Case Report

ACTH - secreting micro adenoma with hypothyroidism - A case report

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Abstract

A 25 year old female was presented with the complaints of weight gain of 15 kg, oligomenorrhea, and hirsutism of 1 year duration. She was known hypertensive. On clinical examination, facial plethora, atrophy of the skin, stria purpurea, hyper pigmented patches over the extremities, over the abdomen, axilla and knees were present, acne was present over the face. On examination, patient was obese; blood pressure (BP) was 150/ 110 mmHg. Bilateral pitting edema was evident and all other systems were normal. On investigations, thyroid stimulating hormone (TSH) and serum cortisol was high. A diagnosis of Cushing's syndrome with Hypothyroidism was entertained. MRI brain (sella) with contrast revealed pituitary microadenoma. Transsphenoidal excision was done. Histopathology features were consistent with Pituitary Adenoma. Normally Cushing's syndrome is dependent on ACTH. Pituitary adenoma is present without any physical signs or symptoms. Among them microadenoma is commonly associated with thyrotoxicosis. But this case was presented with hypothyroidism which is very rare.

Key words

ACTH - secreting micro adenoma, Hypothyroidism, Oligomenorrhea, Hirsutism.

Introduction

The sellar region is a site of various types of tumors, pituitary adenoma are the most common, arise from epithelia pituitary cells and account for 10-15% of intra cranial tumors, tumor >10 mm are macro adenoma and those < 10 mm are micro adenomas, most pituitary adenomas are micro adenomas. Most of the pituitary adenomas are diagnosed accidentally, as they don't have any physical symptoms and signs. Patients with

Prolactin (PRL) - secreting micro adenomas may be treated either with trans-sphenoidal surgery or medically with Dopamine agonists (DA). For patients with Adrenocorticotrophic hormone (ACTH) - secreting adenomas, primary therapy is generally transsphenoidal surgery. Radiotherapy is reserved for the patients who are sub totally resected or remain hypersecretory after surgery. For patients with clinically non functioning adenomas (generally gonadotropin-secreting adenomas on immunocytochemistry), trans-sphenoidal surgery with or without post-operative radiation therapy is performed for all patients with or without visual consequences of the tumor. Thyrotropin (TSH) - secreting pituitary tumors may be found in two opposite clinical situations: the hyperthyroidism secondary to thyrotropin adenomas, also called central hyperthyroidism, and the long-standing primary hypothyroidism which can be accompanied by a compensatory pituitary enlargement. In clinical practice, there are patients with ACTH - secreting micro adenomas have a higher prevalence of central hypothyroidism (HT). In adults, it is due to pituitary macro adenomas, pituitary surgeries or post-irradiation. The availability of medical treatment after surgery is dopamine, DA, agonists, somatostatin analogs, GH-receptor antagonists. It has modified the role of radiotherapy; drugs are now used as a second-line treatment, after surgery (or even as first-line treatment). Radiotherapy is reserved for patients who are sub totally resected or remain hypersecretory after surgery. In waiting for the effects of radiotherapy, adrenal steroidogenesis inhibitors (mitotane, ketoconazole) may be indicated. If drugs are not available or not tolerated, bilateral adrenalectomy may be proposed [1-6].

Case report

A 25 year old female came to M N R Medical College and Hospital, Sangareddy, with the complaints of weight gain of 15 kg since one year, history of oligomenorrhea since 1 year, history of hirsutism since 1 year, and hypertension since 15 days. No history of diabetes, no history of neurological involvement, no history of diplopia or blurring of vision was present. On clinical examination, facial plethora was present, cuticular atrophy was present, stria purpurae, hyper pigmented patches over extremities, over abdomen, axillae and knees, along with Acne and chemosis (**Figure – 1 to 4**). On examination, patient was obese, temperature was normal, pulse rate was 72/ minute, blood pressure (BP) was 150/ 110 mmHg. Heart S1 and S2 were normal, lungs were clinically clear with bilateral pitting edema was evident. Central nervous system (CNS) was normal, Fundus was normal, Media Clear Disc Normal on both the eyes, Obstetric history of P3 L1 A2 with last child was male and alive since 4 years was elicited.

Figure – 1: Cushingoid faces.

