Virilizing adrenal tumor:A Case report

ABSTRACT

Objective : To discuss a rare case of virilizing Oncocytoma of Adrenal Gland.

Discussion: Hirsutism is a common problem affecting 5-10% of the general population. It causes immense psychological burden. The commonest cause of hirsutism is poly cystic ovary syndrome (PCOS). It is seen in 3 out of 4 hirsute women. Sometimes it will be due to rare endocrine diseases like Cushing's syndrome , non- classical congenital adrenal hyperplasia , androgen secreting ovarian tumor or to rare androgen secreting adrenal tumors.

Presentation : we report a 49 Year old lady presented with hirsutism and virilization features to Dermatology department. On further hormonal evaluation by an endocrinologist, it was found to have an elevated Di hydro epiandrosterone - sulfate (DHEA-S). Computerized Tomography (CT) of abdomen was done which showed 45x35x38 mm right adrenal mass. She underwent open right adrenalectomy and histopathology reported as adrenal oncocytoma, a rare adrenal tumor. Functional adrenal oncocytoma is very rare in literature and it is valuable to report.

Conclusion:Adrenal oncocytomas are rare tumors which are commonly present as adrenal incidentalomas. Only histopathology can diagnose oncocytomas and its clinical behaviour. Treatment of choice is excision as open or laparoscopic adrenalectomy. As there are no clear cut guidelines for follow up, it needs further studies and high levels of evidence.

Keywords: Hirsutism, Virilization, DHEA-S, Adrenal Oncocytoma

INTRODUCTION

Oncocytic adrenocortical tumors (OATs) or neoplasms are extremely rare. Most of the cases are nonfunctional and benign, predominantly affecting middle-aged women. About 147 cases have been reported globally in the literature according to a systematic review by Mearini et al. and it is reported that most of the affected patients have been in the age group of 40 to 60 years. Most of these tumors were detected incidentally and 20% of them demonstrating evidence of malignancy. Approximately 10-20% of the OATs were functional in nature. Here we present functional OAT in a 49 year old lady.

Case presentation

A 49 year old lady with no co-morbidities came with history of excessive hair growth over chin and upper lip area of 8 months duration which was progressive in nature. Her Ferriman Gallwey score was 8(Fig 1A). She had history of recent change in voice for 6 months. She attained menopause 1 year back till then she had regular cycles. She had no symptoms of easy bruising, striae or proximal myopathy. Her medical and family history were unremarkable. She had history of thyroidectomy 25 years back, but not on any thyroxine replacement. On examination she was moderately built and nourished with Body Mass Index (BMI) of 28.2kg/m^2. She had hirsutism and male pattern hair loss with features of virilization like acne, atrophied breast and hypertrophied clitoris. She had a large Café-au-lait spot in the upper abdomen and an umbilical hernia which was reducible. There was no mass palpable in the abdomen. There was no features of hypercortisolism like moon facies, facial plethora, ecchymosis, purple striae or acanthosis nigricans. She had a neck scar which was healed with primary intention and had a grade 2 thyroid swelling, which was moved with deglutition and lower border was palpable. Hormonal evaluation was done(Table 1) which showed elevated testosterone and DHEA-S. Contrast Enhanced CT of abdomen was done which showed heterogeneous enhancing mass right adrenal mass of size 45x35x32 mm with Absolute Absolute washout of 58% and Relative washout of 32% (Fig 1B and 1C). Left adrenal gland is seen separate and normal. Lesion is in close contact with inferior vena cava (IVC) and has indiscernible fat planes with segment VI of liver. No obvious infiltration to liver or adjacent structures visualized. Minimal ascites is also seen. Features are suggestive of adreno cortical carcinoma or lipid poor adenoma of adrenal gland. As ascites and indiscernible fat planes with liver segment demonstrated in CT abdomen, Positron Emission Tomography (PET) was done. It showed Fluoro Deoxy glucose (FDG) avid, heterogeneously enhancing well defined soft tissue density lesion in right adrenal of size 43x34x31 mm with SUV max 5.1. It also showed that a minimal ascites, ill defined fat planes with segment VII of liver and closely abutting IVC. Further hormonal evaluation was done for assessing functioning status of adrenal mass which was positive in Free testosterone: 33.12pg/mL (Normal range :0.49-2.87 pg/mL)(Table 1). She underwent open right adrenalectomy about 10 months ago. Intra operatively minimal free fluid was noticed in the abdominal cavity. Liver and other viscera were normal. Approximately 58x40x40 mm mass in the Right adrenal gland was seen and it was partly retro-caval with single right adrenal vein(Fig 1D). She had smooth post operative recovery and her Serum cortisol was low (0.52 mcg/dl) for which hydrocortisone was started and tapered over few months. She was discharged on post operative day 5 and she was on follow up. Histopathology was reported as adrenal adenoma- oncocytic variant(Fig 2A,B,C and D) with absence of major and minor criteria, Lin–Weiss–Bisceglia score (Modified Weiss score) of 0. Now she is off hydrocortisone and symptomatically better.

