

Psychiatric Issues in Endocrinology

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P psychiatric symptoms and syndromes are common in patients with endocrine disorders. This column briefly reviews psychiatric issues in diabetes mellitus, hypoglycemia, thyroid disorders, parathyroid disorders, adrenal disorders, acromegaly, pheochromocytoma, hyperprolactinemia, polycystic ovary syndrome, and testosterone deficiency. A more detailed review is available in the American Psychiatric Publishing Textbook of Psychosomatic Medicine.¹

DIABETES MELLITUS

Type 1 diabetes mellitus (insulin-dependent diabetes), an autoimmune disorder with additional genetic and environmental influences, affects 5% to 10% of diabetics in the United States. Type 2 diabetes is characterized by insulin resistance and is etiologically related to obesity, sedentary lifestyle, and diet. It affects 90% to 95% of US diabetics. Intensive management of both type 1 and type 2 diabetes is known to reduce diabetic complications and improves long-term health outcomes.²⁻⁴ Thus, the goal of achieving optimal glucose values requires complex conscientious daily behaviors, which many patients find difficult. In both types of diabetes, psychiatric disorders have been linked to treatment nonadherence, worse glycemic control, and ultimately greater prevalence of micro- and macrovascular complications.

There is conflicting evidence as to whether stress directly affects the onset of diabetes or its course.¹ Stress hormones are involved in the counter-regulatory response to insulin, so stress is likely to play a role in increasing blood glucose. It is unclear whether stress directly influences metabolic regulation or whether people under stress change their self-care behaviors.

Depression, which is 2–3 times more common in diabetics than in the general population, is associated with poorer glycemic control and increased diabetic complications. The dem-

onstration of such associations raises the question of whether depression is a cause or an effect of poorer diabetic outcomes. There are a number of mechanisms by which depression can increase the risk for or aggravate diabetes. Depression is associated with an increase in the secretion of cortisol and other counter-regulatory hormones. Depression is also associated with reduced physical activity, increased smoking, poor diet, and poor ability to self-monitor. Depression often results in changes in interpersonal functioning that can adversely affect the doctor-patient relationship, which is central to diabetic management. Depression also increases the risk of a variety of other comorbidities, such as coronary disease. There are also a number of mechanisms by which diabetes can result in or aggravate depression. Diabetes can lead to significant restrictions in lifestyle, demoralizing complications (eg, renal failure, blindness, gastroparesis, amputations), and chronic pain. Diabetes is also associated with white matter lesions thought to increase risk for “vascular depression.”

Small randomized controlled trials have demonstrated the efficacy of nortriptyline⁵ and fluoxetine⁶ in the treatment of depression in diabetes. In addition, one small randomized controlled trial of cognitive-behavioral therapy demonstrated that this treatment improved both depression and glycemic control.⁷ A large randomized controlled trial of collaborative care, coordinating medical and psychiatric treatment in

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primary care settings, demonstrated improved depression care and outcome but no improvement in glycemic control.⁸

Given the high prevalence of depression and its adverse effects in diabetes, as well as the availability of evidence-based treatments for depression, aggressive identification and treatment of depression are warranted as early as possible in the course of diabetes. Depression should always be suspected in patients who are having difficulty adapting to diabetes and who show poor glycemic control.

There is also an increased prevalence of diabetes, mainly type 2, in patients with bipolar disorder. Some of this increase is due to the increased frequency of obesity in bipolar patients, some of which is iatrogenic due to the risk of weight gain with most mood stabilizers. The increased prevalence of diabetes may also be related to behavior factors (eg, poor diet, sedentary lifestyle) and other comorbidities. It is unclear whether bipolar disorder might physiologically aggravate diabetes, and whether diabetes and bipolar disorder may share some degree of genetic risk.

Diabetes is 2–4 times more common in patients with schizophrenia than in the general population. While some of this increase can be attributed to the proclivity for some antipsychotics—particularly many of the atypicals—to cause glucose intolerance and obesity, the increased risk of diabetes in schizophrenia preceded the introduction of the atypical antipsychotics.¹ Schizophrenics also tend to have poorer diet and are more likely to be sedentary.

There is also an increased risk of eating disorders in patients with diabetes, with anorexia nervosa and bulimia more frequent in type 1 diabetes and binge-eating disorder more frequent in type 2. For many patients, a downside of optimally tight control of blood glucose is weight gain. In addition, the increased attention to dietary intake may aggravate eating disorders. “Caloric purging” refers to the practice of using less insulin than prescribed in order to lose weight, a practice that has been found in up to 40% of type 1 diabetics 15–30 years of age.⁹ Those who engage in caloric purging have elevated hemoglobin A1c, more frequent hospitalizations and emergency room visits, and more frequent diabetic complications. This practice can be very difficult to detect if it is the only means of purging used by the patient. Thus, in patients who have both diabetes and anorexia nervosa or bulimia, overly intensive diabetic management can backfire. It is important to remember that metabolic stabilization is the primary goal, and to avoid excessive zeal in pursuing ideal blood glucose levels in such patients.

While many clinicians would suspect that frequent hypoglycemic episodes from too much insulin would result in

permanent cognitive dysfunction in diabetics, the evidence is equivocal. There is more evidence that frequent hyperglycemic episodes results in cognitive dysfunction, most likely due to cerebral micro- and macrovascular damage.¹

HYPOGLYCEMIA

“Reactive hypoglycemia” was a popular diagnosis in the past, often offered as an explanation for symptoms of depression, anxiety, inattention, or unexplained fatigue. Currently, a 5-hour glucose-tolerance test is no longer considered necessary in evaluating such patients. Significantly symptomatic hypoglycemia is unusual and is rarely due to an insulin-secreting tumor (insulinoma) or factitious disorder. However, it can be due to insulin, most often insulin that is prescribed. True hypoglycemic episodes are distinguishable from panic attacks in that the latter rarely cause acute confusion or loss of consciousness.

