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Metabolic Syndrome in Adrenal Incidentaloma

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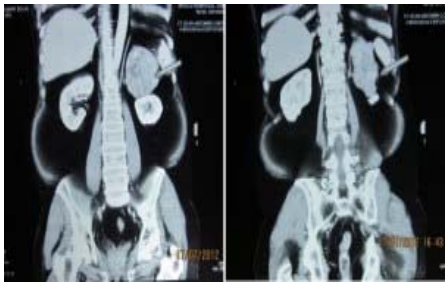
Abstract :
Adrenal incidentaloma is an adrenal mass that is discovered serendipitiously during a radiological examination performed for indications other than evaluation of adrenal disesase. Incidentally discovered adrenal masses are mostly benign, asymptomatic lesions often arbitrarily considered as non-functioning tumours. Recent studies have, however, reported that subtle cortisol production and abnormalities in the hypothalamo-pituitary-adrenal axis are more common than previously thought, and referred to as subclinical Cushings syndrome. Subclinical Cushings syndrome is found more in association with Diabetes Mellitus, Hypertension, Obesity and Hypertriglyceridemia. The purpose of this case study is to investigate a case of adrenal incidentaloma, its hormonal manifestation and associated metabolic conditions, clinical outcome and effectively manage with post-operative follow up to evaluate the improvement in biochemical and clinical parameters. It was concluded that Adrenal incidentaloma should be suspected in a patient presenting with metabolic syndrome and surgery improves metabolic parameters.
Keyword : Adrenal incidentaloma, Metabolic syndrome, Subclinical cushings syndrome, adrenalectomy

Introduction Adrenal incidentaloma encompasses a heterogeneous spectrum of pathologic entities including primary adreno-cortical and medullary tumours, benign or malignant, hormonally active or inactive lesions, metastases and infections. Once an adrenal mass is discovered, investigations should be done to rule out malignancy and to evaluate the endocrine activity of the mass.
Subclinical Cushings syndrome refers to subtle autonomous cortisol hypersecretion that is insufficient to generate the typical, clinically recognizable overt syndrome. Silent cortisol hypersecretion is frequently observed in patients with adrenal incidentalomas. Chronic mild cortisol excess may have important systemic effects on the body. **Diabetes Mellitus, Hypertension and Obesity** could be the clinical effect of cortisol hypersecretion. Also there is increased cardiovascular risk profile in these patients.

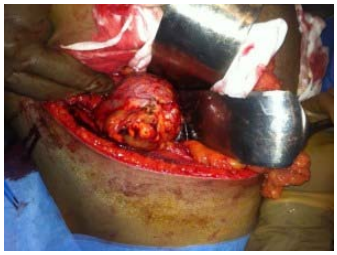
Materials and methods 59 year old male, non-smoker non-alcoholic, known case of **Diabetes Mellitus** for 1 year on T. Glipizide and T.Metformin and **Hypertension** for 4 years with BMI 29 presented with complaints of facial puffiness and pedal edema for past 2 months and H/O headache on and off for past 1 year. There was no history of abdominal pain, fever, dysuria, . No history suggestive of hyperthyroidism or hypothyroidism. Patient was on Telma 80mg OD and Carvedilol 25mg BD with **poor control of Systolic pressure with BP 210/150mmHg**. O/E all systems were found to be normal. Chest X-ray showed normal study. ECG showed incomplete RBBB, LVH with repolarisation abnormality ?lateral ischemia. **Echocardiogram** showed **hypertrophic cardiomyopathy** and **mild cardiomegaly**. PFT signified mild restrictive ventilatory defect. Routine Ultrasound abdomen revealed heterogenous lesion in left suprarenal gland ? of adrenal origin.

