Cortisol Secreting Adrenal Adenoma in a Patient with Schizophrenia, Rheumatic Heart Disease and Myoma Uteri: Difficult to Find but Easy to Diagnose

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Abstract

The presence of cortisol-secreting adenoma concomitantly with rheumatic heart disease, schizophrenia and myoma uteri is rare.

This is a case of a 40 year old female with Schizophrenia who gradually developed Cushing’s syndrome from an adrenal adenoma. She suffered a cardio-embolic stroke from Rheumatic heart disease which delayed hysterectomy for a bleeding intrauterine myoma.

Aside from the physical findings of Cushing’s syndrome laboratory work up revealed an elevated 24 hour urine free cortisol with loss of normal diurnal cortisol secretion, suppressed 8AM ACTH level and negative suppression after a high dose dexamethasone. The patient underwent laparoscopic adrenalectomy for a 3.8 x 2.4 x 3 cm left adenocortical adenoma. She required steroid supplementation. Menstrual flow immediately normalized, functional capacity improved and metabolic parameters such as weight, blood pressure and blood sugar were controlled six months after the surgery. Relapse of psychotic symptoms occurred eight months post-operatively because of non-compliance to antipsychotic medications.

Cushing’s syndrome if untreated can cause significant morbidities such as metabolic, hemodynamic, cardiovascular, bleeding disorder and psychiatric illness. These complications however can also be caused by primary medical illnesses like schizophrenia, rheumatic heart disease and myoma uteri. Treatment of the Cushing’s syndrome may resolve some but not all the metabolic and hemodynamic problems and theoretically should also decrease the risk of complications of other primary illnesses concomitantly present.

The presence of concomitant primary disease that can cause psychosis, cerebrovascular disease and metrorrhagia should also be investigated in a patient who has Cushing’s syndrome. Prompt management of Cushing’s syndrome would lessen the risk of complication attributed to schizophrenia, rheumatic heart disease and myoma uteri.

Keywords: Cushing’s syndrome, schizophrenia, rheumatic heart disease, myoma uteri

Introduction

Cushing’s syndrome is a symptom complex that reflects chronic excessive tissue exposure to glucocorticoid. When iatrogenic causes are excluded, the commonest cause in adult is Cushing’s disease or adrenocorticotropic hormone (ACTH) secreting pituitary adenoma (70%). Adrenal adenomas are responsible for about 10% of cases. Other causes include carcinomas, ectopic corticotrophic releasing hormone (CRH) and ectopic ACTH secreting tumor. Endogenous causes of Cushing’s syndrome are rare and result from loss of the normal feedback mechanism on the hypothalamic-pituitary adrenal axis and normal circadian rhythm of cortisol secretion.¹²

The incidence of adrenal adenoma as a cause of Cushing’s syndrome is 0.6 per million per year. It is 1.5 times more common in women.²

Excessive glucocorticosteroid exposure has widespread systemic effects. The most discriminant features of Cushing’s syndrome are peripheral edema, easy bruising, facial plethora, proximal muscle weakness, reddish purple striae more than one centimeter wide seen over the abdomen, thigh, buttocks and breast area. Proximal muscle weakness is one of the most reliable feature along with ecchymoses. This is due to profound muscle fiber atrophy. The patients often complain of difficulty climbing stairs or combing. This can be verified by formal muscle testing in the clinic or inability of patient to get out of a chair without using her arms.²

Features that are common to both Cushing’s syndrome which are also seen in the general population are depression, dorsocervical fat pad, hypertension, fatigue, facial fullness, weight gain, obesity, vertebral osteoporosis, polycystic ovaries, thin skin and glucose intolerance.³

Cardiovascular disease like hypertension is present in 80% of Cushing’s syndrome. The suspicion of hypercortisolism should be entertained as one of the differential diagnosis in a patient with hypertension that is younger than 40 years. Cardiovascular events are also common in these patients as a result of metabolic disorder like diabetes and dyslipidemia. A Thrombo-embolic phenomenon from atherosclerosis is more common in Cushing’s syndrome than in simple obesity cases. Hypertension may be corrected with treatment of hypercortisolism but may persist in 30-50% due to persistent endothelial dysfunction and essential hypertension.

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hypertension component. Glucose intolerance and diabetes mellitus is present in up to one third of cases. Dyslipidemia is brought about by increased hepatic lipoprotein synthesis. Osteopenia and osteoporosis is present in long standing Cushing’s syndrome. Osteonecrosis in the femoral and humeral heads is also a known feature.

The most common gynecologic complaint of patient with Cushing’s syndrome is menstrual irregularity due to hypercortisolism induced inhibition of pulsatile luteinizing hormone (LH) secretion. There have been reports that hypercortisolism can induce endometrial hyperplasia hence increase menstrual flow. There are features seen in Cushing’s syndrome that may have other causes, these are acne, and villous hypertrichosis.

