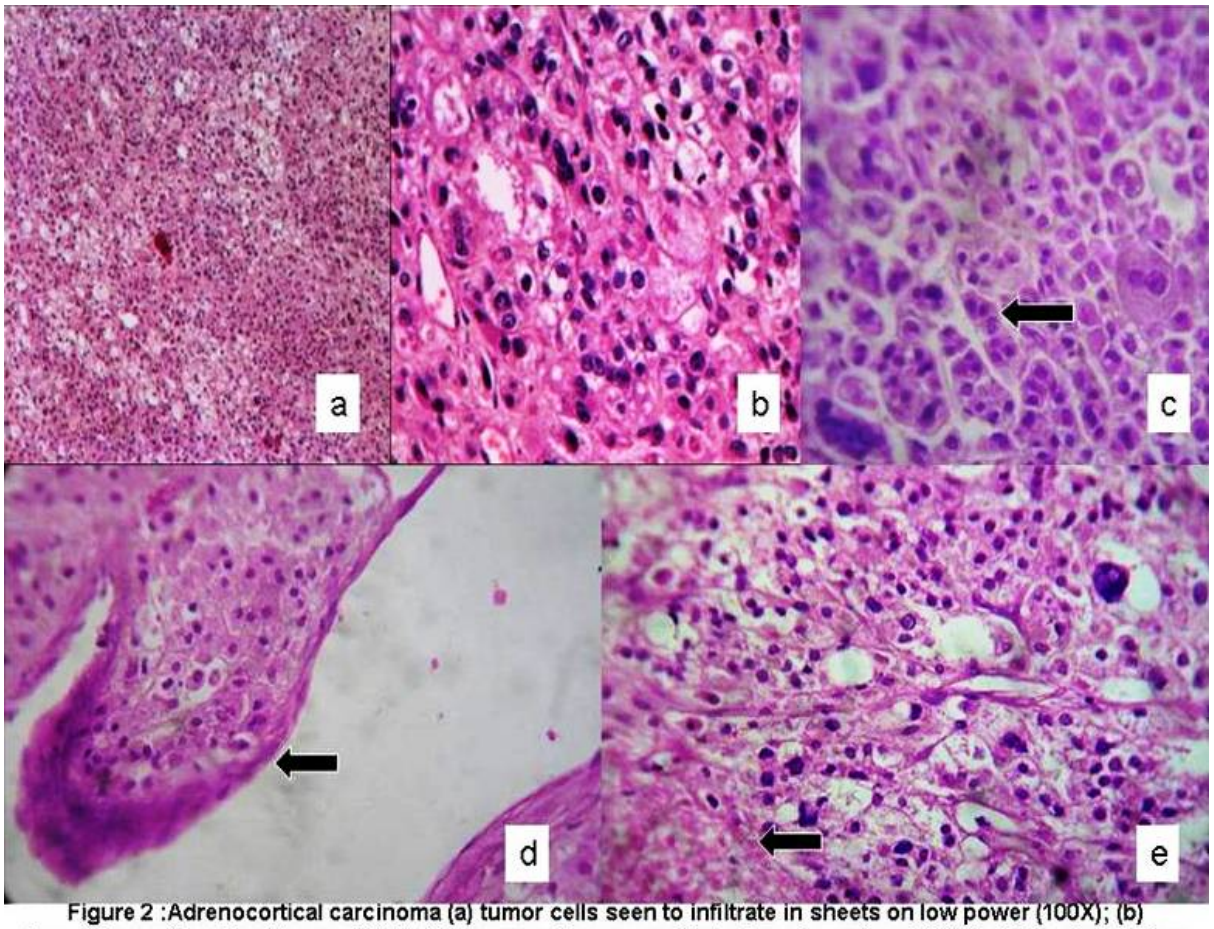

Figure 2 :Adrenocortical carcinoma (a) tumor cells seen to infiltrate in sheets on low power (100X); (b) hyperchromatic cells of tumor (400X); (c) tumor cells arranged in trabecular pattern (400 X); (d) angioinvasion seen as tumor cells covered with endothelial cells protruding into the vascular lumen (400X); (e) large areas of necrosis seen adjacent to sheets of tumor cells (400 X)

