Abstract: Adrenal cortical carcinoma is a rare endocrine neoplasm with a worldwide incidence of two per million population. There is a bimodal age distribution. Tumours may be functional or non-functional depending on whether they produce cortisol, androgens, aldosterone or estrogen. The etiology of adrenal cortical carcinoma is unknown, although recent studies documenting chromosomal abnormalities and alterations in growth factor production have provided insight into possible mechanisms of molecular pathogenesis. Associated with Li-Fraumeni syndrome, MEN-1, Beckwith Wiedman syndrome and carney complex. Complete surgical resection is the curative therapy for localized adrenal cortical carcinoma. 65yrs old female patient presented with CO lower abdominal pain, abdominal swelling, loss of weight, loss of appetite. USG and CT showed Large, lobulated, heterogenous space occupying lesion in the region of left adrenal gland measuring 12 x 8 x 7.5 cms and central necrosis is noted. We did open adrenalectomy. Histopathology report came as adrenal cortical carcinoma. In the past 5 years only two cases are reported in Rajiv Gandhi Government General Hospital, Chennai.

Keyword: functional, non functional, surgery, mitotane, cushing syndrome, virilisation

INVESTIGATIONS:
Routine blood investigations were found to within the normal limit. Serum cortisol:13.27Micg/dl (6.2-13.4) (7 to 10 am) (2.3-11.9) (4 to 8 pm). Cortisol morning sample: 7.8 Micg/dl (3.7 to 19.4). Urine 24 hrs metanephrine: -93.10 (0-350 Micg/day). Serum electrolytes: Na-1139 mmol/L, K - 3.9 mmol/L.

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DISCUSSION

INTRODUCTION:

Adrenal cortical carcinoma is a rare endocrine malignancy with an incidence of 0.5 to 2 cases per million people each year. There is a bimodal age distribution, with incidence peaking in young children less than 5 years old and then again between 40 and 50 years of age. Prognosis tends to be poor because diagnosis is usually delayed, and there is dearth of effective systemic chemotherapy. Complete surgical resection is the only potentially curative treatment. Epidemiological studies have suggested increased incidence of Adrenal cortical carcinoma in association with increased in cigarette smokers in men and the use oral contraceptives in women.

MOLECULAR PATHOGENESIS:

Studies of the genetic alterations in adrenal cortical tumors have revealed the importance of multiple chromosome loci correlate with regions that are involved in familial cancer syndromes. Such syndromes include Li-Fraumeni syndromes (p53 gene on 17p13), Multiple Endocrine Neoplasia type I (MEN 1, MEN1 gene on 11p13), Beckwith-Wiedemann syndrome (11p15.5) which correlates with the overproduction of insulin like growth factor (IGF) II, and the Carney's complex (2p16) (10). The genes h19, insulin-like growth factor II (IGF-II), p57kip2 are important for fetal growth and development. In contrast, IGF-II gene expression has been shown to be high in adrenal cortical carcinomas, especially in tumors producing cortisol and aldosterone. There is also a loss of activity of the p57kip2 gene product in virilizing adrenomas and adrenal cortical carcinomas. Finally, c-myc gene expression is markedly reduced in both nonfunctioning and functioning adrenal cortical carcinomas, especially in tumors producing cortisol and aldosterone. There is also a loss of activity of the p57kip2 gene product in virilizing adrenomas and adrenal cortical carcinomas. In contrast, IGF-II gene expression has been shown to be high in adrenal cortical carcinomas. Finally, c-myc gene expression is relatively high in neoplasms, and it is often linked to poor prognosis. (10) The tumor suppressor gene p53 has also been implicated in the pathogenesis of adrenal cortical (14) cancer.

CLINICAL MANIFESTATIONS:

Patients with adrenal cortical carcinoma usually present with vague abdominal symptoms secondary to enlarging retroperitoneal mass or with clinical manifestations of overproduction of one or more adrenal cortical hormones. Most tumors in children are functional, and virilization is by far the most common presenting symptom, followed by Cushing's syndrome and precocious puberty (1). Among adults presenting with hormonal syndromes, Cushing's syndrome alone is most common, followed by mixed Cushing's and virilization (glucocorticoid and androgen overproduction). Feminization and Conn syndrome (mineralocorticoid excess) occur in less than 10% of cases. Rarely, pheochromocytoma-like hypersecretion of catecholamines has been reported in adrenocortical cancers. (11) Non-functional tumors (about 40%, authorities vary) usually present with abdominal or flank pain, or they may be asymptomatic and detected incidentally. (12) All patients with suspected adrenocortical carcinoma should be carefully evaluated for signs and symptoms of hormonal syndromes. For Cushing's syndrome (glucocorticoid excess) these include weight gain, muscle wasting, purple lines on the abdomen, a fatty "buffalo hump" on the neck, a "moonlike" face, and thinning, fragile skin. Virilization (androgen excess) is most obvious in women, and may produce excess facial and body hair, acne, enlargement of the clitoris, deepening of the voice, coarsening of facial features, cessation of menstruation. Conn syndrome (mineralocorticoid excess) is marked by high blood pressure which can result in headache and hypokalemia (low serum potassium, which can in turn produce muscle weakness, confusion, and palpitations) low plasma renin activity, and high serum aldosterone. Feminization (estrogen excess) is most readily noted in men, and includes breast enlargement, decreased libido and impotence. (10)

The diagnostic evaluation of adrenal mass include measurement of serum electrolytes level to exclude hypokalemia secondary to aldosterone excess. The most sensitive initial screening test for hypercortisolism in patients with adrenal mass is an overnight 1 mg dexamethasone suppression test. Patients with suppressed cortisol levels do not have cushing syndrome and do not require further evaluation for this condition. Patients without suppressed cortisol levels should undergo a 24-hour urine collection for measurement of free cortisol. 24 hour urine collection for free catecholamine levels and their metabolites should be done to rule out pheochromocytoma. (12) RADIOLoGY

Standard preoperative staging in patients with adrenal mass includes HRCT abdomen or MRI. MRI may be helpful in delineating tumor extension in to inferior vena cava. Positron emission tomography when combined with CT imaging helpful in detecting metastasis or recurrence. CT scans of the chest and bone scans are routinely performed to look for metastases to the lungs and bones respectively. These studies are critical in determining whether or not the tumor can be surgically removed, the only potential cure at this time. (2) PATHOLOGY

Adrenal tumors are often not biopsied prior to surgery, so diagnosis is confirmed on examination of the surgical specimen by a pathologist. Grossly, adrenocortical carcinomas are often large, with a tan-yellow cut surface, and areas of hemorrhage and necrosis. On microscopic examination, the tumor usually displays sheets of atypical cells with some resemblance to the cells of the normal adrenal cortex. The presence of invasion and mitotic activity help differentiate small cancers from adrenocortical adenomas. (2) There are several relatively rare variants of adrenal cortical carcinoma:

- Oncocytic adrenal cortical carcinoma
- Myxoid adrenal cortical carcinoma
- Carcinosarcoma
- Adenosquamous adrenocortical carcinoma
- Clear cell adrenal cortical carcinoma
**TREATMENT:**
The only curative treatment is complete surgical excision of the tumor, which can be performed even in the case of invasion into large blood vessels, such as the renal vein or inferior vena cava. The 5-year survival rate after successful surgery is 50–60%, but unfortunately, a large percentage of patients are not surgical candidates. Radiation therapy and radiofrequency ablation may be used for palliation in patients who are not surgical candidates. Chemotherapy regimens typically include the drug mitotane, an inhibitor of steroid synthesis which is toxic to cells of the adrenal cortex, as well as standard cytotoxic drugs. A retrospective analysis showed a survival benefit for mitotane in addition to surgery when compared to surgery alone. The two most common regimens are cisplatin, doxorubicin, etoposide + mitotane and streptozotocin + mitotane. It is unknown which regimen is better. Researchers at Uppsala University Hospital initiated a collaboration between adrenocortical cancer specialists in Europe, USA and Australia, to conduct the first ever randomized controlled trial in adrenocortical cancer (FIRM-ACT study), comparing these two regimens.

**PROGNOSIS:** ACC, generally, carries a poor prognosis and is unlike most tumours of the adrenal cortex, which are benign (adenomas) and only occasionally cause Cushing’s syndrome. Five-year disease-free survival for a complete resection of a stage I–III ACC is approximately 30%. The most important prognostic factors are age of the patient and stage of the tumor. Poor prognostic factors: mitotic activity, venous invasion, weight of 50g+, diameter of 6.5 cm+, Ki-67/MIB1 labeling index of 4%+, p53+

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