

Case Report

Unusually Large Functional Adrenal Adenoma: A Rare Case Report with Review of Literature.

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Abstract: Functional adrenal adenomas of more than 4 centimeters in size are rare. We report a case of adrenal adenoma of 12 centimeters in size, presenting with Cushing's syndrome. **Key words:** adrenal adenoma, large, functional.

INTRODUCTION

Primary diseases of adrenal gland are responsible for up to 20% of cases of Cushing's syndrome. Cortical adrenal adenomas account for 15% of cases. These benign tumors are usually smaller than 4 centimeters (cms) and secrete cortisol.¹ Large adrenal adenoma producing Cushing's syndrome is a rare finding. The presence of large adrenal mass in a patient with Cushing's syndrome is practically always indicative of carcinoma. We present a case of a large adrenal adenoma, measuring 12 cms in size, along with discussion on the clinical, radiological and biochemical features of the case and relevant review of literature.

CASE

A 30-year old female presented with complaints of swelling all over the body for last one year, along with increased body hair and presence of abdominal striae. There was no history of headache, vomiting, visual difficulty, polyuria and polydypsia. Her past medical, personal and family histories were unremarkable. Her blood pressure was 140 / 100 mm of mercury. On examination, patient had moon-facies, increased body hair, proximal muscle weakness, especially involving the pelvic girdle and non-pitting pedal edema. Per abdominal as well as external genitalia examination was within normal limits. No abnormalities were detected in haematological investigation and the values were within normal limits. Routine urine analysis, X-ray chest and electrocardiogram (ECG) revealed no abnormalities. Skeletal survey did not show any symptoms of osteoporosis and there was no seller pathology on skull X-ray. Urinary free cortisol concentration, measured as cortisol / creatinine ratio on two successive 24-hour urine collections were found to be raised to 90 and 169 mol / millimole (reference range 5-55 mol / millimole). On high dose dexamethasone suppression test (dexamethasone 2 milligram orally every six hour for 48 hours), her basal plasma cortisol level was 515 nanomole / litre that failed to suppress after 48 hours and remained raised at 510 nanomole / litre. Computed tomographic (CT) scan of abdomen showed a large mass arising from adrenal gland, suggestive of adrenal neoplasm. Right adrenalectomy of the patient was done and resected specimen was sent for histopathological examination. On gross examination (Figure 1), the operated tumor mass measured 12 cms in size, yellow to brown in color, homogenous, and partly encapsulated. No evidence of necrosis or hemorrhage was

apparent. Various sections from the tumor showed tumor cells disposed in nests, cords and alveolar arrangements (Figure 2). Cells had vacuolated, clear cytoplasm, and variable number of compact type of cells. The nuclear-cytoplasmic ratio was low, although a few cells showed enlarged hyperchromatic nuclei. Scarce mitotic activity was seen, with no abnormal mitotic figures. No necrosis, capsular, venous or sinusoidal invasion was seen. Weiss scoring² of the tumor was calculated to be 2. Post-operative period was uneventful and the patient fully recovered after the surgery.



Fig. 1: Resected specimen of adrenal adenoma.

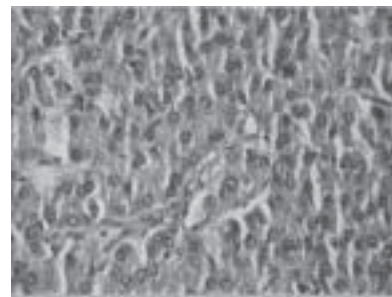


Fig. 2: Microscopic section of adrenal adenoma showing tumour cells in sheets & trabeculae (H & E X 400).

DISCUSSION

Cushing's syndrome is a group of clinical and metabolic disorders characterized by adrenocortical hyperfunction. It is associated with excess production of glucocorticoides. In clinical practice, most cases of Cushing's syndrome are the result of the administration of exogenous glucocorticoides. The endogenous Cushing's syndrome may be associated with primary hypothalamic or pituitary disease associated (70-80%), hypersecretion of adrenocorticotrophic hormone (ACTH) or cortisol by an adrenal adenoma, carcinoma or nodular hyperplasia (10%) or secretion of ectopic ACTH by a non-endocrinal source (10%).