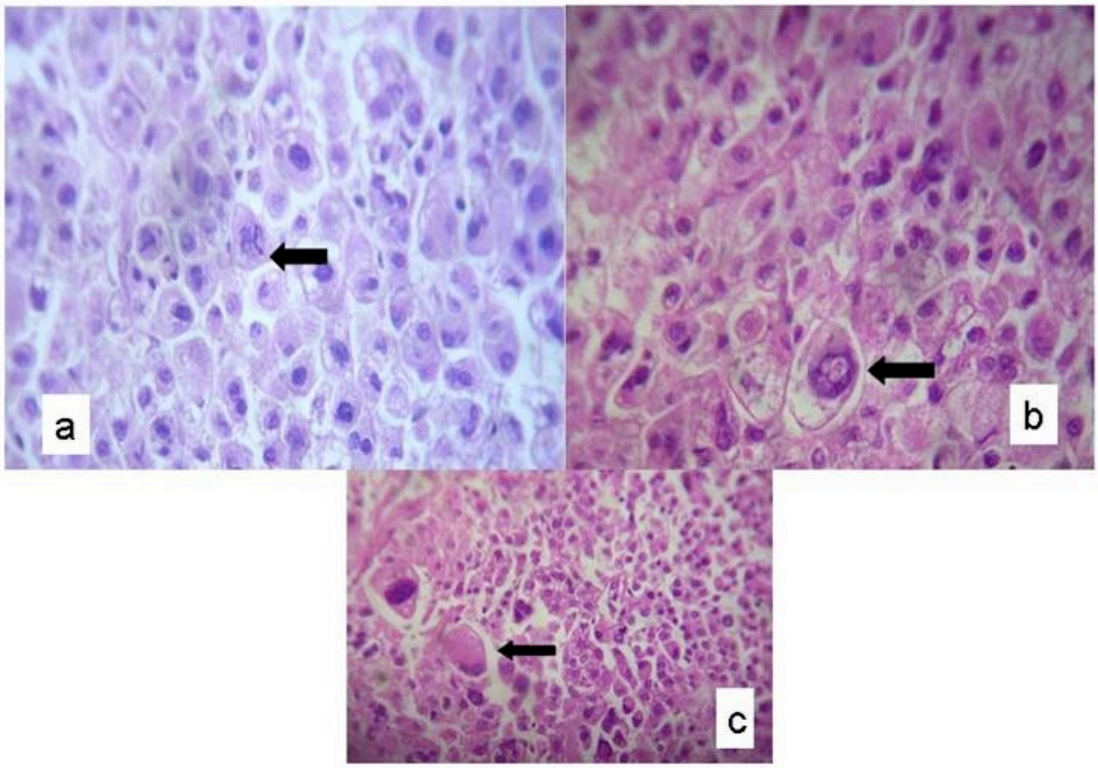

Figure 3. Adrenocortical carcinoma : (a) Brisk mitoses with many atypical mitoses marked by arrow (400 X) (b) Prominent intranuclear cytoplasmic inclusions as marked by arrow (400X) (c) Many tumor giant cells noted (100X)