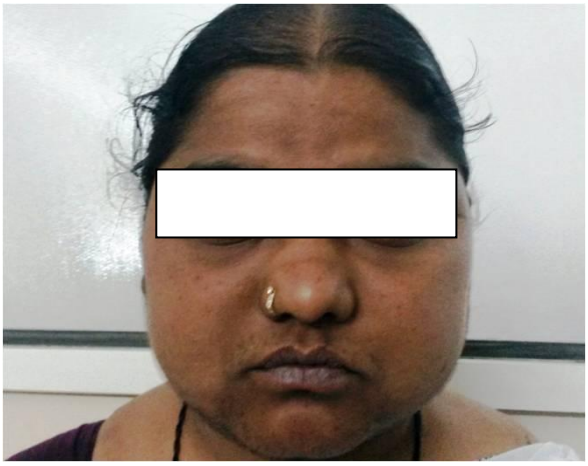


Figure – 2: Hump over the nape of the neck.

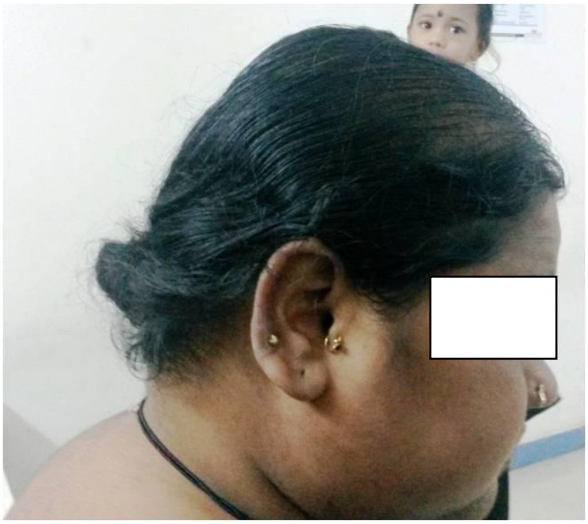


Figure – 3: Pinkish striae on abdomen.

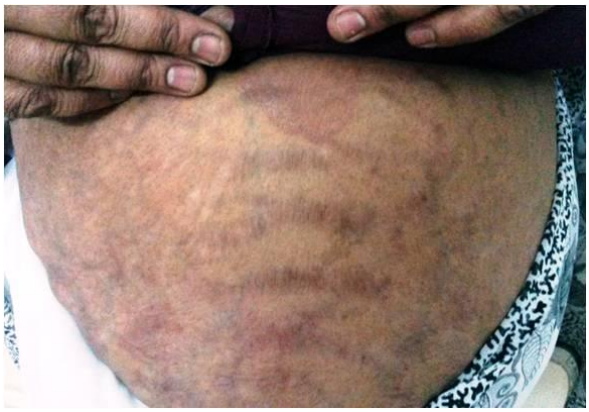
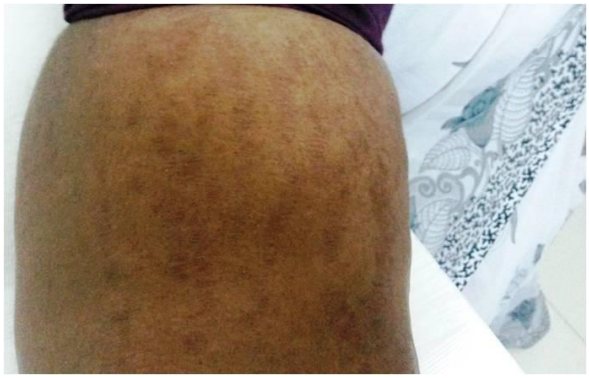


Figure – 4: Striae on right arm.