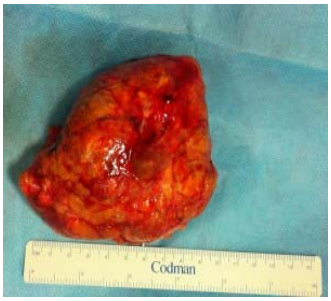


heterogenous mass lesion 8.3 x 6 cm in the region of left adrenal gland containing calcific foci

CT Abdomen was done and well-defined rounded soft tissue mass **lesion 8.3 x 6 cm in the region of left adrenal gland containing calcific foci within heterogenous** contrast enhancement was found. Left adrenal gland could not be separately seen and the plane between lesion and kidney was maintained. Rapid washout of contrast was noted. A diagnosis of adrenal incident aloma was made

and investigations were done to rule out primary malignancy and secondaries. Hormonal study was done and following values were noted. Thyroid function test was within normal limits. **Early morning Plasma cortisol- 29.6mcg/dl**, **Midnight plasma cortisol – 19.1mcg/dl**, Serum ACTH 12pg/ml, Serum aldosterone 23.3ng/dl, urine metanephrines-62mcg/day, urine normetanephrine-250mcg/day, serum sodium-146mEq/l, serum **potassium-2.8mEq/l**, **RBS-147mg/dl,FBS-127mg/dl, serum triglycerides-251mg/dl**. Based on the above values, pheochromocytoma was ruled out. CT chest showed normal bronchial tree with no mediastinal lymphnodes. Patient was provisionally diagnosed with adrenal incidentaloma with subclinical Cushings syndrome. Since mass **lesion is >8cm** and **CT -Abdomen** showed features **suggestive of malignancy** , patient was planned for **open adrenalectomy**.





OPEN ADRENALECTOMY.TRANSABDOMINAL APPROACH-LEFT SUBCOSTAL INCISION

lobulated encapsulated irregular ovoid mass 10 x 7.5 cm, 220gms

Blood pressure was controlled preoperatively with T.propranalol, T.Phenoxybenzamine and Nitroglycerine drip. Patient was started on intravenous hydrocortisone on the day of surgery and was given even after surgery for two days. **Postoperatively Plasma cortisol** on **POD-2** was **4.4mcg/dl**. Serum sodium – 136mEq/l, **Serum potassium- 4mEq/l**. ,serum triglycerides-238mg/dl, FBS – 115mg/dl. Postoperative I.V steroids was given for a week. Postoperative recovery was good. At the time of **discharge on 20th Post operative day** , **blood pressure** recording was **150/90** mmHg and patient was maintained on T.Propranalol and T.Amlodipine and T.hydrocortisone .

HPE specimen revealed **lobulated encapsulated irregular ovoid mass 10 x 7.5 cm, 220gms**. Section shows solid lobulated tan yellow coloured areas. Microscopically, well-defined neoplasm with polygonal cells with clear to eosinophilic cytoplasm and mildly pleomorphic nuclei. Mitosis is not increased. No necrosis. No capsular or vascular invasion. **Impression** in favour of **left adrenocortical adenoma**. On follow up after **two month fasting blood sugar** value was **89mg/dl** and random blood sugar was 115mg/dl.Mid night plasma cortisol was 5.1 mcg/dl.Serum triglycerides was 196 mg/dl . **BMI became 26**.

Discussion

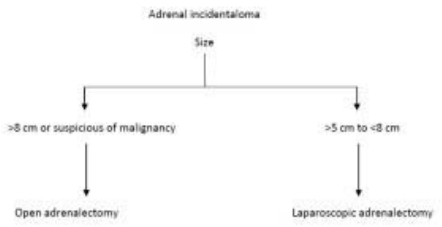
The main objective of this case study was to follow up a case of adrenal incidentaloma and evaluate the improvement in clinical and biochemical parameters post-adrenalectomy in subclincal Cushings syndrome. The **incidence of subclinical Cushings in adrenal incidentalomas is 20%**.

