Case study

Case report :Virilizing adrenal tumor

ABSTRACT

Aim: To discuss a rare case of virilizing oncocytoma of adrenal tumor

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

Presentation : we report 49 Year old lady presented with hirsutism and virilization features to dermatology department and on further hormonal evaluation by endocrinologist found to have elevated Di hydro epiandrosterone - sulfate (DHEA-S). Computerized Tomography (CT) 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 .

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 , needs further studies and high levels of evidence .

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

1. 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 most of the affected patients have been in the age group of 40 to 60 years. Most of these tumors were detected incidentally with 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

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 native (Fig 1A) .She had h/o 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 bruisability , striae or proximal myopathy .Her medical and family history were unremarkable .She had h/o thyroidectomy 25 years back , but not on any thyroxine. On examination she was moderately built and nourished with BMI of 28.2 . She had hirsutism ,male pattern hair loss with features of virilization like acne, atrophied breast and hypertrophied clitoris.She had a large cafe lau 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 by primary intention with grade 2 thyroid swelling which was moved with deglutition ,mobile and lower border palpable . Hormonal evaluation was done(Table 1) which showed elevated testosterone and DHEA-S .Contrast Enhanced CT 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 separately seen, normal. Lesion 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. Minimal ascites present . Features are suggestive of ? adreno cortical carcinoma or lipid poor adenoma of adrenal gland.In view of ascites and indiscernible fat planes

with liver segment , Positron emission Tomography (PET) CT was done which showed Fluoro Deoxy glucose (FDG) avid heterogeneously enhancing well defined soft tissue density lesion in right adrenal 43x34x31 mm SUV max 5.1 with minimal ascites ,ill defined fat planes with segment VII of liver , closely abutting IVC .Further hormonal evaluation was done for functioning status of adrenal mass which was positive for Free testosterone: 33.12pg/mL (Normal range :0.49-2.87 pg/mL)(Table 1). She underwent open right adrenalectomy on 11.1.2022 .Intra operatively minimal free fluid noticed in the abdominal cavity. Liver and other viscera were normal. Approximately 58x40x40mm mass in the Right adrenal gland , partly retro-caval , with single right adrenal vein(Fig 1D). She had smooth post operative recovery and her S.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 is on follow up .Histopathology was reported as adrenal adenoma - oncocytic variant(Fig 2A,B,C and D) .Now she is off hydrocortisone and symptomatically better.

Table 1.Lab reports

TEST	RESULT	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 (Overnight 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 Normetanephrine	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 D :Specimen photograph of right adrenalectomy

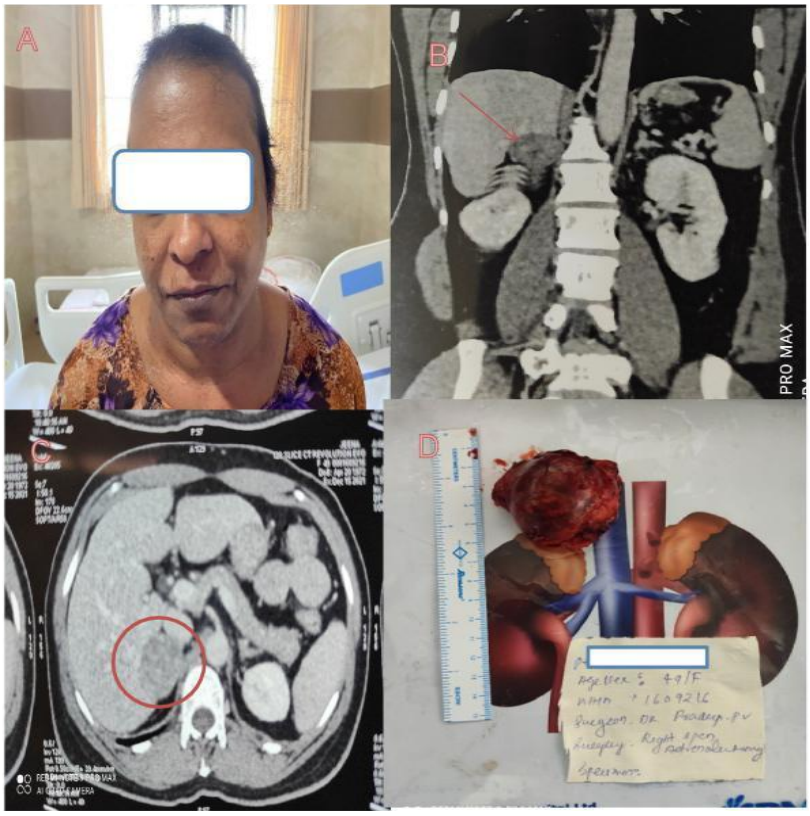
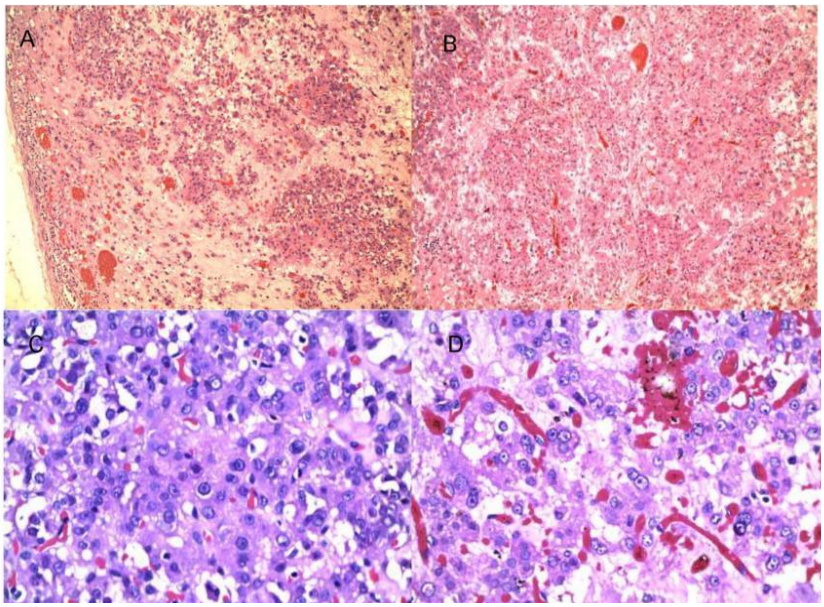