Table 1.Lab reports

HORMONE	Plasma levels	REFERENCE
FSH	5.01 mIU/ml	19.3-100.6mIU/mL
LH	5.01 mIU/ml	14.2-52.3mIU/L
S cortisol Random :	16.6mcg/dl	5-23mcg/dl
Cortisol (Over night Dexamethasone Suppression Test)	0.66 mcg/dl	Suppressed - Normal
Free testosterone	33.12pg/ml	0.49-2.87 pg/ml
Prolactin	4.7ng/ml	Up to 27 ng/ml
Plasma free metanephrine	8.41ng/L	7.9-88.7 ng/dl
Plasma free Nor-metanephrine	33.80ng/L	20.1-136.4 ng/dl
Thyroid stimulating Hormone (TSH) T4	0.316 mIu/L 8.88mcg/dl	0.5-4.5 mIu/L 7.3-11.6 mcg/dl
17 OH Progesterone	2.11 ng/dl	<200 ng/dl

Figure 1 Clinical pictures of the patient

1 A : Patient is having alopecia and virilization

1 B and C : CT Abdomen showing right adrenal tumor

1 C :Specimen photograph of right adrenalectomy

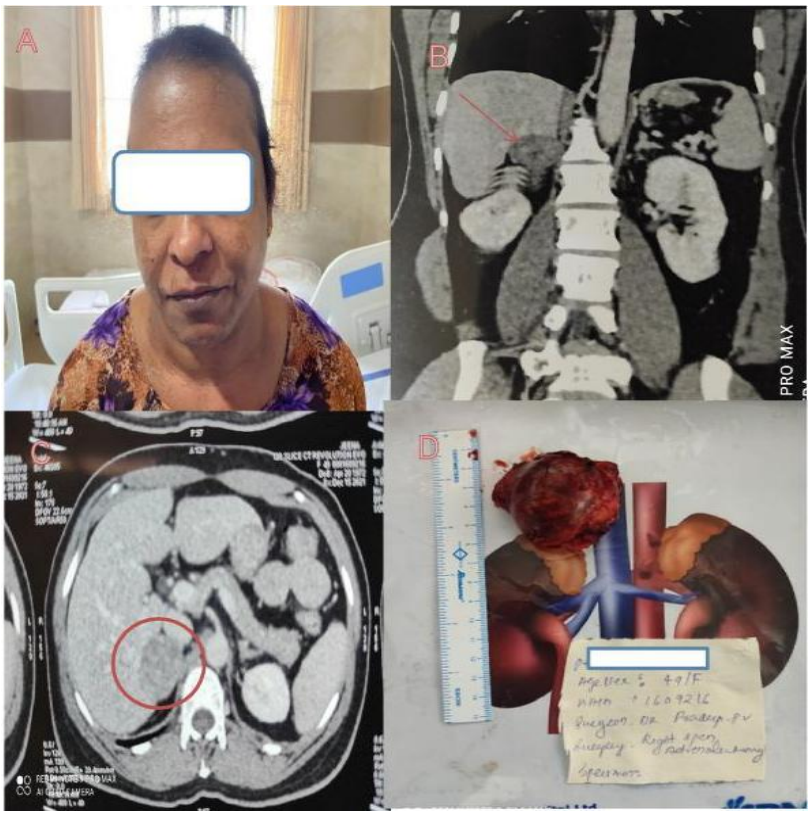

Figure 2 Microscopic features

2A : well circumscribed lesion showing capsule

2B: Nests of cells separated by thin vascular fibrous septae

2C and 2 D : (High power)Cells have abundant granular eosinophilic cytoplasm and irregular vesicular nuclei with prominent nucleoli.

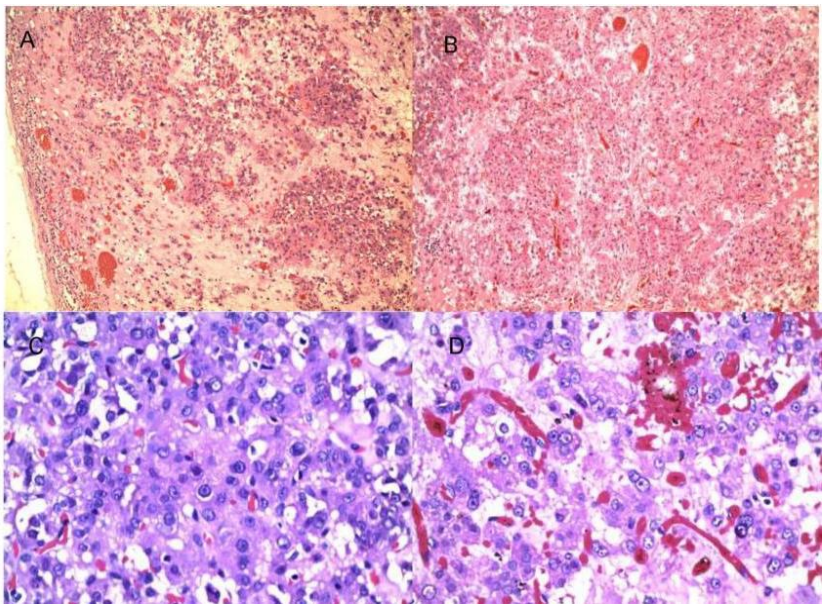

Table 2.