The patient presented with Diabetes Mellitus, Hypertension and Central obesity with facial puffiness and pedal edema secondary to hypertension. The incidence of the metabolic syndrome and its varied etiology, though secondary to adrenal tumour, did not arouse the suspicion of the same until Ultrasonogram abdomen revealed heterogenous adrenal lesion. CECT was done to precisely know the nature of the lesion and metastasis if any. Heterogeneity pointed more in favour of Adrenal carcinoma but rapid washout of contrast was in favour of adrenal adenoma. Though homogenous lesion is more specific for adrenal adenoma, 30% tumours show features of heterogeneity. CT chest revealed normal bronchial tree thus ruling out primary malignancy of the lung. Hormonal study revealed normal levels of urine metanephrines and normetanephrines, making the diagnosis of pheochromocytoma unlikely. Elevated midnight plasma cortisol level is more sensitive for subclinical Cushings syndrome and it was found elevated in this patient. Hypokalemia in this case is due to the mineralocorticoid activity of endogenous cortisol. Thus Diabetes mellitus, hypertension, obesity, elevated lipids and hypokalemia are due to elevated cortisol and it can be said that subclinical Cushings is not actually subclinical. These clinical manifestations could be due to other causes as well making the suspicion of an adrenal tumour difficult.

Increased cortisol is found to be associated with increased cardiovascular abnormalities probably due to metabolic disturbances. In this patient ECG showed changes of incomplete RBBB with repolarisation abnormality and lateral ischemia , and Echo showed HCM changes with normal LV. For a 59 year old male with no previous h/o heart disease , no h/o heart disease in family members with hypertension for 4 years, these cardiovascular changes point to an additional cause other than hypertension which could be due to cortisol and its metabolic effects. Even though the metabolic effects are reversible post surgery, the damage on heart seems permanent.

Other endocrine causes of facial puffiness and pedal edema had to be ruled out before confirming pure adrenal pathology. Patient was euthyroid and no other precipitating factors were found. Serum ACTH was normal thus confirming normal pituitary.

Surgery is indicated for all adrenal incidentaloma with size more than 5cm . laproscopic adrenalectomy is the preferred. But when the size of the tumour is more than 8 cm and if there is any suspicious of malignancy then open adrenalectomy is the best approach. Trans-abdominal approach through sub-costal incision is generally preferred.



Decision on surgery for this patient was made based on the size of the lesion and hormonal status. **Open adrenalectomy was preferred for lesions more than 8cm due to chance of malignancy**. Biopsy turned out to be a benign lesion. However its important to fully evaluate any adrenal neoplasm and choice of surgery should be based on the size of the lesion, nature of the lesion in CT scan, hormonal status or rapid increase in growth of the tumour. 5 cm tumour size is not a strict cut-off and surgery may be justified for smaller tumour if there is a suspicion of malignancy.
Post-operatively patient was evaluated for changes in clinical and biochemical parameters. Clinically, blood pressure dropped by 30mmHg systolic and facial puffiness and pedal edema resolved. Plasma cortisol levels normalized. Serum potassium increased to normal levels. Fasting blood sugar and random blood sugar values decreased post-surgically signifying that it was due to increased endogenous cortisol. Triglyceride levels though dropped continue to be above normal value.

systolic pressure and serum triglycerides dropped though still above normal values

	At the time of evaluation	2nd post operative day	20th post operative day	2nd month follo-up
Blood pressure	210/150 mmHg	160/100 mmHg	150/90 mmHg	150/90mmHg
Midnight plasma cortisol	19.1mcg/dl	4.4mcg/dl		5.1mcg/dl
Fasting blood sugar	127 mg/dl	115 mg/dl		89mg/dl
Serum potassium	2.8 mEq/l	4 mEq/l		
serum triglycerides251 mg/dl		238 mg/dl		196mg/dl
BMI	29			26

Conclusion
Metabolic syndrome in a patient should arouse the suspicion of adrenal incidentaloma with subclinical Cushings syndrome. Missed diagnosis can lead to unresolved hypertension, diabetes and hypertriglyceridemia which inturn cause irreversible cardiovascular damage. Thus imaging of abdomen is a primary investigation in metabolic syndrome. Open Adrenalectomy is preferred for larger lesions i.e >8cm and those suspicious of malignancy. Surgery improves metabolic parameters but end-organ damage is permanent.

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