Figure 2 Microscopic features

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.



Causes of hirsutism

Androgenic hirsutism

Polycystic ovary syndrome (PCOS)

Non-classical congenital adrenal hyperplasia

Cushing syndrome

Androgen-secreting ovarian tumor (eg, Sertoli-Leydig cell tumor)

Androgen-secreting adrenal tumor (eg, adrenocortical carcinoma)

Non-androgenic hirsutism

Idiopathic

Drug-induced

Testosterone, danazol, progestins, anabolic steroids, valproic acid,methyldopa

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 rarely it can be life threatening.[2] Causes of hirsutism is summarized in table 1. Excess androgen secretion in a pre menopausal lady is mainly from ovary or adrenal gland.Testosterone is produced from ovary and DHEA-S is exclusively from adrenals.In post menopausal women , adrenal gland become 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.These oncocytomas are commonly seen in kidney,salivary glands ,thyroid and parathyroid glands .Adrenal oncocytomas are 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 shown that 20% of them are malignant.[6]These tumors are commonly seen in females and clinical signs are of virilizing features and or hirsutism as in our case. 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 , complete resection , without disrupting the capsule is mandatory.Recent studies shown that laparoscopic surgeries are safe in large adrenal masses of more than 6 cm .[8]Even though the experience in laparoscopic approach to these type tumors, could support laparoscopic approach , we opted for an

open approach in view of ACC possibility and to get a complete , en bloc resection.The final diagnosis depended on the histopathological examination. Microscopically, they are composed of large eosinophilic and granular cytoplasm with 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 ,indicative of benign tumor.Because of the rarity of these tumors, clear cut guidelines are not there for post operative treatment and follow up.For benign oncocytomas , there is an excellent prognosis.For borderline oncocytomas only one publication showed a recurrence.For malignant oncocytomas , survival is up to 58 months , more than 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 , needs further studies and high levels of evidence .

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

References

1.Hunter MH, Carek PJ. Evaluation and treatment of women with hirsutism. American family physician. 2003 Jun 15;67(12):2565-72.

2. Martin KA, Anderson RR, Chang RJ, Ehrmann DA, Lobo RA, Murad MH, Pugeat MM, Rosenfield RL. Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2018 Apr;103(4):1233-57

3. Shifren JL, Davis SR. Androgens in postmenopausal women: a review. Menopause. 2017 Aug 1;24(8):970-9.

4. Chang A, HARAWAI S. Oncotype, oncocytosis, and oncocytic tumors. Pathology annual. 1992;27:263-304.

5. Geramizadeh B, Norouzzadeh B, Bolandparvaz S, Sefidbakht S. Functioning adrenocortical oncocytoma: a case report and review of literature. Indian journal of pathology & microbiology. 2008 Apr 1;51(2):237-9.

6. Panizzo V, Rubino B, Piozzi GN, Ubiali P, Morandi A, Nencioni M, Micheletto G. Laparoscopic trans-abdominal right adrenalectomy for a large primitive adrenal oncocytic carcinoma: a case report and review of literature. The American Journal of Case Reports. 2018;19:1096.

7. Kim DJ, Chung JJ, Ryu YH, Hong SW, Yu JS, Kim JH. Adrenocortical oncocytoma displaying intense activity on 18F-FDG-PET: a case report and a literature review. Annals of nuclear medicine. 2008 Nov;22(9):821-4.

8. Machado NO, Al Qadhi H, Al Wahaibi K, Rizvi SG. Laparoscopic adrenalectomy for large adrenocortical carcinoma. JSLS: Journal of the Society of Laparoendoscopic Surgeons. 2015 Jul;19(3).

9. Bisceglia M, Ludovico O, Di Mattia A, Ben-Dor D, Sandbank J, Pasquinelli G, Lau SK, Weiss LM. Adrenocortical oncocytic tumors: report of 10 cases and review of the literature. International Journal of Surgical Pathology. 2004 Jul;12(3):231-43.

10. Wong DD, Spagnolo DV, Bisceglia M, Havlat M, McCallum D, Platten MA. Oncocytic adrenocortical neoplasms—a clinicopathologic study of 13 new cases emphasizing the importance of their recognition. Human pathology. 2011 Apr 1;42(4):489-99.