The Case

A 40 year old housewife with Schizophrenia consulted the endocrinology clinic for weight gain. For the past seven years she has been under the care of a psychiatrist for schizophrenia. Six years prior to consult she noticed gradual development of truncal obesity, rounding of her face, growth of mustache, side burns and leg hair. At around this time she was diagnosed with hypertension and gradually experienced leg weakness, progression of weight gain and increase in abdominal girth.

One year prior to consult at endocrinology clinic she consulted a gynecologist for excessive menstrual flow which was attributed to multiple myoma uteri. Surgery was advised but it was delayed because of psychotic relapse and financial constraints.

At the time she was ready for surgery she developed right sided paresis and slurring of speech. A cranial CT scan showed an infarct over the left middle meningeal artery distribution. This was attributed to a cardio embolic phenomenon from atrial fibrillation and mitral stenosis and regurgitation secondary to rheumatic heart disease. She was put on anticoagulation during her intermenstrual period, digoxin and beta blocker. Diabetes mellitus was documented during this period. She was put on Metformin. She regained her motor function two months later with physical therapy.

During her first endocrinology visit her features were strikingly due to Cushing’s syndrome. She gained 17 kilograms in the past five years and she exhibited Cushiningoid facies when compared to her past photographs. Proximal muscle weakness was confirmed when she could not get up from her chair unassisted. She looked depressed. She denied taking any exogenous steroid or alcohol.

On physical examination she had depressed affect but was coherent and with appropriate behavior. She was obese with a BMI of 29kg/m². Her blood pressure was 160/90 mmHg. Her skin was soft and thin with prominent superficial veins. There were multiple 1-1.5 centimeter striae over her abdomen. She had mild hirsutism distributed over the face and legs. There acneform eruptions over the face. She has prominent supraclavicular and dorsocervical fat pads. Her heart sounds were distinct and the apex beat was not displaced. Cardiac rhythm was irregularly irregular. Her abdominal circumference was 107 centimeters. There were no palpable abdominal or pelvic masses. The extremity muscles were atrophied. Neurologic examination was normal.

Work up for Cushing’s syndrome showed loss of diurnal cortisol secretion. Her 11PM plasma cortisol was higher than her morning plasma cortisol. The diagnosis of Cushing’s syndrome was confirmed with an elevated 24-hour urinary free cortisol. The cortisol hypersecretion was ACTH independent as shown by a low plasma ACTH level of 5 pg/mL. She did not suppress to the overnight high dose dexamethasone suppression test and showed a paradoxical increase. An adrenal CT scan showed a left adrenal adenoma and atrophied right adrenal gland.

Fig. 1a. Patient’s face showing moon facies, buffalo hump, mild hirsutism, acne formation.

Fig. 1b. Patient’s trunk showing abdominal obesity and purple striae
She underwent laparoscopic left adrenalectomy with post operative hydrocortisone infusion. She was discharged on 20mg of Prednisone per day. She developed adrenal insufficiency symptoms three months later when the steroid dose was decreased to 10mg per day. Tapering of steroid was done slower. She had one relapse of psychotic symptoms at six months post-op because of failure to take her antipsychotic medications. Her symptoms resolved after resumption of medication.

Six months after surgery her blood pressure normalized even without her antihypertensive medication.

At one year post surgery her blood sugar was normal even without any medication for diabetes. Her weight was normal for her height. Her abdominal obesity was gone. Her menstrual flow and pattern became normal. Her physical strength has improved and her outlook in life is better. Since she is no longer bleeding profusely during her menstrual period she was assessed to be nearing perimenopausal period. Hysterectomy was deferred and she was advised regular pelvic ultrasonography.

ACTH stimulation done at 14 months post op showed impaired adrenal response so she was maintained on Prednisone 2.5 mg per day.

Discussion

After extensive literature search, we present the first case of cortisol secreting adenoma complicating a case of schizophrenia, rheumatic heart disease and abnormal uterine bleeding in one patient.

Although all the presenting problems of our patient can be explained by the Cushing’s syndrome further investigation showed three other primary disease that were present which needed concomitant treatment. These were schizophrenia, rheumatic heart disease and cardio embolic event and multiple myoma uteri. Of the recommended screening test for hypercortisolism, 24-hour urine free cortisol and low dose dexamethasone suppression test were done salivary cortisol was not done. These tests have comparable sensitivity and specificity. The choice in the local setting is determined primarily by the availability and cost of the test. The 24 hour UFC was elevated and the patient did not suppress to low dose dexamethasone. The low plasma ACTH confirmed an ACTH independent cause. Localization of the tumor was done by high dose dexamethasone suppression and adrenal imaging. This showed and ACTH independent lesion because of failure to suppress cortisol secretion after 8mg of dexamethasone. Computed tomography localized the left cortical adenoma which was removed by laparoscopic adrenalectomy. Evaluations of other medical problems lead to a successful multi disciplinary management.
Conclusion

This case highlights features of Cushing’s syndrome that best discriminate the disease hence management directed to Cushing’s syndrome. On the other hand this case also shows features of Cushing’s syndrome that may be due to other causes (schizophrenia, rheumatic heart disease, myoma uteri). Complete evaluation of Cushing’s syndrome and other medical problems should lead to multidisciplinary and holistic management.

References