Paliperidone-Induced Neuroleptic Malignant Syndrome

To the Editor: Paliperidone, a newer atypical antipsychotic agent, belongs to the chemical class of benzisoxazole derivatives and is the major active metabolite of risperidone. Neuroleptic malignant syndrome (NMS) is the most serious and potentially fatal side effect of neuroleptic medicines.[1] It occurs most frequently with the use of high-potency conventional antipsychotic medicines. This condition may accompany treatment with any antipsychotic agent, including the newer atypical antipsychotics. These patients may have marked muscle rigidity, elevated temperature, diaphoresis, dysphasia, incontinence, altered sensorium, mutism, elevated or labile blood pressure, elevated WBC counts, and elevated serum creatinine phosphokinase.[2] The present case report describes NMS in a 13-year-old boy who was taking paliperidone.

Case Report

A 13-year-old boy reported to the psychiatry department with a complaint of confusion, turning of head toward one side, urinary incontinence, and fever. The patient had had behavioral abnormalities and mental retardation since childhood. When his behavioral abnormalities worsened, his family members decided to take him to a psychiatrist. Three days previously, the patient was given oral paliperidone, 3 mg b.i.d., for behavioral abnormalities by a private psychiatrist. The first day after taking the medication, the patient had difficulty walking, reduced speech, and stiffness of the body. On the second day, the boy failed to recognize his family members; he was febrile, and he had urinary incontinence. He later came to us for further evaluation of his current problem. On general physical examination, he had a fever (103°F), elevated blood pressure (140/80 mmHg), and rapid pulse rate (120 bpm). Neurological examination revealed increased muscle tone in all four limbs, brisk reflexes, bilateral tremors of upper limbs, and positive Babinski's sign. Based on his history and the clinical examination, we made a provisional diagnosis of neuroleptic malignant syndrome (NMS), and the patient underwent a hematological investigation. On investigation, his hemoglobin was 12 g/dL, total leukocyte count was 16,200/mm^3, differential count of neutrophils was 84%, and lymphocyte was 16%. The patient's erythrocyte sedimentation rate was 18 mm at the end of first hour and platelets were 1,052,000/mm^3. The patient also showed decreased serum iron (8 μg/dl [reference range: 35–150]) and increased creatinine phosphokinase (2,120 U/liter [reference range: 35–232]). SGOT was 123 U/liter (reference range: 15–37) and SGPT was 86 U/liter (reference range: 30–65). His renal function, CSF analysis, and serum electrolytes were within normal limits. One of the incidental findings was increased head circumference (56 cm). The patient's CT scan showed congenital hydrocephalus. Later an assessment was made using the NMS scale;[3] the score was 24/36. All these above findings strengthened our final diagnosis of NMS and made us immediately withdraw the oral paliperidone. Later on, the boy was managed with IV fluids, antipyretics, and benzodiazepines. The patient's confusion decreased after a day of supportive management, and he reached a premorbid state within 1 week, with no neurological deficits at 3-week and 4-week follow-up visits. The parents were advised on behavioral management for temper tantrums. The patient was later referred to a neurosurgeon for management of congenital hydrocephalus.

Discussion

Paliperidone is a newer atypical antipsychotic drug available in extended-release formulation. It has efficacy and adverse effects similar to those of risperidone. NMS is historically associated with the classic or "typical" antipsychotic drugs, and it is also a potential adverse effect of atypical antipsychotic drugs. A review of the literature on NMS with atypical antipsychotic agents by Khaldi et al.[4] states that NMS is reported with all of the atypical drugs, such as clozapine, olanzapine, risperidone, aripiprazole, ziprasidone, amisulpride, and quetiapine. In 2007, Duggal et al.[5] described a suspected case of NMS with paliperidone in a 63-year-old woman. Initially, she was taking oral quetiapine and trifluoperazine; after paliperidone was added, NMS symptoms appeared.

NMS is common in patients who have risk factors like dehydration, rapid rate of neuroleptic loading, depot neuroleptics, age extremes, prolonged use of restraints, use of other medications with neuroleptics (especially lithium), poorly controlled neuroleptic-induced extra-

pyramidal symptoms, treatment-resistant extrapyramidal symptoms, withdrawal of antiparkinsonian medications, a diagnosis of an affective disorder, alcoholism, organic brain syndrome or previous brain injury, extrapyramidal disorder, iron deficiency, and catatonia.[6] The risk factors for causing NMS in the current case report are the pediatric age, presence of mental retardation and hydrocephalus, iron deficiency, and the longer-acting antipsychotic with higher dosage. To conclude, paliperidone has the potential to cause NMS, and special precautions must be taken with children and with those who are at high risk for NMS.

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