Neuroleptic malignant syndrome in severe vascular dementia: Diagnostic challenge due to baseline impaired mental status

Thein Swe, Akari Thein Naing

ABSTRACT

Introduction: Neuroleptic malignant syndrome (NMS) is a life-threatening disease more often considered than truly diagnosed. The NMS is a life-threatening neurologic emergency associated with the use of antipsychotic drugs and characterized by a distinctive clinical syndrome of mental status change, rigidity, fever, and dysautonomia.

Case Report: A 69-year-old wheelchair bound male with past medical history of severe vascular dementia with behavioral problems, schizoaffective disorder referred from nursing home due to fever for 1 day. According to his room-mate, his baseline mental status use to be drowsy and disoriented. Vitals showed temperature 102°F (38.8°C), tachycardia, high blood pressure 140/90 mmHg, tachypnea and low oxygen saturation of 87% on room air. Arterial blood gases showed hypoxia and respiratory alkalosis with high A-a gradient. Also suspected infection due to leukocytosis with neutrophilia. However, we kept neuroleptic malignant syndrome (NMS) in mind since patient was taking haloperidol for episodic agitation although haloperidol dose was unchanged and no new drugs were added. When total creatine kinase came back as 3142 IU/L, he was managed successfully with dantrolene and amantadine.

Conclusion: Neuroleptic malignant syndrome can be difficult to diagnose in the presence of baseline altered mental status. It is important to have early diagnosis of NMS in patients who presented with altered mental status and muscle rigidity with underlying dementia and psychiatric illness.
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Conclusion: Neuroleptic malignant syndrome can be difficult to diagnose in the presence of baseline altered mental status. It is important to have early diagnosis of NMS in patients who presented with altered mental status and muscle rigidity with underlying dementia and psychiatric illness.

Keywords: Altered mental status, Dantrolene, Amantadine, Dementia, Neuroleptic malignant syndrome

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a life-threatening disease more often considered than truly diagnosed. Initial diagnosis of NMS would be difficult if a patient has severe dementia. Muscle rigidity and elevated total creatine kinase play an important role in considering diagnosis. Many of NMS cases are due to change in class or dose of antipsychotic medications, however, it can also occur in patients on long-term stable dose and sometimes it is unrelated to dose.
CASE REPORT

A 69-year-old wheel-chair bound male with past medical history of severe vascular dementia with behavioral problems, schizoaffective disorder, seizure disorder, hypertension was referred from nursing home to emergency room (ER) for fever for one day.

He had a history of hospitalization in a psychiatric ward one month before because of agitation. After that he was discharged with oral haloperidol 2 mg twice daily and this dose remained the same for the next six months. He was also taking carbamazepine 200 mg per os ibid and divalproex sodium 750 mg per os ibid for seizure, and amiodpine 5 mg per oral once daily for hypertension.

At the admission, the patient was drowsy and less responsive than usual. He did not open his eyes in response to verbal stimuli, he was not communicative at all, was minimally responsive to painful stimuli but presented involuntary movements of his upper extremities. He was more awake, alert and oriented to time and place before coming to ER. Physical examination was also conducted in ER and patient was also drowsy and less responsive. Vital signs upon admission were: temperature 102°F (38.8°C), heart rate 110 beats/min, blood pressure 150/90 mmHg, respiratory rate 20 breaths/min, oxygen saturation 87% on room air. Neck was supple. Pupils were normal, equal and reactive to light. Respiratory, cardiovascular and abdominal examinations were normal apart from tachypnea and tachycardia. Neurological examination revealed muscular rigidity of upper limbs even if they were moving spontaneously sometimes. Reflexes were normal and Babinski sign was downgoing. Lower limbs motor exam and sensory exam in 4 limbs could not be assessed well because patient was drowsy and not cooperative. However, they were moving spontaneously against gravity and motor of both upper and lower limbs were at least 3/5.

