Review Articles

Psychiatric Manifestations in Endocrine Disorders

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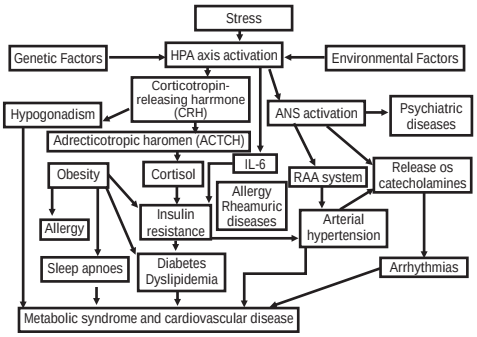
The clinical study of hormone fluctuations and their relationship to human behaviour is called as Psychoneuroendocrinology. A number of psychiatric symptoms are seen to be associated with multiple endocrine disorders. These may be a direct result of either hyper- or hypo secretion of the hormones from the endocrine glands. At times, many psychiatric or neurological conditions affect the hypothalamus or the pituitary gland and interfere with the physiological endocrine functions. Often common endocrine disorders present with psychiatric symptoms and may be mistaken for primary psychiatric disorders.

An interdisciplinary team comprising of a physician, an endocrinologist, a gynaecologist, a urologist, and also a psychiatrist, is required to help identify, diagnose and treat the comorbid psychiatric symptoms to help achieve the best possible outcome and an improved quality of life for the patients.



Stress and Psychoneuroimmuno endocrinology axis

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Adrenal Glands

Hypercortisolaemia or Hypocortisolaemia may be a result of a central cause, increased ACTH production, or a local cause at the level of the adrenal glands.

The relationship between the Hypothalamic Pituitary Adrenal (HPA) axis and mood disorders is complex. Glucocorticoids can be both anabolic and catabolic in nature. They are stress hormones that prepare an individual for the demands placed by a stressful environment and create a fight or flight response.

Depression is related to hyperactivity of the HPA axis. However, depressive disorders are seen in both hyper and hypo-cortisolaemic states.

1. Cushing's Syndrome

Major Depressive Disorder (MDD), Panic Disorder and Generalised Anxiety Disorder (GAD) are seen in over 50% of cases of both the pituitary dependent and the pituitary independent form of Cushing's syndrome.[3] Symptoms include attention and memory disturbances, slowing of thought process, irritability, emotional lability, anxiety, fatigue, reduced sexual drive, increased appetite, and insomnia. Risk factors include female gender, older age, severity of the condition, high urinary cortisol levels, and an absence of pituitary adenoma.[3] Sudden withdrawal of steroid treatment may also produce a similar condition.

Correction of the hypercortisolism with cortisol inhibitors such as the anti-fungal - ketoconazole appear to be more effective

than antidepressants in treating the psychiatric symptoms.[3] Persistent symptoms are due to the excess glucocorticosteroids causing cortical atrophy and resultant neurocognitive symptoms.

Symptoms of mania and hypomania have also been reported, with a higher risk in those with doses of prednisone of over 80 mg/ day.

2. Addison's Disease

Depression and irritability are seen in Addison's Disease, although the causative mechanisms are unknown. Both the physical and psychiatric symptoms respond well to treatment with steroid replacement, with glucocorticoids being more effective than mineralocorticoids. Patient education to adjust doses of medication is important.

3. Phaeochromocytoma

Anxiety symptoms, that almost present like a panic attack are often reported. This is so prevalent, that often anxiety is listed as a symptom in patients. Therefore physicians should exercise caution and consider a diagnosis of phaeochromocytoma in patients with anxiety with hypertensive episodes that persist or worsen.[3] Surgical removal of the tumour results in alleviation of symptoms.

Pituitary Gland

1. Oestrogen & Progesterone Abnormalities

A. Amenorrhoea in Anorexia Nervosa (AN)

Amenorrhoea in Anorexia Nervosa is associated with hypothalamic dysfunction. It is reversible and improves with weight gain.[2]

B. Premenstrual Dysphoric Disorder (PMDD)

PMDD or late-luteal phase disorder is a prime example of mood dysregulation in women. Lifestyle management with diet, exercise and stress reduction are first-line treatment options. Often patients may require antidepressants for the relief of the key symptoms of depressive mood and irritability.[2]

C. Polycystic Ovary Syndrome (PCOS)

Symptoms of depression and anxiety are often seen in young girls with PCOS. Sodium valproate has also been implicated in the development of PCOS, especially in young women. It has been reported that PCOS develops in about 10% of women with bipolar disorder who are on valproate therapy (compared with 1.5% of women treated with lithium and other antiepileptic mood stabilisers), most within the first 6 to 12 months of treatment.

