

Intentional Overdose in a Young Male Patient: Limitations of Current Mental Health Models at the Initial Point of Care for High-Risk Patient Cohorts

Rishi Sood¹ Vikram Anumakonda^{1*}

¹The Department of Acute Medicine, Dudley Group NHS Foundation Trust, UK.

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Corresponding Author: Vikram Anumakonda FRCP, FFICM, Consultant Physician, Department of Acute Medicine and Critical Care, The Dudley Group NHS Foundation Trust, UK.

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Abstract

A male in his early 20's presented to the ED of a district hospital within the West Midlands following an intentional mixed overdose of prescribed medications; Citalopram, Chlorpromazine, and Diazepam. Following ingestion of an unknown quantity of these medications at around 2 PM, he was found an hour later in an unresponsive state by family members. The patient reported a separation from their partner preceding the event and had a history of PTSD and extreme anxiety. Post overdose the patient reported significant muscle aches and pains. This combination of drugs placed the patient at an increased risk for developing Neuroleptic malignant syndrome (NMS). NMS is a life-threatening idiosyncratic reaction associated with exposure to dopamine antagonists, commonly antipsychotics [1] characterized by fever, altered mental status, muscle rigidity, and autonomic dysfunction [2]. NMS has been associated with virtually every neuroleptic agent but is more commonly reported with typical antipsychotics [3]. There is also a concurrent increase in the risk of developing rhabdomyolysis secondary to the overdose of antipsychotic drugs. Rhabdomyolysis (lysis of skeletal muscle cells) is a potentially lethal syndrome with a broad spectrum of clinical and biochemical findings [4]. Antipsychotic use is a risk factor for rhabdomyolysis and seems to be more common in those taking multiple agents [5]. This case highlights the potential risk of developing both NMS and rhabdomyolysis in the context of a mixed antipsychotic drug overdose. It highlights the challenges with the assessment of these high-risk patients presenting with self-harm that are assessed by liaison psychiatry teams or models in the United Kingdom.

Background

The case highlights the potential risk for the development of NMS in the context of a mixed drug overdose involving antipsychotics. This particular case will explore the development of rhabdomyolysis associated with the use of antipsychotics, such as chlorpromazine one of the offending drugs consumed in the overdose. Being aware of the risks associated when a patient presents with a mixed overdose of antipsychotics is essential as NMS is life-threatening. It is an emergency situation and needs to be managed accordingly. NMS is mostly seen with high-potency first-generation antipsychotics, such as haloperidol, but can occur with any antipsychotic class [1].

This case illustrates the issue of chlorpromazine-induced rhabdomyolysis in an otherwise healthy 20 + year-old male patient. The patient was known to have a long-standing history of depression and mental health issues. He was prescribed all the drugs that were taken in this episode of overdose. It was established that within this episode there was no concomitant use of alcohol or illicit drugs. The overdose comprised only the aforementioned drugs. Overdose is a significant contributor to mortality in England and Wales, 4,907 deaths related to drug poisoning were registered in 2022, equivalent to a rate of 84.4 deaths per million people [6]. However, NMS is a rare complication of treatment with neuroleptics [7] nonetheless, timely recognition and appropriate management are necessary to prevent associated morbidity.

Citalopram is a selective serotonin reuptake inhibitor (SSRIs). It is the most prescribed treatment for individuals experiencing major depressive disorder [8]. Chlorpromazine, a first-generation antipsychotic is used to treat schizophrenia, bipolar disorder, and acute psychosis [9]. Its antipsychotic effect is believed to be due to the post-synaptic blockade at the D2 receptors in the mesolimbic pathway [9]. The risk of severity of central nervous depression can be increased when Chlorpromazine is combined with 1,2-benzodiazepine [10,11,12,14].

NMS is largely iatrogenic and is often precipitated by medications such as antipsychotics. First-generation antipsychotics are more likely to cause NMS than second-generation antipsychotics [13]. Neuroleptic malignant syndrome is a rare, but potentially life-threatening adverse event associated with the use of neuroleptic agents [15]. Its pathophysiology is mostly due to the blockade of dopamine receptors. Key issues of NMS are those of diagnosis, treatment, and reintroduction of antipsychotic treatment [16].