Blood tests showed white blood cells 11.6x10^9/L, neutrophil percentage (auto) 71.3 % (normal = 40–70%), normal potassium, blood urea nitrogen 34 mg/dL, creatinine 1.9 mg/dL, glomerular filtration rate 28.1 ml/min, glucose 135 mg/dL, calcium 9.4 mg/dL, aspartate aminotransferase 95 IU/L, bilirubin 0.6 mg/dL, alanine aminotransferase 55 IU/L, alkaline phosphatase 49 IU/L, Lactic acid was 13.5 mg/dL and total creatine kinase 3142 IU/L. Urinalysis showed normal except large blood with muscle injury (e.g., elevated creatine kinase). However, muscle rigidity and elevated total creatine kinase play an important role in considering diagnosis. Many of cases are due to change in class or dose of antipsychotic medications. However, it can also occur in long-term stable dose and sometimes it is unrelated to dose. According to the Diagnostic and Statistical Manual of Mental Disorders, (4th Edition), Washington, DC, American Psychiatric Association, 1994, diagnosis of NMS is made when the individual exhibit severe muscle rigidity and elevated temperature associated with the use of antipsychotic medication and have at least two of the following associated symptoms: (a) diaphoresis, (b) dysphagia, (c) tremor, (d) incontinence, (e) changes in level of consciousness ranging from confusion to coma, (f) mutism, (g) tachycardia, (h) elevated or labile blood pressure, (i) leukocytosis, or (j) laboratory evidence of muscle injury (e.g., elevated creatine kinase). However, while monitoring intake and output. Vancomycin 1 gram IV and meropenem 1 gram IV were given one time as infection could not be ruled out at that time. Dantrolene 1 mg/kg IV pushed and amantadine 100 mg per oral twice daily were given as bromocriptine was not available at that time. Cooling blanket was applied because patient was persistently febrile (103.6°F or 39.7°C) since admission. Enoxaparin 60 mg subcutaneously was given twice daily for three days since CT scan of chest with PE protocol could not be done due to patient’s poor renal function. Head CT scan showed no acute intracranial pathology. However, lumber puncture was not done since meningoencephalitis was less likely.

After two days, mental status was improving and he opening his eyes upon calling, less muscle rigidity, total creatine kinase was trended down to 1125 IU/L and blood urea nitrogen was 5 mg/dL, creatinine was 1.1 mg/dL and glomerular filtration rate (GFR) was improved to 71 mL/min. Computed tomography (CT) scan of chest with pulmonary embolism (PE) protocol was done and showed negative for PE. Enoxaparin was stopped. Dantrolene was stopped after giving one day due to deranged liver function tests. Amantadine was increased to 200 mg per oral twice daily and continued for 14 days. Patient was downgraded from ICU to medical floor after three days of ICU stay. Patient was discharged from medical service four days after admission to psychiatric ward to continue evaluation and adjustment his schizoaffective disorder. Finally, he was discharged from psychiatric service as his psychiatric symptoms were well controlled. Medications upon discharge were amantadine 200 mg per oral twice daily, carbamazepine 200 mg per oral twice daily and valproate 250 mg per oral thrice daily for seizure and divalproex 250 mg per oral three times daily to control his impulse control.

DISCUSSION

Neuroleptic malignant syndrome (NMS) a life threatening disease more often considered than truly diagnosed. Muscle rigidity and elevated total creatine kinase play an important role in considering diagnosis. Many of cases are due to change in class or dose of antipsychotic medications. However, it can also occur in long-term stable dose and sometimes it is unrelated to dose. According to the Diagnostic and Statistical Manual of Mental Disorders, (4th Edition), Washington, DC, American Psychiatric Association, 1994, diagnosis of NMS is made when the individual exhibit severe muscle rigidity and elevated temperature associated with the use of antipsychotic medication and have at least two of the following associated symptoms: (a) diaphoresis, (b) dysphagia, (c) tremor, (d) incontinence, (e) changes in level of consciousness ranging from confusion to coma, (f) mutism, (g) tachycardia, (h) elevated or labile blood pressure, (i) leukocytosis, or (j) laboratory evidence of muscle injury (e.g., elevated creatine kinase). However,
these symptoms should not be caused by neurological or a mental disorder (e.g., Mood Disorder with Catatonic Features).

