Case report

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Neuroleptic malignant syndrome – severe atypical case with electroconvulsive therapy

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Abstract

Neuroleptic malignant syndrome (NMS) is an idiosyncratic life-threatening condition requiring prompt recognition and management. This case illustrates severe, atypical NMS with rhabdomyolysis and a creatinine-phosphokinase of 113,300 IU/L. Due to the diagnostic challenge of NMS, electroconvulsive therapy (ECT) has shown benefits in managing severe, atypical, refractory, unresponsive and undifferentiated NMS cases. Further research is needed to confirm ECT's efficacy through randomised control trials and establish specific inclusion and exclusion criteria for ECT treatment in NMS.

Keywords: neuroleptic malignant syndrome, electroconvulsive therapy

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Neuroleptic malignant syndrome (NMS) is an idiosyncratic life-threatening condition occurring within 72 hours of dopamine antagonist administration with an incidence rate of 0.1-0.2% among antipsychotic treated patients (1). Whilst, the exact pathogenesis remains unclear, theories revolve around the blockade of central dopamine receptors precipitating symptoms of hyperthermia, dysautonomia, rigidity and mental status changes (1,2,3). Due to its varied clinical presentation, NMS is primarily a diagnosis of exclusion, (1,3). Given its poor differentiation, electroconvulsive therapy (ECT) has shown benefit in several complex clinical cases (4). This report details a diagnostically challenging case of severe atypical NMS where possible continued ECT treatment would have benefited.

Case report

A 32-year-old female tuition teacher with a 19-year history of Bipolar Type 1 Disorder presented with manic features including grandiosity, hyperactivity, irritability, disinhibition, overfamiliarity, hypersexuality, and pressured thoughts and speech. She denied recent psychotic symptoms, cognitive decline, or medication nonadherence. Previous severe relapse was partially treated with ECT, and a past autokabalesis attempt was noted. Further history was unremarkable. Upon admission, she was orientated, afebrile, agitated and verbally aggressive, with no neck stiffness or rigidity.

Her medication regime included lithium carbonate 750mg nocte, haloperidol 5mg twice daily (BD), olanzapine 10mg BD, benzhexol 2mg mane and clonazepam 4mg nocte. Upon admission, she was prescribed lithium carbonate slow-release 800mg nocte, sodium valproate immediate-release 500mg BD, chlorpromazine 50mg mane and 100mg nocte, continuing olanzapine, benzhexol and clonazepam as before, and haloperidol was ceased.

Immediate ECT was initiated due to symptom severity, normal vitals, absence of fever, and past positive response to ECT. Two bitemporal ECT stimulations were administered (54mC and 59mC) with intravenous propofol and suxamethonium. Seven hours post-ECT, she was febrile (38.3°C), diaphoretic, agitated and slurring speech. Clonazepam 2mg, haloperidol 10mg, promethazine 50mg, midazolam 5mg and paracetamol was administered.

On the second day, the patient remained manic, febrile (40°C), hypertensive (167/89mmHg), tachycardic (145bpm), tachypneic (24bpm), drowsy, disinhibited, irritable and hyperreflexic with a Glasgow Coma Scale (GCS) of 13. Patient was declared unfit to continue ECT. Ten hours later, rigidity and bilateral ecchymosis on her upper limbs was noted. A provisional diagnosis of sepsis was made due to fever spikes, elevated C-reactive protein (CRP) 49.12mg/dL, and leukocytosis (16.6×10^9/L). Intravenous ceftriaxone, paracetamol, alprazolam 0.5mg and promethazine 50 mg were administered for agitation and sepsis. Sedation aspiration risk was managed via nasogastric tube and imaging.

