CASE REPORT
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Olanzapine-Induced Hypoglycemic Encephalopathy: A Case Report

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Antipsychotic medications are associated with increased risks of metabolic abnormalities. We present a 44-year-old woman with underlying bipolar disorder who had been treated with atypical antipsychotics, olanzapine. After taking 50 mg olanzapine to commit suicide, she developed altered mentality. The serum glucose level was 15 mg/dL and she was treated with glucose infusion immediately. Brain MRI findings were compatible with hypoglycemic encephalopathy. Olanzapine may induce serious hypoglycemia, even in the absence of any risk factors of hypoglycemia.

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KEY WORDS: Hypoglycemic encephalopathy · Olanzapine · Diffusion-weighted image.

Introduction

Atypical antipsychotic drugs offer important benefits to many patients with disorders such as schizophrenia, including a lower risk for the extrapyramidal side effects compared to conventional antipsychotics. However, certain treatments with antipsychotic medication are associated with increased risks for weight gain, dyslipidemia, insulin resistance, hyperglycemia, and hypoglycemia.[1-3]

The mechanism of these metabolic abnormalities, especially glucose metabolism is still unclear. Mechanisms such as antagonism of histamine and serotonin, and increased leptin secretion may play a role in the lowering of serum glucose levels.[4,5]

We report a case of severe hypoglycemia with encephalopathy induced by olanzapine overuse.

Case

A 44-year-old woman was admitted to our hospital due to a comatose mentality. She had previous history of bipolar disorder and treated with olanzapine, valproic acid for 10 years. After taking 50 mg olanzapine at once to commit suicide, she developed an impaired consciousness. She was admitted to emergency room after 8 hours. On admission, her vital signs were stable. Her body weight checked 67 kg and the body mass index was 26.8. On neurologic examination, her mental state was semi-coma. Vestibulo-ocular reflex and corneal reflex were not shown. No other definitive upper motor neuron signs were observed. Her serum blood glucose levels were 15 mg/dL on admission. Intra-venous infusion of 500 mL 50% dextrose was administered immediately, but her mental state was not improved. Laboratory findings showed Hb A1c 5.3%, insulin level 2.66 μU/mL and fasting total cholesterol level was normal. Valproic acid level was 11.6 μg/mL, which were lower than the therapeutic level. Blood gas analysis revealed no hypoxia. Some possible causes of hypoglycemia in non-diabetic patient including hepatic, renal disease, infection, insulinoma, non-β-cell tumor were evaluated and the results were negative. Diffusion-weighted brain MRI (DWI) showed increased signal intensity at the bilateral globus pallidi, fronto-parietal subcoritical white matter, corpus callosal splenium symmetrically, and left inferior cerebellar hemisphere, but negative on fluid attenuated inversion recovery (FLAIR) images (Fig. 1).

Electroencephalography showed nearly persistent intermixed synchronous or independent moderate amplitude semi-rhythmic delta slow waves, compatible to decreased cortical function without seizure activities.

On neurologic examination after the 2 days of symptoms onset, her mental status improved to drowsy. She showed bradyphrenia, bradykinesia and symmetric fair grade motor weakness in whole extremities without other sensory abnormality,

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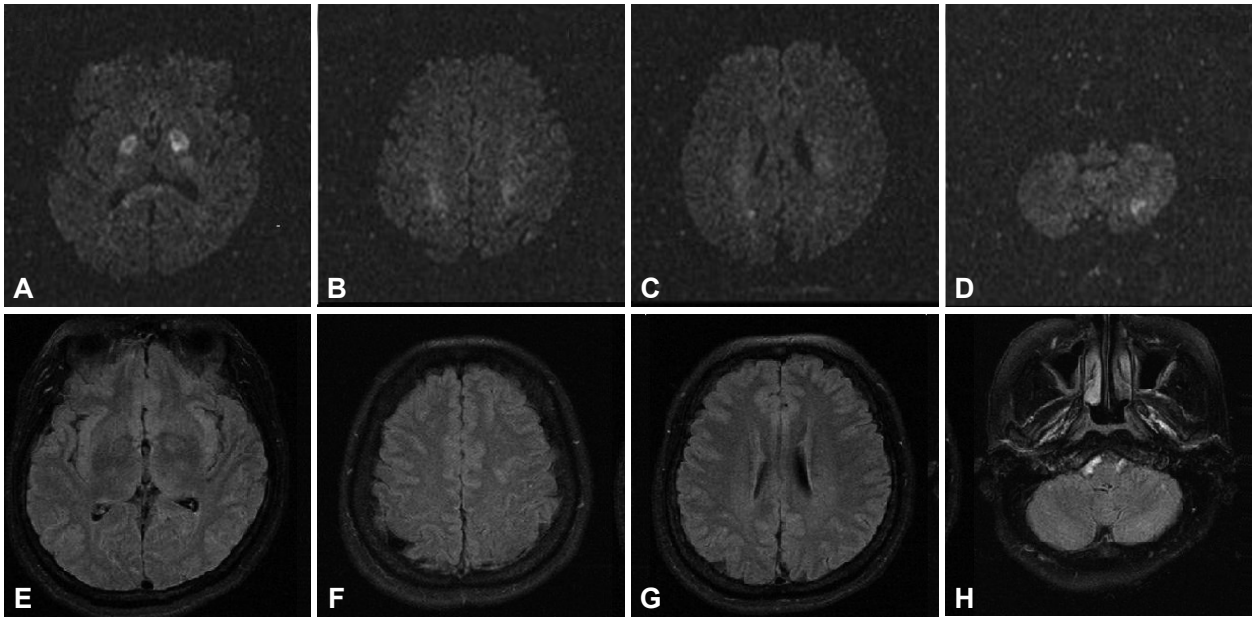

FIGURE 1. Initial diffusion-weighted brain MRI on admission showing hyperintense lesions in the bilateral globus pallidi, corpus callosal splenium (A), bilateral fronto-parietal subcoritical white matter (B, C), and left inferior cerebellar hemisphere (D). On fluid attenuated inversion recovery images, these lesions are not shown (E-H).