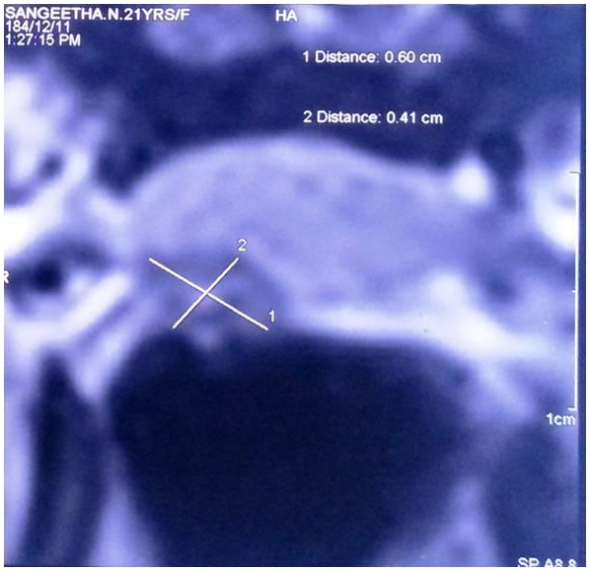
On investigation, her complete blood picture (CBP) showed hemoglobin (Hb) was 14.9 gm/dl, RBC count was 4.7 million/cubic mm, WBC count was 10,900 cell/cubic mm, and differential count (DC) showed - N 75, L 20, E 2, M 3, B 0 with Platelets count was 3.24 lakhs /cubic mm. Blood picture of Normocytic Normochromic was present with ESR was 32 mm, Blood Group was O positive, BT was 2 min 0 sec, CT was 4 min, Blood sugar was 102 mg/dl , Blood urea was 18 mg/dl, Serum creatinine was 0.56 mg/dl, Chest X-ray PA view showed no any defect, Serum sodium was 139 meq/ dl, Serum potassium was 3.3 meq/ dl , Serum chloride was 109 meq/ dl, Serum cortisol was 272 microgram/ dl (Normal 8 AM: 5-23 microgram/dl, 4 PM: 2.3-11.9 microgram/dl), ECG was normal, liver function test (LFT) was normal, complete urine examination (CUE) showed Albumin and Sugar - Negative, ONDST - 772 mmol/ lt [7], LDDST - 702 mmol/ lt [8], Serum Proteins - 10.2 gm/ dl, Serum TSH - 4.69 IU/dl (N- 0.35 To 5.5 IU/ dl).

As the Serum cortisol and TSH was high, it was suggesting Hypothyroidism and Cushing's Syndrome, which may depend on ACTH secreting tumor, MRI brain was done to rule out Pituitary tumour. MRI brain (sella) with contrast was done on 15/12/2011. It revealed, Pituitary Gland - maximum thickness was 8 mm; there was 5X5 mm ill defined non - enhancing focal lesion in the right side of the Pituitary Gland. Pituitary stalk was 2 mm. Post Pituitary bright spot was seen. Bilateral cavernous sinuses were normal. Supra sellar region was normal. Impression of small focal lesions in the right side of the anterior Pituitary Gland suggested of Micro Adenoma (**Figure – 5**). As the patient was having Micro Adenoma, patient was posted for surgery for excision Transsphenoidal excision was done on 24/12/2011. Histopathology revealed three grey brown soft tissue bits together measuring 0.4 X 0.4 cm. Section of the specimen submitted showed a cellular tumour composed of more or less uniform cells in acinar and trabecular pattern. The cells showed moderate to abundant cytoplasm and centrally to eccentrically placed nucleus, areas of hemorrhage seen, no mitosis discerned, no necrosis. Impression features consistent with Pituitary Adenoma. Immunophenotyping of the tissue revealed ACTH- Positive, Prolactin V - Postive, GH - Negative. Post-operatively patient was kept on Anti-hypertensives and Ketoconazole. No steroid replacement was given, and the patient was discharged. Patient stopped treatment on her own.

On review examination on 17/3/2015, her weight was 92 kg, blood pressure (BP) was 190/90 mmHg, Complete blood picture (CBP) showed normal limit, Hemoglobin was 10.3 gm/dl, ESR was 60 mm - 1 hour, complete urine examination (CUE) showed Albumin was nil, Sugar was nil, random blood sugar (RBS) was 119 mg/dl, Blood Urea was 16 mg/dl, T3 was 41.18 pg/ml, T4 was 6.2 ng /dl, TSH was 0.56 IU/dl, Serum Cortisol was 24.55 micro gm/ dl [4, 5], Chest X-

ray PA view showed cardiomegaly with left ventricular configuration, ECG showed left ventricular hypertrophy, Ultrasound of the abdomen revealed bilateral renal calculi, both ovaries showed multiple small follicles - Poly cystic ovarian disease. MRI scan didn't reveal any neuroparenchymal abnormality.

Figure – 5: MRI scan of pituitary fossa.



Patient was kept on following treatment.

