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CASE REPORT

Neuroleptic Malignant Syndrome Associated with Ischemic Injury of the Bilateral Basal Ganglia

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INTRODUCTION

Neuroleptic malignant syndrome (NMS) is an uncommon and potentially fatal untoward drug reaction associated with neuroleptic agents.[1] It presents with panoply of clinical manifestations including fever, muscular rigidity, altered sensorium, leukocytosis, and elevated serum creatinine kinase. Signs of autonomic instability such as tachycardia, hypertension, diaphoresis, and tachypnea also can be present. Together with supportive measures and the withdrawal of the offending agent, administration of the skeletal muscle relaxant, dantrolene, along with dopamine agonists, bromocriptine or amantadine, are necessary interventions in most cases. Although incidence is reported at only 0.02 to 3% in patients using neuroleptic medications,[2] mortality rates approach 10% and are related to complications arising from acute renal failure, acute respiratory failure, cardiac injury, and sepsis.[3] Therefore, preventions and identification of risk factors associated with NMS are crucial.

We present a patient with hypoxic-ischemic injury to the basal ganglia secondary to a provoked asthma attack who received the atypical antipsychotic, quetiapine, in rehabilitation and subsequently developed neuroleptic malignant syndrome.

CASE REPORT

A 48-year-old male asthmatic developed a hypoxic respiratory arrest. His past medical history was significant for severe asthma with frequent exacerbations. He had no neurologic history and was otherwise healthy. He was employed as a painter for a local vehicle resale company and endeavored to paint a project car at home without proper ventilation. Overcome by paint fumes, he developed a respiratory arrest and emergency medical services were contacted.

Upon their arrival, the patient was cyanotic and bradycardic. He entered asystole and treatment measures, in accordance with Advanced Cardiovascular Life Support guidelines, were administered with return of spontaneous circulation approximately six minutes after arrest. The patient was intubated and transferred to the intensive care unit (ICU). Upon extubation, he exhibited difficulties with speech, weakness in the right arm, cognitive and motor slowing, and agitation.

Magnetic resonance imaging (MRI) of the brain displayed diffusion restriction in bilateral cortical areas and basal ganglia, consistent with hypoxic injury (Figure 1). Due to agitation, he was placed on 50 milligrams of quetiapine and 50 milligrams of trazodone at bedtime. He slowly improved and was transferred to an inpatient rehabilitation facility.

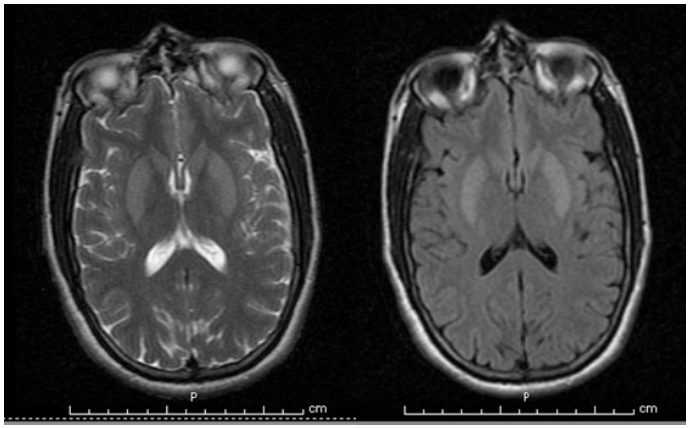

Figure 1. T2-MRI (left) and FLAIR MRI (right) taken within five days of the paitent's cardiopulmonary arrest revealed high signals involving the putamen and caudate bilaterally, indicating ischemia.

The patient was treated at the rehabilitation center for seven days, during which time quetiapine and trazodone were continued. Increased spasticity in his extremities developed and baclofen was added to his medication regimen, however, he experienced progressive tightness and rigidity of the extremities and decreased responsiveness. Tachypnea and a fever of 38.1°C developed. He was transferred to the ICU at an acute care hospital for evaluation of a possible infectious cause, none of which was found via imaging or laboratory studies.

