Case Report

Olanzepine-induced neuroleptic malignant syndrome in a case of multiple sclerosis

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Abstract

Suspicion of neuroleptic malignant syndrome (NMS) is a frequent cause of emergent psychiatric consultation. Despite early recognition, NMS has remained a syndrome that causes high rates of morbidity and mortality. A 25-year-old male with multiple sclerosis presented to the accident and emergency department and E with ataxia. He was started on steroids. On the third day, he became tearful and anxious. A diagnosis of multiple sclerosis-induced psychosis was made and he was started on olanzepine 2.5 mg BD. On the sixth day the patient was tachypneic and had tachycardia. Temperature recorded in the axilla was 45°C. Patient was intubated and electively ventilated. A diagnosis of NMS was made and treated accordingly. This case report highlights the importance of recognizing and treating NMS in a patient on anti-psychotics.

Key words: Multiple sclerosis, neurolept malignant syndrome, olanzepine

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Introduction

Suspicion of neuroleptic malignant syndrome (NMS) is a frequent cause of emergent psychiatric consultation. This uncommon syndrome, characterized by muscular rigidity, autonomic instability, hyperthermia, and mental status changes, has been associated with conventional dopamine D_2 receptor antagonist treatments such as haloperidol or fluphenazine. Recent literature suggests that it also occurs in atypical antipsychotics with low dopamine antagonism. Despite early recognition, NMS has remained a syndrome that causes high rates of morbidity and mortality.[1] A review in 2009 suggests that, in general, NMS associated with atypical antipsychotic drugs manifests in a typical manner. One notable exception is clozapine-induced NMS, which appears less likely to manifest with extra-pyramidal features, including rigidity and tremor.[2] A significant incidence and prevalence of psychological disorders in multiple sclerosis (MS) has been reported. Their underlying mechanisms and the extent to which they are reactive to psychosocial factors or symptoms of the pathological process itself, remain unclear. It is concluded that psychiatric onset of MS may occur in up to 1% of patients, and that in previously healthy persons with acute psychotic disorder even the slightest neurological abnormality justifies a cranial magnetic resonance imaging (MRI) examination.

Case Report

A 25-year-old man, with a background history of multiple sclerosis in remission for two years came to the Accident and Emergency department with weakness in his right arm and leg for 6 h. He also had ataxia. There was no focal/urinary incontinence or visual disturbances. He was started on methyprednisolone 1 g intravenously. On the third day, the patient had jerky movements and shivering. Axillary temperature was recorded at 38.6°C. He also had dysarthria, past pointing and blurring of vision and nystagmus. He was very anxious, tearful, and apprehensive; diagnosis of psychosis was made, and the patient was started on olanzepine 2.5 mg BD. He also had a lumbar puncture done for nystagmus and ataxia. On the sixth day patient was tachypneic and had tachycardia. He was very drowsy. Temperature recorded in the axilla was 45°C. Leucocyte count was 22,000 cells/mm^3. Creatinine kinase (CK) levels

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were 15,650 u/L [normal 30-190 u/L], serum alanine aminotransferase was 146 [normal 15-45] and alkaline phosphatase was 660 [normal < 300]. Patient was tachycardic, diaphoretic with incontinence and altered consciousness. Patient was intubated and electively ventilated. His CK levels continued to rise. His urine output decreased with increasing levels of creatinine and urea. Hemodialysis was initiated due to oliguria and rising renal parameters. The temperature was measured continuously via a rectal probe. At all times temperature was above 40°C. A diagnosis of Neuroleptic malignant hyperthermia was made. Arterial lines and a central line were inserted. Patient was well hydrated. Active cooling measures were initiated. Bloods were closely monitored for evidence of Disseminated intravascular coagulation (DIC) and electrolyte imbalance. An antipyretic was started. Patient was started on bromocryptine 5 mg NG TDS, Dantrolene 200 mg IV QDS, baclofen 10 mg TDS and clonidine 100 micrograms BD. The symptoms of NMS started resolving after nearly 4 h. The tachycardia and muscle rigidity had significantly reduced by the first day. Patient made a complete recovery in two days. MRI of the brain revealed extensive plaques in brainstem and swelling of the brain. A diagnosis of multiple sclerosis with superimposed acute demyelinating encephalomyelitis was made. The patient was extubated three days.

Discussion

Neuroleptic malignant syndrome (NMS) refers to the combination of hyperthermia, rigidity, and autonomic deregulation that can occur as a serious complication of the use of antipsychotic drugs. Delay first used the term in 1960, after observing patients treated with high-potency antipsychotics.[3] The syndrome can occur after any duration of treatment, although two-thirds of cases occur within the first week. The frequency has been variably reported as 0.07-2.2% of patients taking neuroleptics.[4] Data largely come from case control studies rather than prospective randomized trials.

Several criteria systems have been used for diagnosis of NMS. We used the DSM-IV-TR Criteria.[5] Criteria A included muscle rigidity and fever and criteria B consisted of diaphoresis, incontinence and altered consciousness. Our patient had both parameters of criteria A and had two parameters of criteria B. This was consistent with the diagnosis of NMS. The serotonin syndrome can be distinguished from NMS in most cases by a detailed history of medication used with particular attention to recent dosage changes and the absence of severe rigidity.[6] NMS pathophysiology is largely speculative. Neuroleptic drugs block dopaminergic receptors, creating a functional dopamine-deficiency state. Dopaminergic receptor blockade in the substantia nigra causes muscle rigidity and alters thermoregulation in the hypothalamus. Increased heat production from muscle rigidity causes fever, impaired heat dissipation (by reducing cutaneous vasodilatation or by sweating), and possibly a higher core temperature set point in the hypothalamus.[7]

Although rhabdomyolysis is a rare side-effect (<1%) of olanzapine, this adverse event should be evoked when a patient with olanzapine presents with muscle pain, unexplained fatigue or weakness. Creatinine kinase levels should be checked in all patients with suspected NMS. However, it remains uncertain whether a mild and asymptomatic muscle enzyme increase without any metabolic disorder requires the discontinuation of olanzapine therapy.[8]

An algorithm has been suggested to treat both NMS and seronergic syndrome (SS), as it is not possible to differentiate them sometimes. The suggested algorithm includes: (1) Supportive care and withdrawal of all potentially offending agents; (2) Laboratory evaluation with prompt initiation of treatment for both disorders—cyproheptadine for SS and dantrolene for NMS; (3) Do not use bromocriptine (contraindicated in SS) or chlorpromazine (contraindicated in NMS) initially; (4) Add bromocriptine when serotonergic agent has long half-life.[9] The efficacy of using dantrolene as a mode of treatment in NMS has been questioned.[10]

In our case, the patient had psychotic features, which is commonly treated with olanzepine. Though there have been many reports of NMS with high-dose olanzepine,[10] there is little evidence to show that low-dose olanzepine causes NMS. The other feature in this case was the time taken for the onset of NMS. Reports normally mention weeks to months for NMS to set in after initiating low-dose olanzepine, in our case the symptoms started 3 days after starting low-dose olanzepine. The most important factor which predicts mortality in a case of NMS is onset of renal failure. Our case also had renal failure but prompt initiation of renal replacement therapy was life-saving. The most important cause of renal failure is myoglobinuria which leads to acute tubular necrosis. The relapse rate of NMS is nearly 80%. Electroconvulsive therapy (ECT) has been used as an alternative method for treatment of psychosis in patients with increased risk of NMS with medications.[11]

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