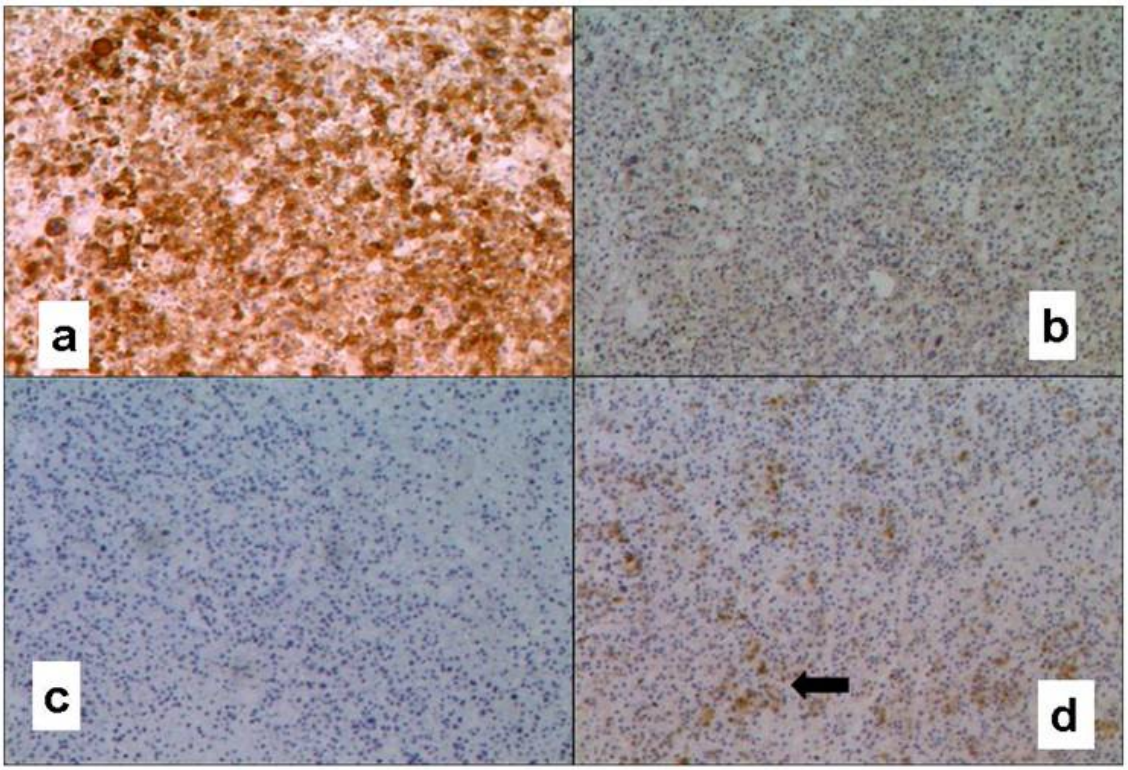

Figure 4 Immunohistochemical staining of Adrenocortical carcinoma: (a) Synaptophysin positive (100 X) ; (b) Chromogranin negative (100 X); (c) EMA negative (100 X); (d) Inhibin focal positive (100 X)

DISCUSSION

Although the exact aetiopathogenesis of ACC is unknown, gene mutations of tumor suppressor genes (like TP 53, TP 57 etc), DNA repair genes; activation of protooncogenes and others have been implicated in some studies[4].

Patients with non-functioning tumors present with non-specific symptoms related to tumor burden, like abdominal fullness, early satiety, pain, weight loss, weakness, fever or mass. In such cases on physical examination and radiology, the adrenal mass may be found incidentally[7,8]. In the present case the mass was detected on USG and CT for symptoms of mass effect. Although most incidentalomas are non-functional adenomas, some of the larger ones (5-15cm in diameter) could be ACCs presenting with mass effect[3,5,6].

Inspite of advances in imaging techniques, only a few adrenal lesions like simple cyst, myelolipoma and obvious local malignant invasion can be adequately categorized by radiology[1,8,9]. Venography is essential in all adrenal masses that are to undergo surgical resection to detect or to exclude thrombotic tumor masses in the suprarenal vein, renal vein or inferior vena cava (IVC)[1]. In the present case on contrast CT a nonfilling IVC was seen with a large right adrenal mass the exact nature of which could not be discerned.

Percutaneous biopsies and FNACs are unwarranted in cases of adrenal masses due to potential hazard of tumor seeding into the retroperitoneum, and are often inconclusive[1,8]. Resection of adrenal masses is therefore essential for diagnosis and necessary as a curative approach for ACC in all cases inclusive of recurrent disease, metastasis and non functioning adrenal masses[1].

In most studies so far histopathologic criteria of Weiss appeared to predict survival and prognosis of ACC most accurately whereas immunologic markers, cytoskeletal markers, DNA ploidy, cell phase markers and oncogenic probes have yielded inconsistent results[7,9-11]. In addition to Weiss criteria, gross factors predicting malignancy and prognostically important were: weight >400gms; tumor size >10.5cms; variegated appearance, fibrous bands, nodularity, intratumoral haemorrhage and nuclear cytoplasmic pseudoinclusions[7,10-12].

In some studies tumor size, mitotic count and haemorrhage predicted 5 years survival of 0-83%[10]. Mitotic index was found to be the single most important factor in predicting prognosis in many studies. Stojadinovic found 30-85% of cases to have distant metastasis at presentation and hence to carry a dismal prognosis. Patients without distant metastasis but presence of >4 factors of the 6 viz. venous invasion, capsular invasion, adjacent organ invasion, tumor necrosis, high mitotic rate and atypical mitoses on resection had a worst survival of 0% compared to those without resection who had a 8.6% survival[11].

The main differential diagnosis of ACCs are pheochromocytoma, renal cell carcinoma, hepatocellular carcinoma, metastatic carcinoma and liposarcoma. Most of the other tumors can be separated from ACC by performing immunohistochemistry. In pheochromocytoma both synaptophysin and chromogranin are positive while in ACC only synaptophysin is positive (upto 90% of ACCs). In renal cell carcinoma, hepatocellular carcinoma and metastatic adenocarcinoma, epithelial membrane antigen (EMA) is positive but synaptophysin is negative, while in ACC, EMA is negative. In liposarcoma, synaptophysin as well as inhibin are negative both of which are positive in ACC.

In the present case almost all of Weiss' prognostic criteria were found to be present viz. venous invasion, capsular invasion, tumor necrosis, >45mitoses/50hpf, atypical mitoses, high nuclear grade, nuclear pseudoinclusions and diffuse architecture of tumor cells amongst others. Also the tumor was strongly positive for synaptophysin, negative for EMA and chromogranin and focal positive for inhibin thus fitting into the diagnosis of ACC[1,12].

CONCLUSION

ACC is a rare and highly malignant tumor with poor prognosis probably due to late presentation with advanced and metastatic disease especially the non-functional types. The Weiss histologic criteria appear to correlate best with disease prognosis. Complete resection still appears to be the best form of treatment in all cases. Future advances in management of ACC would depend on better understanding of molecular pathogenesis.(eg. development of tyrosine kinase inhibitors).

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