The patient remained tachypneic, rigid, feverish, and became obtunded. Upon medication review, it was discovered that he was inadvertently given at least 100 milligrams of quetiapine and 50 milligrams of trazodone each evening at the rehabilitation facility for an unknown length of time. Given this information and the clinical picture, neuroleptic malignant syndrome was suspected. A repeat MRI of the brain showed evolution of the hypoxic changes in the basal ganglia (Figure 2). At this time, a neurology consultation was obtained and treatment with dantrolene and amantadine was initiated. The patient exhibited significant improvement within the first 24 hours of treatment, especially with muscle rigidity. Fortunately, there were no renal or cardiac complications from the event and most symptoms were resolved within one week.

His arousal and attention improved, but the hypoxic encephalopathy continued. On discharge, the patient returned to inpatient rehabilitation.

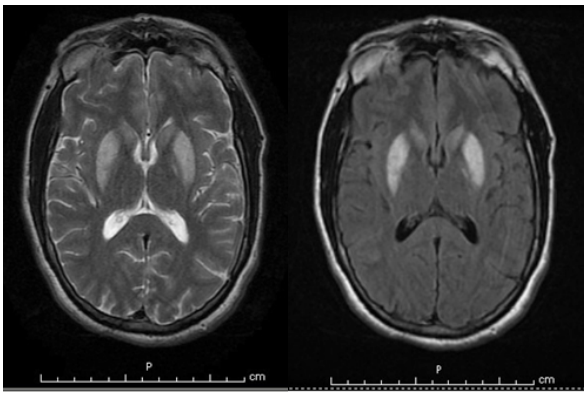

Figure 2. T2-MRI (left) and FLAIR MRI (right) taken approximately 19 days after arrest, showing evolution ischemic damage in bilateral basal ganglia.

DISCUSSION

Neurologic sequelae arising in survivors of cardiopulmonary arrest are a significant cause of morbidity. In acute ischemic stroke, cerebral hypoperfusion generally is confined to a focal vascular distribution, whereas in cardiac arrest, the lack of cerebral blood flow is global in nature, leaving the entire brain vulnerable to injury via both direct and reperfusion mechanisms. Areas especially prone to hypoxic injury include the cerebellum, hippocampi, cortex, and basal ganglia; all areas of high metabolic demand for oxygen and glucose.[4,5] Basal ganglia involvement has been described in neuroleptic malignant syndrome,[6,7] likely due to its dopaminergic neural circuitry involving the nigrostriatal pathways.[2]

Prior to receiving neuroleptics, our patient suffered from hypoxic-ischemic damage of the basal ganglia, particularly involving the putamen and caudate bilaterally, from a cardiopulmonary arrest. The cause of NMS is suspected to be due to excessive dopaminergic blockade within the brain, explaining the risks associated with antipsychotic agents, which act as dopaminergic antagonists. First generation antipsychotics are implicated more commonly than second generation, or "atypical," antipsychotics due to their higher affinity for dopamine receptors. However, both classes have been implicated in NMS. Additionally, high doses and rapid dose escalation of antipsychotic agents place patients at increased vulnerability to NMS.[8] Other factors also contribute to the development of NMS, such as preexisting central nervous system disorders, dehydration, and malnutrition.[9-12]

The blockade of dopamine in already damaged nigrostriatal dopaminergic circuits may have contributed to the emergence of NMS in this patient. To our knowledge, he had never been exposed to quetiapine in the past. During his hospitalization, he received a therapeutic dose of quetiapine daily but began receiving double the dose in error at rehabilitation before developing NMS. This error highlights the need for all medical facilities to have proper dosing precautions in place and effective medication administration.

CONCLUSION

We recommend that dopamine receptor antagonists should be used with caution or avoided in patients with hypoxic or ischemic injury to the basal ganglia, as the risk of further dopamine blockade could place the patient at risk for neuroleptic malignant syndrome. We also recommend early neurological consultation in patients with hypoxic-ischemic encephalopathy, as this may direct therapy and improve outcomes.

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