Vascular dementia is the second most common type of dementia after Alzheimer disease. In subcortical pathology, patients can present with personality and mood changes, abulia, apathy, depression, emotional disturbance. And cognitive disorder characterized by relatively mild memory deficit, psychomotor retardation, and abnormal executive function. Behavioral and psychological symptoms are common in patients with small-vessel and large-vessel vascular dementia presenting with especially more apathy in small-vessel vascular dementia and more agitation or aggression in large-vessel vascular dementia [1, 2]. The prognosis of the NMS patients in presenium and senium tends to be worse. It is important to diagnose NMS early and treat them as soon as possible for better prognosis [3].

Neuroleptic malignant syndrome (NMS) is most often seen with the “typical” high potency neuroleptic agents such as haloperidol. However, every class of neuroleptic drug could be a risk factor for NMS including the newer atypical antipsychotic drugs such as clozapine and olanzapine. Although symptoms usually develop during the first two weeks of neuroleptic therapy, the association of the syndrome with drug use is idiosyncratic. Neuroleptic malignant syndrome (NMS) can occur after a single dose or after treatment with the same agent at the same dose for many months or years. It is not a dose-dependent phenomenon, but higher doses are a risk factor. NMS may not predictably develop even in predisposed individuals upon neuroleptic exposure and that additional cofactors must be present for the full syndrome to occur [4]. A significantly lower rate of mortality from haloperidol-induced NMS (7%) and a high rate of mortality (38.5%) among patients with organic brain syndrome were also noted. Myoglobinemia and renal failure are strong predictors of mortality, indicating a mortality risk of approximately 50% [5]. One study demonstrated that psychopathological features such as psychomotor agitation, confusion and disorganized behavior may be risk factors for the neuroleptic malignant syndrome [6].

Changes in either mental status or rigidity were the initial manifestations of NMS in most of cases with a single presenting sign and were significantly more likely to be observed before hyperthermia and autonomic dysfunction [7]. It is important to include differential diagnosis such as meningitis, encephalitis, systemic infections, catatonia and serotonin syndrome.

Malignant catatonia is another differential diagnosis characterized by psychosis, agitation, and catatonic excitement. The motor symptoms are also characterized by more positive phenomena (dystonic posturing, waxy flexibility, and stereotyped repetitive movements) than are described in NMS. Laboratory values are usually normal. Lethal catatonia often starts with extreme psychotic excitement, which, if persistent, can lead to fever, exhaustion, and death. NMS starts with severe extrapyramidally induced muscle rigidity. Their early clinical differentiation is important because lethal catatonia often needs neuroleptic treatment and neuroleptic malignant syndrome necessitates immediate cessation of neuroleptics [8]. In this case, patient was drowsy and did not exhibit agitation and lethal catatonia was unlikely.

Serotonin syndrome is one of the differential diagnoses and it is usually caused by use of selective serotonin reuptake inhibitors and has a similar presentation that is difficult to distinguish from NMS. Typical features in these patients that are not often found in NMS patients are shivering, hyperreflexia, myoclonus, and ataxia. Nausea, vomiting, and diarrhea are also symptoms of serotonin syndrome and are rarely described in NMS. Rigidity and hyperthermia, when present, are less prominent than in patients with NMS. In this case, it is unlikely because patient did not take selective serotonin reuptake inhibitors drugs.

Treatment NMS is mainly supportive with stopping offending neuroleptic agent, hydration to prevent kidney failure from rhabdomyolysis, cooling blankets and cardiopulmonary support. Additional treatment includes dantrolene, bromocriptine or amantadine although their efficacy is unclear and disputed [9].

CONCLUSION

Neuroleptic malignant syndrome (NMS) can be difficult to be diagnosed in the presence of baseline altered mental status. It is important to have early diagnosis of NMS in patients who presented with altered mental status and muscle rigidity with underlying dementia and psychiatric illness.

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Author Contributions

Thein Swe – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Akari Thein Naing – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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