Rhabdomyolysis is an emergency syndrome caused by skeletal muscle cell damage and the release of intracellular components such as potassium, creatine kinase (CK), myoglobin, and lactate dehydrogenase into the bloodstream [17]. Elevated creatinine Phosphokinase is the hallmark of rhabdomyolysis. It rises within 12 hours of the onset of muscle injury, peaks in 1-3 days, and declines 3-5 days after cessation of muscle injury [4].

In this life-threatening manifestation of NMS, the patient presents with "lead-pipe" muscle rigidity, autonomous instability, hyperpyrexia of more than 40 degrees Celsius, altered mental status, leucocytosis, and elevated serum creatinine kinase [18,19].

Case Presentation

A male in his early 20's presented to the Emergency Department and was post-taken with the Acute Medicine Consultant during the ward round. The patient had a significant history of depression and suicidal ideation. It was noted they had recently suffered a separation from a long-term partner. The latter in addition to a long-standing history of mental health issues placed a great burden upon the patient and may have contributed to the patient's actions with regards to consuming the overdose. The patient was unemployed and lived at home with his parents. There was no underlying medical history of note in the patient's medical records. Prior to the event, they were noted to be fit and healthy. They were known to be treated with oral chlorpromazine for their mental health issues. They presented via ambulance service after an intentional mixed overdose after being found obtunded and thereafter developing intense generalized whole-body muscle aches. During post, the patient was neurologically stable and gained consciousness with a Glasgow coma scale (GCS) of 15.

His treatment course was brief requiring IV Fluids and repeat bloods before discharge. After the initial onset of the overdose, he was found to have worsening kidney function. There was concern regarding the patient's blood test results which revealed a Creatine Kinase (CK) of approximately 25,500. Since the patient's Creatinine Kinase (CK) came back elevated at 25,494 it was correlated with his physical symptoms of muscle aches and pains which were consistent with rhabdomyolysis. The patient was examined thoroughly, and his physical exam was largely unremarkable. Pathologies such as compartment syndrome were promptly excluded. Other than the pronounced muscle ache the patient did not mention any other complaints. Upon checking the patient's flow sheets it was confirmed there had been no episodes of significant pyrexia. Had the latter been present a concern for Neuroleptic malignant syndrome (NMS) could have been also considered. Pyrexia in the context of new-onset renal failure in the setting of rhabdomyolysis on antipsychotics would be suspicious for NMS. This was also ruled out by the fact that the patient had no muscle rigidity or hemodynamic instability. The patient's Creatinine Kinase (CK) peaked at around 25,494 the day after the overdose. The management of the patient included IVI fluids and close monitoring of the CK until return to baseline. The patient recovered baseline function. However, the patient was very reluctant to engage with the liaison psychiatric team and needed a lot of constant persuasion and negotiation to accept psychiatric input. He was subsequently discharged.

Investigations If Relevant

The patient had serial blood tests taken from admission to discharge and there was largely no degree of severe derangement save for the Creatinine Kinase. The following comprise the most significant investigation results for this patient.

20/05: pH 7.412, BE -0.5, ECG SR

21/05: eGFR>90, K 4.2, Na 139, CRP 4, WCC 8.3.

19/05: CK [25494]

Differential Diagnosis

The peak CK level of 24,500 U/L associated with muscle pain confirmed the diagnosis of severe rhabdomyolysis secondary to Chlorpromazine overdose. Rhabdomyolysis refers to significant muscle cell damage that results in the release of waste products and creatine kinase (CK) into the bloodstream. Although CK levels above 1,000 U/L are typically viewed as concerning, there is no universally accepted definition, as factors like gender, ethnicity, muscle mass, age, and kidney function can affect CK levels and the need for urgent treatment. It can potentially cause life-threatening complications like acute kidney injury [5,21].

The present case seeks to inform regarding the potential development of NMS and rhabdomyolysis. Neuroleptic Malignant Syndrome (NMS) is linked to the use of antipsychotic medications and other drugs such as L-dopa, antidepressants, and antihistamines. In this case, there were no documented signs like altered mental status, new-onset catatonia, or episodes of tachycardia or tachypnea, which made the suspicion for NMS low during the post-admission review. If any of these symptoms had been present, it would have raised concern. Evidence strongly suggests that dopamine is involved, as most drugs associated with NMS are D2 dopamine receptor antagonists [22].