Six hours later, laboratory results showed creatinine phosphokinase elevation of (CPK) 113,300IU/L,

aspartate-aminotransferase 133IU/L, alanine-amino-transferase 242IU/L, CRP 65.06mg/L and normal serum lithium levels. The patient was febrile (39.4°C), disorientated, autonomically unstable and rigid with decreased urine output (0.625ml/kg/hr) of dark-tea coloured urine indicating rhabdomyolysis. In conjunction with the medical team, lithium carbonate, sodium valproate, chlorpromazine, olanzapine, benzhexol and clonazepam were ceased. Bromocriptine 5mg thrice daily (TDS), promethazine 25mg TDS, diazepam 10mg TDS, and a meningitic dose of ceftriaxone was commenced. By day five, the patient was afebrile, clinically improving, and GCS 15. Midazolam 7.5mg and increased diazepam (15mg TDS) were administered for agitation. Nephrology was consulted for persistent myoglobinuria despite hydration and fluid management.

On the sixth day of admission, the patient was afebrile, CPK was 41,537IU/L and midazolam (2.5mg) was given for severe agitation unresponsive to diazepam. By the eighth day, CPK decreased to 9950IU/L and ceftriaxone and bromocriptine doses were tapered. By day 10, the patient was afebrile, oriented, and mobilizing without rigidity, irritability, or autonomic instability, and a CPK of 2346IU/L. On day 11, patient was cleared for discharge with no manic cognition and prescribed a three-day diazepam course (15mg mane, 10mg vespa, 15mg nocte) for ongoing agitation.

Four days post-discharge, rhabdomyolysis resolved, and CPK dropped to 556IU/L. Due to her antipsychotic sensitivity, lithium carbonate slow-release 400mg nocte was commenced for 5 days, then increased to 800mg nocte with diazepam. Five days later, CPK was 156IU/L. Seven weeks after discharge, lithium carbonate, sodium valproate, olanzapine and diazepam were commenced with ongoing clinic reviews and monitoring of CPK and serum lithium.

Discussion

This case underscores the complexity of diagnosing and managing NMS. Diagnostic features like hyperthermia, diaphoresis, mental status changes and autonomic instability appeared only seven hours after ECT, with pathognomonic generalised rigidity and elevated CPK manifesting at 13 and 32 hours respectively (1). Studies show hyperthermia and profuse diaphoresis occurred in 98% of cases, autonomic instability in 95%, elevated CPK in 95% and generalised or severe lead-pipe rigidity associated myonecrosis in 97% (3). Due to delayed cardinal symptom presentation, the patient was initially misdiagnosed with sepsis, indicated by fever, raised CRP, leucocytosis, and possible meningitic signs.

High-potency first generation neuroleptics are the most common NMS triggers, but low-potency antipsychotics, atypical antipsychotics, tricyclic antidepressants, antiemetics and lithium are also culprits (1,2,3,4). NMS usually occurs within therapeutic dosing range (1). Within this case, the patient was prescribed lithium carbonate, haloperidol, and olanzapine before admission, and was administered chlorpromazine, haloperidol, and promethazine for sedation during admission. This medication administration, coupled with severe psychomotor activity – a significant factor in NMS and subsequent rhabdomyolysis – potentially led to NMS development (1,3,4).

NMS has a reported fatality rate of 10-20% in unrecognized cases, highlighting its life-threatening nature (1). As mental status changes and neurological signs often precede systemic signs, NMS resembles various pathologies (1,3). Bromocriptine and Dantrolene are predominantly used for pharmacotherapy, with benzodiazepines for agitation management (1,2), as seen within this case. Owing to its reported efficacy, ECT must be considered for NMS in cases of catatonia, atypical presentations, failure of standard pharmacotherapy, refractory medication-rechallenging, and when the underlying condition responds to ECT (2,4). Studies show decreased mortality rates amongst severe NMS cases treated with ECT compared to pure symptomatic therapy. (5). However, suxamethonium associated malignant hyperthermia risks with ECT have also not been substantiated (4). Notwithstanding, limited support from randomised controlled trials, ECT remains a valuable option (4,5). Hence, the benefit of continued ECT for this case must be considered.

This atypical NMS case highlights the need for early detection and intervention. Despite ECT's reported efficacy, further research must classify NMS intervention based on severity and establish specific inclusion and exclusion criteria for ECT treatment in NMS.

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