Abstract: A 31 years old headmistress presented with headache weight gain, increased blood pressure unresponsive to antihypertensive medication and was referred to the Department of Endocrine surgery. Clinical examination revealed puffiness of face and striae of arms and waist but no truncal obesity. She had classical biochemical features of ACTH dependent Cushing’s disease with partial cortisol suppression in response to dexamethasone. MRI revealed a pituitary microadenoma. The outcome of surgery of the pituitary microadenoma is highlighted in this paper since surgery for microadenoma is a rarity.

Keyword: pituitary microadenoma, Cushing’s disease, Cushing’s syndrome, transsphenoidal surgery

HPE-Basophilic Pituitary Microadenoma

Aim: The aim of this paper is to highlight the characteristics of Cushing’s Disease and discuss the outcome of surgery in ACTH secreting pituitary microadenoma.

Introduction—By Definition CUSHING’S DISEASE – is caused by excessive secretion of ACTH by a pituitary tumour usually an adenoma. Cushing’s disease is responsible for roughly 2/3 of cases of endogenous Cushing’s syndrome and the remainder 1/3 is Ectopic ACTH secreting tumours and primary adrenal neoplasms. Cushing’s disease is pituitary dependent with elevated ACTH levels whereas Cushing’s Syndrome-long term exposure to excessive glucocorticoids.
The diagnosis of Cushing’s disease is a vital part to establish the ACTH secreting micro adenoma with the aid of the response pattern to dexamethasone suppression test and the CT/MRI imaging patterns. When it is confirmatory and the diagnosis is certain it is not mandatory to carry out petrosal sinus sampling which is recommended if there is uncertainty in diagnosis. Petrosal sinus sampling is helpful to confirm pituitary source of ACTH and laterisation of adenoma. The option of surgery an the optimal therapy depends on individual patient and in this patient the outcome of surgery had been favourable. Surgery for pituitary micro adenoma is generally not undertaken except for Cushing’s disease with ACTH secreting micro adenoma and hence this is highlighted.

Case report:
A 31 years old lady a Headmistress by occupation was referred from Department of Internal Medicine to Endocrine surgery with Head ache, Weight gain, Increased Blood Pressure unresponing to antihypertensives she was in the Reproductive age group and had completed her family with two children. Clinical examination revealed Striae on the arms and waist, acne, puffiness of face and her blood pressure was 150/100 mm Hg. She did not have truncal obesity. Cranial nerves were examined and found to be normal. She had facial hair but no evidence of virilisation or any other over stigmata of Cushing’s syndrome. Her serum cortisol was 26.88 at 8 am estimation (normal 6.2-19.4 mcg/dl)A 1 mg overnight dexamethasone suppression test revealed a suppression of serum cortisol and low dose (0.5mg four times a day) dexamethasone partially suppressed serum cortisol from 35.88 microgram/dl to 28.43 microgram/dl (normal is 6.2-19.4 microgram/dl). Serum cortisol was suppressed not fully though by high dose (2mg 4 times a day) to 23.96 mcg/dl. Her serum prolactin was 14.04 ng/ml (normal 4.79-23.3 ng/ml). Plasma ACTH levels was measurable at 136.71 pg/ml (normal 7.2-63.3 pg/ml). Though a corticotrophin releasing hormone test was planned to evaluate an exaggerated response of serum cortisol consistent with pituitary disease it was not carried out and inferior petrosal sampling was not done. Biochemical evaluation confirmed pituitary dependent Cushing’s syndrome= Cushing’s disease. MRI revealed a prominent circumscribed lesion suggestive of a PITUITARY MICRO ADENOMA.

Medical management with ketoconazole 200 mg once daily dose for three weeks which was later withdrawn due to altered liver function test and raised bilirubin levels and UNREMITTING HEADACHE. Though Cabergoline a potent dopamine receptor agonist can be used they were attributed to tumour shrinkage in residual tumours after surgery with a 8-45% success rate. Somatostatin analogues on the other hand caused shrinkage of 5-25% after one year of octreotide therapy. Temozolomide/tazoeoctride has been tried but not systematically studied. According to the Endocrine society’s clinical guidelines 2011 recommendations states that the indications for surgical therapy includes...
A Visual field deficit due to the lesion

- Other visual abnormalities such as ophalmoplegia or neurological compromise due to compression by the lesion
- Lesion abutting or compressing the optic nerves or chiasma on MRI
- Pituitary apoplexy with visual disturbance
- Hypersecreting tumours other than prolactinomas as recommended by other guidelines of the endocrine society and pituitary society

According to the endocrine society’s clinical guidelines 2011 recommendations, surgery maybe considered for patients if they have the following:
- Clinically significant growth of the Pituitary incidentaloma
- Loss of endocrinological function
- A lesion close to the optic chiasma and plan to become pregnant
- Unremitting headache.