Adrenal adenomas are uncommon in patients younger than 30 years. Most of them are small in size. Only a few (d"10%) of them are functional with production of glucorticoides (Cushing's syndrome), mineralocorticoides or sex hormones. Approximately 80% of patients are females, and in only 20% of cases, the syndrome occurs before puberty. The adrenal adenomas are usually unilateral although bilateral cases are on record.³

The most significant point in an adrenocortical neoplasm is the differentiation between adrenocortical adenoma and carcinoma. Truly speaking, there is no single histological criteria by which we can reliably differentiate the two. Several studies have been done in past to reach a convincing guideline to solve the puzzle. The most relevant and widely used one was given by Weiss² in 1984 who proposed nine histopathological criteria to distinguish adenomas from adrenal cortical tumors that had metastasized or locally recurred. Malignant ones met four or more of these histological criteria.² The low threshold for malignancy was mentioned by Weiss and the presence of three or more of these of histopathological criteria was suggestive for a malignant clinical behavior. However, Weiss criteria are exclusively histopathological in nature, which can be assessed only after the tumor has been resected. In practice, the clinicians need to know before surgical intervention if the lesion they are dealing with is benign or a malignant one as adrenocortical carcinomas are usually associated with a dismal prognosis. Both CT and magnetic resonance imaging (MRI) are useful in evaluation; CT is currently regarded as the most accurate imaging modality for the preoperative localization of these tumors.⁵ Besides signs of local invasion, lymphadenopathy, distant metastasis and few other imaging parameters, size of the tumor remains to be one of the most important pre-operative predictor in making such differentiation.

Several studies have been done in past to evaluate size of the tumor as a marker of malignancy. Barnett CC Jr et al⁶ in their retrospective study evaluated the value of tumor size and other clinical parameters in the prediction of the adrenal malignancy. They found size of the tumor to be the single best predictor of malignancy. In their study, the median size of the adrenal cortical adenomas was found to be 3 cms and 9.2 cms respectively. In their study, Lumachi et al⁷ found that there was a significant difference in size between benign neoplasms (range, 3–6 cms; median, 4 cms) and malignant neoplasms (range, 3–12 cms; median, 6 cms), while no benign lesion exceeded 6 cms in size. In another study by Jain et al,⁸ the mean size and weight of the malignant tumors were found to be statistically significantly; higher than those of the benign tumors, with no adenoma was being larger than 5 cms and no carcinoma was smaller than 6 cms. According to Fassnacht M et al,⁹ the probability of malignancy is clearly related to tumor size as almost all lesions of < 3 cms in size are benign whereas diameter of > 3 cms indicate a higher risk of malignancy.

Thus, the previous studies show that the adrenal adenomas are mostly smaller in size, that is, less than 5-6 cms and adrenal carcinomas often more than 5 cm, though smaller carcinomatous lesions might be detected. However, the problem in suggesting

the larger lesions to be the malignant ones is that rarely, large histopathologically proven (as per the Weiss criteria) adenomas also occur, as in our case where gross size is 12 cms. Barnett CC Jr et al⁶ too concluded that although size remains a good predictor of the histological features and clinical behavior of adrenal neoplasm, both small and large benign adrenal cortical tumors occur with measurable frequency. A subgroup of adrenal adenomas are larger, more heterogeneous, and more frequently calcified than those with the usual imaging findings. Central necrosis, hemorrhage, or both are responsible for many of the imaging features. Differentiation of these lesions from other large adrenal masses, including adrenal carcinoma, cannot be made by means of imaging alone; resection is required for the definitive diagnosis. Adrenal adenomas may occasionally undergo intratumoral hemorrhagic degeneration with development of avascular and cystic internal regions and subsequent fibrosis. They then become much larger and display focal liquefaction, central or peripheral calcification and fibrosis, internal soft-tissue nodules, and patchy heterogeneous contrast enhancement, features that are commonly associated with adrenocortical carcinomas and other lesions. These lesions can be misdiagnosed histologically also if the criteria for malignancy, which include mitoses, a trabecular growth pattern, and an increased nuclear-cytoplasmic ratio, are not applied correctly¹⁰.

To conclude, we suggest that tumor size determined by imaging techniques does help in deciding malignant potential of the adrenal tumors but is not infallible. High-quality imaging studies (CT and MRI), imaging-guided fine needle aspiration cytology (FNAC)⁷ and diagnostic laparoscopy may be useful in establishing a preoperative diagnosis. Ultimately, histopathological examination continues to be the benchmark for diagnosis.

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