New-onset Diabetic Ketoacidosis Induced by the Addition of Perospirone Hydrochloride in a Patient Treated with Risperidone

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Abstract

A 32-year-old man with a family history of type 2 diabetes mellitus presented with circulatory collapse and deep coma after 9 days of treatment with perospirone hydrochloride, a recently developed atypical antipsychotic agent available only in Japan. The new drug had been added to the long-standing treatment with risperidone. Diagnosed with diabetic ketoacidosis, he was given insulin and saline with discontinuation of all antipsychotics. Ultimately, diabetes was controlled by dietary therapy alone despite reintroduction of risperidone. The risk of new-onset diabetic ketoacidosis in patients with diabetic risk factors who are taking perospirone hydrochloride or other atypical antipsychotics should be kept in mind.

Key words: perospirone hydrochloride, atypical antipsychotics, type 2 diabetes mellitus, diabetic ketoacidosis

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Perospirone hydrochloride (Lullan) is a newly developed atypical antipsychotic agent clinically available only in Japan. Details of its adverse effects are not widely known.

Case Presentation

A 32-year-old Japanese man being treated for schizophrenia was admitted to the emergency department with circulatory collapse and deep coma. He had taken risperidone (2 to 4 mg daily) for 3 years, during which he gained 20 kg to result in a body mass index of 33.4 kg/m². His father had type 2 diabetes mellitus. Annual serum glucose examinations had been normal, most recently 11 months before admission (110 mg/dL). During the preceding 9 days, perospirone hydrochloride (8 mg daily) had been added to risperidone (4 mg daily) to treat worsening of auditory hallucinations. During the 4 days preceding admission, he had experienced severe thirst, taking about 5 L daily of fruit juices and tea.

On arrival at the hospital, the patient was unresponsive to any stimulus. Blood pressure was 78/42 mm Hg, and heart rate was 128 beats/min. Laboratory examinations indicated hemococoncentration (hematocrit, 59.9%), severe metabolic acidosis (pH, 7.120; HCO₃⁻, 12.0 mmol/L; base deficit, 16.6 mmol/L), hyperglycemia (glucose, 1708 mg/dL; creatinine, 4.92 mg/dL), electrolyte abnormalities (sodium, 134 mEq/L; potassium, 6.2 mEq/L; chloride, 79 mEq/L), and ketonemia (3+ by reagent strip testing; acetoacetic acid, 3010 μmol/L; 3-hydroxybutyric acid, 5260 μmol/L). Hemoglobin A₁c was 10.7%. Serum level of C-peptide was 1.2 ng/mL.

The patient was diagnosed with diabetic ketoacidosis complicated by hypovolemic shock. Continuous intravenous infusion of insulin and volume resuscitation with saline were begun. All previous medications including risperidone and perospirone hydrochloride were discontinued. Serum glucose was controlled at concentrations between 150 and 200 mg/dL, although large doses of intravenous insulin initially were required. Two weeks after admission, psychotic symptoms worsened, including auditory hallucinations. Risperidone (2 mg daily) was reinitiated; the dose was increased to 5 mg followed by gradual tapering as symptoms responded. On the other hand, intravenous administration of insulin first was replaced by intermittent subcutaneous administration, and finally by dietary therapy alone (28 kcal/kg/day). The patient was diagnosed with type 2 diabetes mellitus. On day 93 the patient left the hospital with a body mass index of 29.1 kg/m² while receiving risperidone at 1 mg daily.

Discussion

Previous reports suggested that atypical antipsychotic agents such as clozapine, olanzapine, risperidone, and quetiapine may be associated with new-onset diabetic ketoacidosis as well as type 2 diabetes mellitus (1, 2). However, no previous reports have described an initial episode of ketoacidosis in patients taking perospirone hydrochloride.

During 3 years of therapy with risperidone, our patient with a family history of type 2 diabetes mellitus had a considerable weight gain. As suggested by the hemoglobin A₁c value on admission, hyperglycemia may have existed even before additional treatment with perospirone hydrochloride...

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was begun. After onset of ketoacidosis and admission, all antipsychotics were discontinued. Diabetes was controlled upon discharge from the hospital by dietary therapy alone, despite reintroduction of risperidone. Most likely the patient’s weight gain, a well-known adverse effect of risperidone, induced type 2 diabetes mellitus, with subsequently added perospirone hydrochloride or/and massive ingestion of soft drinks being the main contributor to development of life-threatening diabetic ketoacidosis. In the present case, risperidone with a known risk of inducing type 2 diabetes had been administered to the patient with an increasing body weight as well as a family history of type 2 diabetes mellitus. At least monthly examinations of serum glucose level should have been undertaken. The risk of new-onset diabetic ketoacidosis in patients with risk factors for diabetes who receive perospirone hydrochloride or other atypical antipsychotics should be kept in mind. We explained the purpose of this report to the patient and obtained written consent.

References