that are atypical and refractory to pharmacotherapy.

Case Report

A 42-year-old man was referred to our clinic for evaluation of recurrent seizures which had begun to occur 10 months before and were usually seen in the early morning or during tiring work. He had been diagnosed with epilepsy and anxiety disorder by a neurologist, and phenytoin and alprozolam treatment had been prescribed. The frequency of attacks had increased up to four times a week in the previous 3 months. He was referred to our clinic after these complaints. Also, he had no response to carbamazepine and levetiracetam treatment, and the electroencephalogram (EEG) performed shortly after an episode showed diffuse rhythmic theta activity.

The typical attack was seen on the first morning of hospitalization after a fast of 10 hours. It began with fatigue and psychomotor slowing. Some bizarre behaviors, like crying, "I will die" and moving his extremities aimlessly were observed, followed by loss of consciousness. The peripheral glucose level was 30 mg/dl. Upon administration of intravenous glucose solution, he became alert and all symptoms subsided after a few minutes. The blood sample sent for investigations prior to therapy also revealed the low plasma glucose (21 mg/dl) and high circulating insulin level (15 μU/ml). The attacks did not recur with continuous intravenous glucose administration.

An abdominal MRI revealed a 17 mm round nodular mass located over the pancreatic tail. Surgical removal of the tumor resulted in complete resolution of the symptoms and reversion of the insulin and glucose levels back to normal levels. The microscopic evaluation of removed material also confirmed the diagnosis of insulinoma.

Comment

Insulinomas are rare neoplasms recognized by an inappropriately high circulating insulin level, for the ambient blood glucose concentration. The most common neurological feature at presentation is confusion. As the disorder evolves, coma, motor deficits, or convulsions begin to occur.[1] Unless there is the presence of localized abnormalities in the cerebral circulation, low glucose level affects all cerebral neurons, resulting in a generalized dysfunction which may present as diffuse slow activity in EEG and lead the clinician to prescribe antiepileptics, as in our case. The episodic nature of hypoglycemia in insulinoma also causes the symptoms to fluctuate, and delays the diagnosis.

Confusion or bizarre behavior which could be misdiagnosed as an epileptic disorder are much more common (approximately 25%), although nearly six percent of the hypoglycemic cases present with seizures.[2] Hypoglycemia itself can also induce unawareness of the autonomic and neuroglycopenic symptoms and decrease the counterregulatory hormonal responses in insulinoma.[3] So, the unawareness of autonomic symptoms might play a critical role in misinterpretation, as in our case.

Once diagnosed as a refractory epileptic disorder, a significant proportion of patients receive aggressive and escalating pharmacotherapy. Remembering that the metabolic causes of seizures are almost always curable, and may be fatal if untreated, this report highlights the need for careful assessment of every seizure. The critical importance of assessment of blood glucose level in patients with altered level of consciousness is again impressed. Insulinoma, though uncommon, is a potentially recognizable and treatable disease, as long as there is a high index of suspicion. It should always be considered among the diagnostic possibilities in any patient with unusual or inexplicable neurological features, including atypical seizures refractory to pharmacotherapy.

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Modafinil-Induced Reversible Hyperkinetic Nondystonic Movement Disorder in a Patient With Major Depressive Disorder

SIR: Fatigue, lack of energy, and lassitude are commonly reported symptoms in major depressive disorder and are likely to persist as residual conditions in patients with partial response to antidepressant therapy. Modafinil, a newer psychostimulant, has been used as an augmentation strategy to treat persistent fatigue and sleepiness in patients with major depression who are partial responders to antidepressant treatment.[1] Furthermore, modafinil may fasten the onset and

degree of resolution of symptoms of depression with fatigue when combined with selective serotonin reuptake inhibitor treatment.[2] Modafinil seems to be generally well tolerated; frequent adverse events include headaches, nausea and nervousness, which are transient in most cases.

Case Report

A 76-year-old female patient with a history of major depressive disorder (DSM-IV), was admitted to the psychiatric department with a severe major depressive episode (Hamilton Depression Rating Scale) in August 2003. After partial response with venlafaxine 150 mg/d and concomitant treatment with zopiclone 7.5 mg/d for insomnia, she still suffered from severe lack of energy, persistent fatigue and lassitude. Modafinil 200 mg/d was then administered as augmentation to ongoing antidepressant therapy with rapid improvement of residual symptoms and full remission from depression after 2 weeks of treatment (Hamilton Depression Rating Scale). The patient was discharged with venlafaxine 150 mg/d and modafinil 200 mg/d and subsequently was followed at our outpatient clinic. After 4 months of continuous treatment, the patient presented with bothersome, nondystonic, hyperkinetic, involuntary movements affecting the orofacial region and the lower limbs, which had developed over the past 4 days. After discontinuation of modafinil, the drug-induced movement disorder improved and then finally disappeared completely within 4 days.

Comment

The authors report a case of a severe and disabling, but reversible, orofacial and lower limb hyperkinetic, nondystonic, modafinil-induced movement disorder. No such movement disorders have been observed in patients treated with modafinil for daytime sleepiness or narcolepsy even in large-scale trials.[3] Neither have there been any reports on those disorders in depressed patients receiving modafinil as an augmentation strategy. A causal relationship between the intake of modafinil and the movement disorder described seems probable, because the movement disorder developed within a timeframe of 4 months of continuous treatment with modafinil, which is in line with a case report on orofacial dyskinesias following a 10-month period of treatment with the modafinil derivative adrafinil.[4] Furthermore, the movement disorder completely resolved within 4 days after discontinuation of modafinil. This case report supports further evidence that, like in the case of antipsychotics,[5] elderly patients might have a greater risk for developing hyperkinetic movement disorders.

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