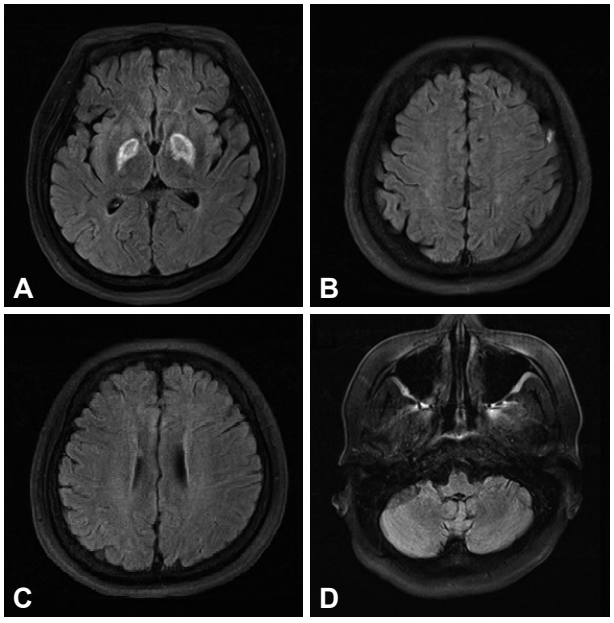

FIGURE 2. Follow-up fluid attenuated inversion recovery MRI after the 20 days of symptoms onset revealing hyperintense lesions in bilateral globus pallidi, which had seen diffusion-weighted brain MRI on admission (A). The fronto-parietal subcoritical white matter and left inferior cerebellar hemisphere lesion are not shown any more (B, C, D).

cerebellar dysfunction and abnormal movement. Her consciousness improved gradually and after 3 weeks on admission, her mental status became alert but bradyphrenia and bradykinesia persisted. Follow-up brain MRI showed bilateral symmetric patchy high signal intensity on FLAIR images at the globus pallidi, had seen on DWI initially. The fronto-parietal subcoritical white matter, corpus callosum and left inferior cerebellar hemisphere lesions were not shown (Fig. 2).

She was discharged with no further improvement on 1 month after hospitalization.

Discussion

Olanzapine is known as a common cause of hyperglycemia and hypertriglyceridemia. Recently published randomized controlled study demonstrated that olanzapine has a relationship to weight gain and insulin resistance.[3] It was suggested that metabolic abnormalities caused by olanzapine are related to the insulin resistance.[6,7]

In this patient, however, olanzapine induced hypoglycemia and it might be related to an induced metabolic abnormality that olanzapine promote insulin resistance and excessive insulin secretion. In our patient, serum insulin levels were not elevated during the episodes of hypoglycemia. Two possible explanations for normal serum insulin level deserve comment. First, it is possible that hypoglycemia is related to noninsulin mechanism such as antagonism of histamine and serotonin, and increased leptin secretion. Second, as the patient was treated with immediate infusion of glucose before sampling of serum insulin, rapid rising serum glucose level might halt insulin secretion and lower the increased serum insulin level.

Usually, even if olanzapine stimulates insulin secretion, homeostatic mechanisms act to regulate blood sugar levels and to prevent the onset of hypoglycemia. From the perspective of this patient, it might lack reserve capacity with regard to

glucose homeostasis, why she developed hypoglycemia.

In the cases of hypoglycemic encephalopathy, lesions mainly involve the cerebral cortex, basal ganglia, hippocampus, splenium, and bilateral internal capsule. The mechanisms of cytotoxic edema are shrinkage of the extracellular space as a result of hypoglycemia, and failure of ionic pumps of neuronal membrane, which cause hyperintense lesion on DWI.[8] Some studies reported that hyperintense lesions which were detected in white matter such as corpus callosum, internal capsule, or corona radiata, regressed on follow-up imaging. These features exhibit relatively good prognosis. If lesions were detected in the cerebral cortex, basal ganglia, or hippocampus and did not regress on second imaging, the outcome will be poor.[8,9] In our patient, follow-up brain MRI showed disappeared subcoritical white matter, corpus callosum, cerebellar hemisphere lesions, but persistent high signal intensity in the bilateral basal ganglia. Her clinical outcome was not so good because the patient was left with bradyphrenia and bradykinesia, which is correlated to previous reports. Regarding above unequal vulnerability, basal ganglia may be more vulnerable to oxidative stress after glucose reperfusion because of their lesser glucose transporter efficiency.[10]

Hypoglycemia is a serious medical condition which causes neurologic damages. We should consider the metabolic effects when we use atypical antipsychotic drugs and monitor any hypoglycemic symptoms, body weight, fasting glucose and insulin intolerance.

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