Patients should be counselled about diet and exercise at the start of valproate therapy in an effort to avoid weight gain since obesity will worsen insulin resistance and hyperandrogenaemia. At each visit, patients should be asked about menstrual irregularity, hirsutism, and acne. When present, appropriate referral to a gynaecologist or endocrinologist is advised. Therapy for PCOS may include an oral contraceptive or progestin, insulin sensitisers such as metformin, antiandrogens, and local/topical treatments for hirsutism and acne. Since other mood stabilisers such as lithium and lamotrigine do not appear to cause PCOS, a switch to either one of these medications could also be helpful.

D. Postpartum Depression (PPD)

The sudden changes in the levels of oestrogen and progesterone in the postpartum period alter the serotonin levels in the brain resulting in the

postpartum depression. Often it may be an emergency, as the new mother may experience either suicidal or infanticidal ideas. Treatment includes antidepressants, and often inpatient care along with Electroconvulsive Therapy (ECT).

5. Menopause

The association of depression in women in the peri-menopausal and post menopausal phase has been well documented. Oestrogen replacement therapy (ERT) has been used to treat women with depressive symptoms in the post menopausal state.

2. Androgens Abnormalities

Anger, impulsivity, dominant behaviour, anti social behaviour, competitive behaviour and aggression are strongly correlated with higher levels of testosterone, in both men and women. Sodium valproate had been associated with the development of hyperandrogenism in young women.

Patients with male hypogonadism often have undiagnosed anxiety and depression. The symptoms are seen to abate with testosterone replacement therapy for 3 months.

3. Hyperprolactinaemia

Symptoms of anxiety, hostility, depression and sexual dysfunction have been reported in women with both pituitary related and psychotropic medication (especially atypical antipsychotics such as risperidone and olanzapine) induced hyperprolactinaemia. The approximate relative potency of antipsychotics in causing hyperprolactinaemia is (in order of decreasing potency) risperidone, haloperidol, olanzapine, ziprasidone, quetiapine, clozapine, and aripiprazole. Women tend to have higher prolactin responses to antipsychotics than men.

Risk factors include childhood traumatic events, other stressful life events, hypothyroidism and use of oral contraceptives.

During drug therapy, the physician should inquire about menstruation, nipple discharge, breast enlargement, sexual functioning, and (if appropriate) pubertal development. If these are normal, there is no need to measure serum prolactin. However, if problems in these areas are uncovered that are temporally related to antipsychotic therapy, serum prolactin level should be measured.

If the level of serum prolactin is elevated but less than 200 ng/mL in a symptomatic patient, other causes of hyperprolactinaemia (such as pregnancy, hypothyroidism, and renal failure) should be excluded by measuring serum human chorionic gonadotropin, TSH, and creatinine levels. If these tests are negative, one might try to decrease the dosage of the antipsychotic medication or change treatment to an agent less likely to elevate serum prolactin. If it is not possible to lower the dosage or switch to a different medication, it may be helpful to add a small dose of aripiprazole, which will usually suppress serum prolactin by virtue of its partial dopamine-agonist properties. Dopaminergic drugs, such as bromocriptine or cabergoline, can also be given but may occasionally worsen the underlying psychosis.

4. Acromegaly

Excessive production of pituitary growth hormone results in an altered appearance of skeletal growth and therefore sometimes psychiatric sequelae such as irritability, impulsive behaviour, and mood changes.

5. Cushing's Syndrome

Major depressive disorder (MDD), Panic disorder and generalised anxiety disorder (GAD) are seen in over 50% of cases of both the pituitary dependent form (central cause) of Cushing's syndrome.[3]

Pancreas

1. Type I Diabetes

Eating disorders and depression are also seen frequently in patients with Type I diabetes. Often patients may deliberately omit their insulin to induce hyperglycaemia to lose weight.[3] Non-compliance in these patients is governed by the presence of depression and parenteral and peer influence. Eating disorders should be ruled out in patients with poor glycaemic control and those with multiple episodes of diabetic ketoacidosis.[3]

2. Type II Diabetes

Clozapine and olanzapine have been shown to have the greatest propensity to lead to weight gain and obesity; quetiapine and risperidone rank intermediate; and, aripiprazole and ziprasidone appear to be least associated with adverse effects on body composition. Weight gain and obesity are associated with increased rates of Diabetes and lipid abnormalities. Atypical antipsychotics increase glucose and lipid levels, and responsible for metabolic syndrome (Type II Diabetes, dyslipidaemia and hypertension).

Type II Diabetes and depression have a bidirectional relationship. Depression is seen in almost 1 out of every 4 patients suffering from Type II diabetes. Hence a thorough assessment for the same should be a part of the protocol for all patients. Poor self image and poor quality of life are frequently seen as accompanying symptoms. The burden of treatment to the patient is much greater if the accompanying depression remains undiagnosed or untreated.

Prevalence of Type II DM is 2 to 3 times more common in patients with Schizophrenia and bipolar disorder. The high comorbidity in multifactoral and complex, with genetics, lifestyle and atypical antipsychotic medications playing a role.