Causes of hirsutism

Androgenic hirsutism	**Non-androgenic hirsutism**
Polycystic ovary syndrome (PCOS)	
Non-classical congenital adrenal hyperplasia	Idiopathic
Cushing syndrome	Drug-induced Testosterone, danazol, progestins, anabolic steroids, valproic acid,methyldopa
Androgen-secreting ovarian tumor (eg, Sertoli-Leydig cell tumor)	
Androgen-secreting adrenal tumor (eg, adrenocortical carcinoma)	

Discussion

Hirsutism is defined as as an unwanted androgen-dependent hair growth in females, that is on the face, chest and back.[1] Most of the causes of hirsutism are benign like polycystic ovary syndrome, however it can rarely be life threatening.[2] Causes of hirsutism is summarized in Table 2. Excess androgen secretion in a pre-menopausal lady is mainly from ovary or adrenal gland. Testosterone is produced from ovary while DHEA-S is exclusively from adrenals. In post menopausal women adrenal gland becomes major source for androgens.[3] Oncocytomas are tumors composed of oncocytic cells; these cells are first described by Hamprel in 1931 in thyroid gland as large eosinophilic, granular cells.[4] These granular cytoplasm is due to large number of mitochondria. The oncocytomas are commonly seen in kidney,salivary glands ,thyroid and parathyroid glands. Adrenal oncocytomas are an extremely rare cause of adrenal tumors and the functional ones are only 30% as per the literature.[5] They usually present as benign, non functional adrenal incidentalomas.

Recent studies have shown that 65% of them were either malignant or had malignant potential .[6] These tumors are commonly seen in females and clinical signs are of virilizing features and or hirsutism. In our case DHEA-S was elevated as in all other cases of adrenal oncocytoma reported in the literature. There are no specific signs in CT/MRI to reach the diagnosis. Mostly these may confuse with adreno cortical carcinoma(ACC) in non invasive investigations like CT/MRI. As we have a differential diagnosis of adreno cortical carcinoma, guided biopsy is contraindicated. FDG PET scan is used to differentiate benign and malignant lesions in adrenals, but only few reports are there in literature for adrenal oncocytomas and the findings are paradoxical.[7] The treatment for adrenal oncocytomas is surgical excision . As it has a malignant potential and a differential diagnosis of adreno cortical carcinoma, a complete resection without disrupting the capsule is mandatory. Recent studies have shown that laparoscopic surgeries are safe in large adrenal masses of more than 6 cm.[8] Even though the experience in laparoscopic approach could be taken for these type tumors, we opted for an open approach in view of ACC possibility and thereby getting a complete resection.

The final diagnosis of oncocytoma depended on the histopathological examination. Microscopically, they are composed of large cell with eosinophilic and granular cytoplasm and central pyknotic nuclei. There are specific criteria for benign, borderline or malignant oncocytomas as described by Bisceglia et al in 2004.[9] Prognosis of these tumors will depend up on the cited criteria for adreno cortical oncocytic neoplasm known as Lin-weiss-Bisceglia system. These system includes 3 major criteria, 4 minor criteria and definitional criteria. If any one major criteria is present, it is carcinoma. Presence of any four minor criteria indicative of uncertain malignant potential and if there is no major or minor criteria, it is indicative of benign tumor. Because of the rarity of these tumors, clear cut guidelines are not there for post operative treatment and follow up. As far as benign oncocytomas concerned,

there is an excellent prognosis. As for borderline oncocytomas only one publication showed a recurrence. For malignant oncocytomas survival is up to 58 months which is more than the survival of adreno cortical carcinoma.[10]

4. CONCLUSION

Adrenal oncocytomas are rare tumors which are commonly present as adrenal incidentalomas. Only histopathology can diagnose oncocytomas and its clinical behaviour.Treatment of choice is excision as open or laparoscopic adrenalectomy. As there are no clear cut guidelines for follow up, it needs further studies and high levels of evidence.

ACKNOWLEDGMENTS

No funding sources

COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

'Author 1' designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. 'Author 2' and 'Author 3' managed the analyses of the study. 'Author 4 managed the literature searches.All authors read and approved the final manuscript.

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Informed consent is obtained from the patient

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