Since the patient had unremitting headache and declining endocrine function, it was decided to undertake Transsphenoidal microadenomectomy with the aim to normalise hypothalamic-pituitary-adrenal function through the endonasal approach. Recently endoscope with inbuilt high powered microscope are available which improves cure rate to 87% from 76%. Sublabial approach is an alternate to endonasal route. Steroids were used as twice daily dose prior to surgery.
striae - waist region
MRI-suggestive of PITUITARY MICRO ADENOMA

Transsphenoidal microadenomectomy Technique
The transsphenoidal procedure as used today was described and successfully performed almost a century ago by bold pioneer surgeons such Cushing and Hirsch. The patient is positioned supine and the throat packed with roller gauze tied to the endotracheal tube for removal post procedure. The pack prevents operative blood from draining into the stomach and causing postoperative nausea and vomiting.

Endonasal Exposure is achieved by retracting the nostril with nasal speculum exposing the middle turbinate and the mucosa is detached from the bony posterior septum.

The rostrum of the sphenoid and the sphenoid sinus ostia are exposed. The anterior wall of the sphenoid sinus is opened widely. After the sphenoid sinus has been entered, the sellar floor is usually easily identified as a recognizable convex surface. The floor of the sella is then opened and the dura is exposed. Once the dura has been exposed adequately, it is opened in a cruciate fashion and the tumour comes into view. The tumor, was soft and suctionable, and removed with a ring curette with suction and an enucleator. The floor of the sella is reconstructed using either bone, cartilage. The sella can be packed with fat, especially if there is a cerebrospinal fluid leak which in our case was not necessary.

Post operative sequelae was the notable diuresis effect resulting in Urine output 10000 ml beyond first 5 days which settled with Vasopressin spray and after 5th POD onwards- the urine output was 5000 ml that further came down to 3000 ml on
Post operatively patient was followed up with Prednisolone 10 mg tapered to 5 mg after a week and then discontinued on 10th day. Amlodipine 5 mg was administered for two weeks. The Histopathology results were Basophilic pituitary microadenoma. Discussion By Definition CUSHING’S DISEASE is caused by excessive secretion of ACTH by a pituitary tumour usually an adenoma. Cushing’s disease is responsible for roughly 2/3 of cases of endogenous Cushing’s syndrome Remainder 1/3 – Ectopic ACTH secreting tumours and primary adrenal neoplasms. Clinical presentation includes Buffalo hump, Weight gain, Moon Facies, striae, Hypertension, Impaired GTT Usually Microadenomas (by definition 10 mm or less). Clinical manifestations can be

- Asymptomatic—do not cause mass effect
- Macroadenomas (Uncommon in CUSHING'S DISEASE)
- Mass effects when size exceeds 15 mm
- Suprasellar extension / optic chiasma compression/local bone erosion / cavernous sinus compression

PAN HYPOPITUITARISM as macroadenoma enlarges.

The Adrenal manifestations include BILATERAL ADRENAL HYPERPLASIA (any ACTH elevation-pituitary/ectopic)

- Diffuse

Nodular (micronodular and macronodular) Definitive diagnosis can be arrived with Urinary free cortisol screening test (24 hrs urine) Low dose/high dose dexamethasone suppression tests

- Coricotrophin assay
- Coticotrophin releasing hormone stimulation test

- Inferior petrosal sinus catheterisation Inferior Petrosal sinus sampling should be carried out by an Experienced interventional neuro radiologist. Blood from right half of pituitary gland drains into right inferior petrosal sinus and vice versa and blood samples are taken from each sinus and a vein below the heart. If ACTH level differs in comparison—pituitary

If ACTH level same in comparison—ectopic SURGICAL APPROACH includes

- Endoscopic endonasal transsphenoidal
- Endoscopic translabial
- Minimally invasive keyhole craniotomy
- Lateral parietal approach-open
- Pterion approach
- Lateral frontal-open

PERSISTENT OR RECURRENT CUSHING'S can be treated with mitotane but we ought to be aware of incomplete resection and dealing with Double adenomas CONCLUSION Pituitary micro adenomas are operable and in Cushing's disease - offers effective cure. The outcome is good with minimal complications, but surgeons must have a thorough knowledge of the surrounding anatomy and potential complications.
Table 1 Dexamethasone suppression

<table>
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<tr>
<th></th>
<th>Serum Cortisol (6.2-19.4mcg/dl)</th>
<th>Plasma ACTH (7.2-63.3pg/ml)</th>
<th>Serum Prolactin (4.79-23.3) ng/ml</th>
<th>Electrolytes</th>
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<tbody>
<tr>
<td>Pre-op</td>
<td>35.88mcg/dl</td>
<td>96.71pg/ml</td>
<td>14.04ng/ml</td>
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<tr>
<td>Low dose dextro</td>
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<td>High dose dextro</td>
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<td>AFTER SURGERY</td>
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<td>1.97pg/ml</td>
<td>12.06ng/ml</td>
<td>WNL</td>
</tr>
</tbody>
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