Cushing’s Disease presenting as Suicidal Depression

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Abstract
A case of Cushing disease, who presented with suicidal depression as the main cause of Cushing’s disease, not only had features of hypercortisolaemia but also remitted depression fully.

Introduction
Cushing syndrome (CS) results due to chronic exposure to excess secretion of glucocorticoids by the adrenal cortex, which could be adrenocorticotropic hormone (ACTH) dependent or ACTH independent. Among ACTH dependent causes, pituitary corticotropic adenoma (Cushing disease (CD)) is the most common cause whereas, an extra pituitary tumour (ectopic ACTH syndrome) is less frequent and a tumour secreting corticotrophin-releasing hormone (CRH) (ectopic CRH syndrome) is a rare cause of CS. ACTH independent causes include benign or malignant unilateral adrenocortical tumours or bilateral adrenal hyperplasia. CS presents with wide variety of symptoms, however, it less likely known to present with severe (suicidal) depression.

Case Report
A 25 year old male was brought for psychiatric consultation with the complaints of decreased verbal communication, sadness, weeping spells, loss of interest, decreased sleep, weight gain, suicidal thoughts and visual hallucinations for the last two months. Except for depressed affect, his general physical examination including blood pressure (128/84 mm Hg) and routine laboratory parameters including fasting plasma glucose (96 mg/dl) were normal. He was diagnosed as a case of severe (suicidal tendency) depression. Fluoxetine 20 mg, duloxetine 20 mg and clonazepam 0.5 mg at bedtime with supportive psychotherapy was instituted. Two-month follow-up did not show improvement. However, the patient noticed multiple stretch marks on his abdomen and both thighs and weight gain of 8 kg., hence the psychiatrist referred him for Medicine consultation. Examination revealed a healthy young male, communicating in monosyllables (Figure 1a). Multiple wide purple striae were present on abdomen and bilateral thigh, the largest being 27 cm in length and 2.5 cm in width (Figure 2a). Mental state examination was marked by depressed affect, psychomotor retardation, depressive and suicidal ideation. His blood pressure was 140/86 mmHg and pulse rate was 84 beats/minute. One month later, he returned with laboratory investigations for abdominal striae and was found to have developed hypertension (170/100 mmHg), proximal muscle weakness and impaired glucose tolerance (random sugar 193 mg/dl). Two-hour oral glucose tolerance plasma glucose was 240 mg/dl thereby confirming diabetes. His 24-hour urine cortisol was 3679.2 µg (28-213µg/24 h normal range), morning (8 a.m.) serum cortisol was 32.4 µg/dl (4.3-22.4 µg/dl normal range) and there was lack of suppression of serum cortisol after 1 mg overnight dexamethasone (8 a.m. serum cortisol was 31.40µg/ml after 1mg dexamethasone at 11pm). These findings were confirmed on repeat testing. His plasma ACTH was 147 pg/ml (normal < 46pg/ml); suggestive of ACTH dependent Cushing disease. Ultrasonogram abdomen revealed hepatomegaly with fatty infiltration, dual energy x-ray absorptiometry (DEXA) scan showed osteopenia in spine, abdominal CT scan showed bilateral adrenal hyperplasia. MRI brain showed pituitary mass 3.5×2.5cm in size (Figure 3a, 3b). His diagnosis was revised to severe depression caused by Cushing’s disease and was referred to neurosurgery consultation. During investigation, he was being treated with antihypertensives, oral hypoglycemic agents and antidepressants (fluoxetine, sertraline, duloxetine, and imipramine) and clonazepam, quetiapine, risperidone and olanzapine for sedative and augmenting purpose. However, there was no response in depressive symptoms. He under-went trans-sphenoidal resection of pituitary adenoma. The histopathological appearance was consistent with a pituitary corticotrophin adenoma. Post-operatively, serum cortisol normalized within five days, a marked improvement in depressive symptoms was seen within a week and patient achieved nearly complete depressive remission over a period of one month. At 12-month follow-up patient was in depressive remission, his blood pressure and plasma glucose was normal and there was no purple abdominal striae and proximal weakness (Figure 1b, 2b).

Discussion
Cushing’s disease (CD) was first described by Harvey Cushing in 1932 and is defined by ACTH hypersecretion, induced by pituitary adenomas, leading to hypercortisolaemia. In our case was diagnosed on the basis of hypercortisolaemia and pituitary macroadenoma and major depression was its initial presentation. Major depression is the most common psychiatric disorder seen in CS with no significant differences between pituitary-dependent and -independent forms. Rates for major depression vary from 12% to 50-70% in different studies. Depression can be an early manifestation of CS and found to correlate with the severity of the clinical...
Fig. 2a, b: Multiple purple striae at presentation and after treatment

Fig. 3a, b: Precontrast and post contrast T1W sagittal image showing heterogeneous signal intensity in pituitary gland suggestive of pituitary macroadenoma

presentation. Increased glucocorticoid signalling via glucocorticoid receptors and decreased serotonin and increased dopamine cerebral activity is responsible for the depressive symptom in CS. Patients with CD and depression have been found to suffer from a more severe form of illness, both in terms of clinical presentation and cortisol production compared to non depressed counterparts. Treatment unresponsiveness of depression in CD suggests involvement of hypothalamic-pituitary-adrenal axis and indicates severe clinical presentation and connotes poor outcome. Such depression responds to drugs like ketoconazole, metyrapone and aminoglutethimide (which inhibit corticosteroid production) rather than antidepressants. Although antidepressants prove less effective yet have been considered as the only treatment option while patients are being investigated for persistent hypercortisolism. Sharing this view, we had also tried antidepressants to treat depression in our patient, which however were ineffective. Normalization of cortisol, after surgery has been considered as the main - stay of treatment of depression. Our patient had marked improvement in depressive symptoms within a week post-operatively and it continued thereafter. However, for the hormonal replacement and other supportive follow-up treatment, our patient did not require any psychotropic medications. Some studies report that psychiatric and neurocognitive disorders can persist, even long-term after the resolution of hypercortisolism and occasionally they can even exacerbate with the decrease and resolution of hypercortisolism i.e. depression after disease remission. Reason for this has been suggested to be due to the relative glucocorticosis deficiency, which seems to allow unrestrained increase in catecholamines. And also, the brain volume loss which occurs with active disease, has been demonstrated to be partially persistent after remission. So patients of CS, should be followed up long after resolution of hypercortisolaemia for depression.

Conclusion

Depression is a common presentation in clinical practice and is primarily considered as a psychiatric disorder and most often not investigated for secondary forms of depression. Moreover, the symptoms of Cushing disease and depression are similar and could delay the diagnosis and treatment of CD.

Cushing’s disease can prove fatal in the absence of treatment, therefore, it is necessary that the patients who present with depression and other signs or symptoms of Cushing (obesity, easy bruises, striae, facial plethora, proximal muscle weakness and hypertension) must be screened for CS so that an early appropriate treatment could be initiated to minimise morbidity and mortality.

References