THYROID DISORDERS

Hyper- and hypothyroidism, with the exclusion of the pituitary or hypothalamic types, are common and easily screened for with a serum thyroid-stimulating hormone (TSH). Somatic symptoms of hyperthyroidism include sweating, fatigue, heat intolerance, weight loss, weakness, fine tremor, and tachycardia. The psychiatric symptom pattern in hyperthyroidism most often resembles generalized anxiety, but depression, irritability, hypomania, and cognitive dysfunction are all common. In severe hyperthyroidism (thyrotoxicosis, “thyroid storm”), patients may be manic.

The somatic symptoms of hypothyroidism include weakness, fatigue, cold intolerance, weight gain, constipation, and somnolence. The psychiatric presentation of hypothyroidism closely mimics depression, but cognitive dysfunction is not uncommon. Severe hypothyroidism rarely presents with psychosis (“myxedema madness”).

Subclinical hypothyroidism refers to the clinical condition in which TSH is elevated, but T4 is low or normal and the patient has few or no symptoms. Subclinical hypothyroidism appears to be a risk factor for depression and is a common cause of rapid cycling in bipolar disorder. Patients with subclinical hypothyroidism often show subtle signs of cognitive dysfunction. At what point to treat with thyroid replacement in subclinical hypothyroidism, if at all, remains controversial.

PARATHYROID DISORDERS

Symptoms in hyperparathyroidism directly reflect serum calcium levels. It is common for a person with mild-to-moderate hypercalcemia (10–14 mg/dL) to experience depression, apathy, irritability, lack of initiative, and lack of spontaneity. In severe hypercalcemia (>14 mg/dL), patients are usually delirious with psychosis, catatonia, or lethargy, and may progress to coma. Symptoms in hypoparathyroidism similarly reflect calcium levels. In mild hypocalcemia, patients have anxiety, paresthesias, irritability, and emotional lability. Mania, psychosis, tetany, and seizures are common in severe hypocalcemia.

ADRENAL DISORDERS

Hyperadrenalism (Cushing's syndrome) most commonly results from exogenous corticosteroids, but may also be the result of adrenocorticotropic hormone (ACTH) secretion by a pituitary tumor (Cushing's disease), or corticosteroid secretion by an adrenal tumor. In addition to somatic consequences—including diabetes, hypertension, muscle weakness, obesity, and osteopenia—psychiatric symptoms are common in hyperadrenalism and may actually appear before physical signs. Depression is most common, but anxiety, hypomania/mania, psychosis, and cognitive dysfunction are all common.

Addison's syndrome may be primary (a result of adrenal destruction by autoimmune disease, metastatic cancer, tuberculosis, or human immunodeficiency virus infection) or secondary, through suppression of ACTH secretion by chronic corticosteroid therapy. Common physical symptoms in Addison's syndrome include postural hypotension, anorexia, nausea and vomiting, and weakness. Psychiatric symptoms include apathy, anhedonia, fatigue, and depressed mood. Adrenal insufficiency may sometimes be mistakenly diagnosed as major depressive disorder. While anorexia is common in both, the presence of nausea and vomiting should suggest the former.

ACROMEGALY

Acromegaly is the result of excess growth hormone secretion by a pituitary tumor. Common physical symptoms and signs include headache, disfiguring facial and bodily features, glucose intolerance, and hypertension. Psychiatric symptoms include mood lability, personality change, and depression. Any psychosis reported was usually due to treatment with dopamine agonists such as bromocriptine.

PHEOCHROMOCYTOMA

Pheochromocytomas are rare catecholamine-secreting tumors. They cause tachycardia, labile hypertension, headache, sweating, and palpitations. They may also cause anxiety symptoms that mimic panic attacks. Pheochromocytomas have occasionally been reported to be unmasked after the prescription of an antidepressant. Screening by testing for urinary catecholamines produces frequent false positives. The best diagnostic test is a plasma metanephrine level which is more specific. However, these tumors are quite rare, and it is unnecessary to screen for pheochromocytomas in most anxious patients even if they also have hypertension.

HYPERPROLACTINEMIA

Excessive secretion of prolactin may be caused by pituitary adenoma, pregnancy, antipsychotics (eg, conventionals, risperidone), and antidepressants. Hyperprolactinemia in women is manifested by galactorrhea, irregular menses, and infertility. Men usually have no physical symptoms, but both genders may experience reduced libido, depression, and anxiety.

POLYCYSTIC OVARY SYNDROME

Polycystic ovary syndrome (PCOS) is common, affecting 5% to 10% of women of childbearing age. The cause of PCOS is unknown, but there is increased risk in women receiving valproate. Physical signs of PCOS include oliguria, amenorrhea, hirsutism, infertility, obesity, hypertension, and insulin resistance. Depression is very common, but it is unclear whether its origin is hormonal or an emotional reaction to the changes in appearance and reproductive function associated with PCOS.¹

TESTOSTERONE DEFICIENCY

In men, testosterone deficiency may be the result of aging or primary or secondary hypogonadism. Physical symptoms in men include reduced libido, sexual dysfunction, low energy, muscle weakness and atrophy, and reduced hair growth. The concept of a male climacteric is controversial. There is evidence of an increase in depression associated with reduction in testosterone levels in men.¹⁰ However, results have been mixed in randomized controlled trials using testosterone to treat depression in hypogonadal men.¹

In women, testosterone deficiency results in decreased libido, low energy, and depression. However, the level considered

to constitute deficiency has not been clearly defined, and the indications, risks, and benefits of testosterone-replacement therapy in women are even less clear than in men. *PP*

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