- Eltroxin 100 mcg/ OD
- Glyciphage 500 mg/ TID
- Diabetic diet.
- Mild physical exercise walking.
- Stamlo 5 mg/ OD
- Tab. Cyproheptadaine 4 mg/ TID

Discussion

Thyrotropin (TSH) - secreting pituitary tumours may be found in two opposite clinical situations: the hyperthyroidism secondary to thyrotroph adenomas, also called central hyperthyroidism, and the long-standing primary hypothyroidism which can be accompanied by a compensatory pituitary enlargement. TSH - secreting pituitary adenomas belong to the syndromes of "Inappropriate Secretion of TSH" (IST). The adjective "Inappropriate" indicates the lack of the expected suppression of TSH secretion when free thyroid hormone levels are actually elevated, as in the other forms of thyrotoxicosis. Moreover, TSH-omas have to be differentiated from the non-neoplastic form of IST which is due to resistance to thyroid hormone. Differently, pituitary hyperplasia, which is reversible on thyroid hormone replacement, is the more frequent cause of a pituitary mass occurring in the context of untreated primary hypothyroidism. Failure or delay in the recognition of the above clinical situations may cause dramatic consequences, such as unnecessary pituitary surgery in hypothyroid patients or improper thyroid ablation in those with central hyperthyroidism. In contrast, early diagnosis and proper treatment of TSH-secreting pituitary tumors prevents the appearance of signs and symptoms of mechanical compression of the adjacent structures by the expanding tumor mass (visual field defects, headache and hypopituitarism) [2].

Pituitary tumors cause symptoms by secreting hormones like Prolactin (PRL), responsible for amenorrhea-galactorrhea in women and decreased libido in men; growth hormone (GH), responsible for acromegaly; Adreno Cortico Tropic Hormone (ACTH) , responsible for Cushing's syndrome; Thyroid Stimulating Hormone (TSH), responsible for hyperthyroidism, depressing the secretion of hormones (hypopituitarism), or by mass-related effects (headaches, visual field abnormalities). All patients with pituitary tumors should be evaluated for gonadal, thyroid and adrenal function as well as PRL and GH secretion. Specific stimulation and suppression tests for pituitary hormones are performed in selected situations for detecting the type of hypersecretion or the response to treatment. Imaging procedures like CT scan, MRI determine the presence, size and extent of the lesion. The classification of pituitary tumors is based on the staining properties of the cell cytoplasm viewed by light microscopy and immunocytochemistry revealing the secretory pattern of the adenoma. Treatment of pituitary adenomas consists of surgery (performed in more than 99% of cases via a transphenoidal route) and radiotherapy. The

availability of medical treatment (dopamine, DA, agonists, somatostatin analogs, GH-receptor antagonists) has profoundly modified the indications of radiotherapy, drugs being now generally used as a second-line treatment, after surgery (or even as first-line treatment). The treatment summarized as follows. For treatment of GH-secreting adenomas, trans-sphenoidal surgery is the first-line therapy except when the macroadenoma is giant or if surgery is contra-indicated; postoperative radiation therapy (fractionated, or by gamma-knife) is performed for partially resected tumors or when GH levels remain elevated (eventually after a trial of somatostatin analog). Somatostatin analogs, are proposed when surgery is contra-indicated, or has failed to normalize GH levels, or in waiting for the delayed effects of radiation therapy. If the probability of surgical cure is low (e.g. in patients with very large and/or invasive tumors), then somatostatin analogs may be reasonable primary therapeutic modality provided that the tumor does not threaten vision or neurological function. Pegvisomant, the new GH-receptor antagonist, is indicated in case of resistance to somatostatin analogs. Patients with PRL-secreting microadenomas may be treated either with trans-sphenoidal surgery or medically with DA agonists. In patients with macroadenomas, even in the presence of chiasmatic syndrome, DA agonists are now proposed as primary treatment. Indeed, effects on visual disturbances are often very rapid (within a few hours or days) and tumoral shrinkage is usually very significant. For patients with ACTH-secreting adenomas, primary therapy is generally trans-sphenoidal surgery by a skilled surgeon, whether or not a microadenoma is visible on MRI. Radiotherapy is reserved for patients who are subtotally resected or remain hyper-secretory after surgery. In waiting for the effects of radiotherapy, adrenal steroidogenesis inhibitors (mitotane, ketoconazole) may be indicated. If drugs are not available or not tolerated, bilateral adrenalectomy may be proposed. For patients with clinically non functioning adenomas (generally gonadotropin-secreting adenomas on immunocytochemistry), trans-sphenoidal surgery with or without postoperative radiation therapy is performed for all patients whether or not they have visual consequences of the tumor. Selected patients with small, incidentally microadenomas may be carefully followed without immediate therapy [6].

Unlike pituitary macroadenomas, microadenomas (micros) are not commonly associated with hypopituitarism. In clinical practice, we have observed that patients with ACTH - secreting micros have a higher than expected prevalence of central hypothyroidism (HT), and we speculated that this effect might be because of glucocorticoid-induced suppression of the hypothalamic-pituitary-thyroid axis [1].

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