Therefore a thorough screening of all patients should be carried out prior to starting atypical antipsychotics. This includes evaluating weight, waist circumference, blood pressure, fasting glucose, lipids, and documentation of family history of diabetes and cardiovascular illness. Metabolic monitoring at regular intervals is recommended for early intervention. Switching to antipsychotic drugs such as ziprasidone or aripiprazole that cause the least weight gain is recommended.

Increased body weight, female gender, a history of depression or dieting and body dissatisfaction promote the development of eating disorders in these patients. Tell tale signs that must set off an alarm in physicians include missed appointments, recurrent hypoglycaemia due to intentional insulin overdose, recurrent episodes of diabetic ketoacidosis, poor self esteem, dietary manipulation, and poor glycaemic control.[3]

Thyroid Gland

1. Hyperthyroidism

The thyroid hormone enables the sympathetic system to act. Thus a hyperthyroid state induces a sympathetic hyper activation, creating a fight or flight response. Fear, aggression or anxiety are the emotional components of a fight or flight situation. These are also seen in

patients with anxiety disorders, along with other psychological symptoms such as irritability, rapid speech, exaggerated startle response, panic attacks, and insomnia, resulting in a misdiagnosis and often a delayed diagnosis of the endocrine disorder.

Significant hyperactivity may be misdiagnosed as a manic or psychotic episode in approximately 10% of patients with severe hyperthyroidism. Severe hyperthyroidism can also induce delirium, especially during thyrotoxic storms.

Along with the management of the cause of hyperthyroidism, beta blockers such as propranolol, metoprolol, and atenolol, may provide symptomatic relief.

2. Hypothyroidism

Patients with hypothyroidism show a generalised slowing of both mental and physical activities, along with easy fatigability, reduced concentration, and other symptoms that mimic the symptoms seen in clinical depression. This was a rationale for the use of thyroid hormone augmentation for the treatment of resistant depression, even in those with a euthyroid state. Primarily depression, attention deficit disorders and cognitive disturbances (due to the changes in metabolic activity in the CNS) have been reported.[3] Severity of symptoms can range from mild depression to psychotic depression with suicidal thoughts.

Congenital hypothyroidism results in profound intellectual and developmental deficits (cretinism).

In patients of dementia with hypothyroidism, the memory deficits may not reverse even with treatment.

"Myxoedema Madness" - although now rare, described the relationship between severe hypothyroidism and psychosis. In patients suffering from severe hypothyroidism, there may be a reduced level of consciousness, and a delirious state often misinterpreted as psychosis

3. Thyroid Augmentation in Mood Disorders

An elevated TSH level is the most sensitive index of underlying hypothyroidism. However there is no consensus on how best to treat the subclinical hypothyroidism seen in patients with mood disorders (depression and mania). One theory postulates that these patients may be suffering from early thyroid hormone deficiency without any disturbances in their physical functions, resulting in successful trials with the addition of T3.[2]

4. Mood Stabilisers-induced Subclinical Hypothyroidism

Lithium, Carbamazepine and sodium valproate are often used as a mood stabilising agents in the treatment of various mood disorders such as recurrent depression, resistant depression, bipolar disorder and in mania. All 3 of these can induce subclinical hypothyroidism at anytime during treatment. 20% of patients treated with Lithium can develop hypothyroidism, with women and rapid cyclers being more vulnerable, and up to 50% develop goitre.[2] Therefore all patients on Lithium, Carbamazepine and Sodium valproate should be regularly screened with a baseline thyroid function test. Tests should be repeated 1 to 2 months, 6 months, and 12 months after starting Lithium, and yearly thereafter.

If hypothyroidism occurs during treatment, replacement thyroid hormone therapy with levothyroxine should be started, and the dosage increased as needed to normalise serum TSH.

Parathyroid Gland

1. Hyperparathyroidism

The mechanism/s for psychiatric symptoms in patients with hyper parathyroidism is unknown. High prevalence rates of depression are correlated with the severity of symptoms and high serum calcium levels. Depressive symptoms and quality of life improve significantly after treatment with surgery - parathyroidectomy. Anxiety, delirium and personality changes have also been reported.

2. Hypoparathyroidism

Neuropsychological dysfunctions and psychiatric symptoms are reported. For conventional psychopharmacological agents to work, serum calcium levels and vitamin D levels also need to be corrected.

Conclusion

The prevalence of psychiatric co morbidity in endocrine disorders is significant. This may be either due to the effects of the hormonal disturbances or independent or them due to other factors such as family history, stressful life events or personality factors. It is important for family physicians to inquire about and evaluate for psychological symptoms. When required a Psychiatric consultation should be sought. The assessment and treatment of the symptoms would help achieve better compliance, better treatment outcomes and an improved quality of life for the patients.

References

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