Treatment

Treatment of NMS is individualized and based on the clinical presentation, but the first step in essentially all cases consists of cessation of the suspected offending neuroleptic pharmacologic agent. If the syndrome has occurred in the setting of an abrupt withdrawal of a dopaminergic medication, then this medication is reinstated as quickly as possible. The next key step in the management of NMS is the initiation of supportive medical therapy. Aggressive hydration is often required, especially if highly elevated CPK levels threaten to damage the kidneys (as was the case in the presentation), and treatment of hyperthermia with cooling blankets or ice packs to the axillae and groin may be needed.

Metabolic abnormalities may need to be corrected, and bicarbonate loading should be considered in some cases as it may be beneficial in preventing renal failure [23]. In summary, the mainstays of treatment consist of immediate cessation of the dopamine antagonist (or restarting or continuing the dopamine agonist) and supportive measures (rehydration, cooling, and treatment of rhabdomyolysis if present). Additional treatment may be considered if supportive interventions fail [24]. A delay of at least 2 weeks in restarting antipsychotic treatment is advised following full resolution of NMS.

In more severe cases of NMS, empiric pharmacologic therapy is typically tried. The two most frequently used medications are bromocriptine mesylate, a dopamine agonist, and dantrolene sodium, a muscle relaxant that works by inhibiting calcium release from the sarcoplasmic reticulum [23]. The patient was treated with IVI fluids and repeat blood until it was ascertained that the CK levels were approaching baseline. The patient was treated with IVI fluids and repeat blood until it was ascertained that the CK levels were approaching baseline.

Outcome And Follow-Up

This case presentation highlights that oral antipsychotic use can be a risk factor for significant complications, namely the development of NMS and rhabdomyolysis. This patient went on to develop rhabdomyolysis without the rest of the clinical findings associated with NMS and was appropriately managed. The outcome for this patient was favorable with no long-term complications being sustained in terms of renal function. The patients' routine investigations returned to baseline rapidly following treatment with IV fluids necessitating only a short stay in the hospital of only one day.

The patient was referred to their mental health team following treatment. The patient was initially very hesitant to engage with the liaison psychiatric team and required ongoing persuasion and negotiation to accept psychiatric support. He was eventually discharged with a mental health follow-up.

This case highlights the limitations of the current model of psychiatric liaison operational in the UK in high-risk patients. The case highlights the need for prompt recognition of the potential complications in the context of mixed overdose particularly when the patient is prescribed 1st generation antipsychotic medications. Early intervention with IV fluids, when CK is elevated due to rhabdomyolysis, is crucial to improve patient outcomes and prevent long-term renal impairment. This case report highlights the significance of managing chlorpromazine-induced rhabdomyolysis. CK elevation should be rigorously investigated bearing in mind factors known to modulate CK levels before making any precipitate decisions.

Discussion

Studies conducted in the U.K. reveal that individuals with a history of self-harm are **50 to 100 times** more likely to die by suicide than the general population. In both global and U.K. contexts, deliberate self-harm is a significant predictor of future suicide risk, highlighting the need for targeted interventions and long-term support for these high-risk individuals.

The provision of mental health support for acute deliberate self-harm (DSH) varies worldwide, with different models in place. In the **U.K.** a multidisciplinary approach is common, involving mental health assessments in emergency departments, followed by referral to crisis intervention teams and specialized psychiatric services. This model emphasizes comprehensive risk assessment and safety planning. However, one flaw is that not all hospitals have immediate access to psychiatric professionals, potentially delaying care and delayed engagement of mental health services in high-risk patients could lead to huge dropouts. In the **U.S.**, emergency departments often serve as the first point of contact, with subsequent referrals to outpatient services or psychiatric units. The system can be fragmented, leading to gaps in follow-up care, but it provides swift crisis intervention in emergencies. In countries like **Australia**, specialized mental health triage services and community mental health teams work together to ensure ongoing support, offering a more continuous care model, though accessibility can still vary by region.

In **Scandinavian countries**, integrated healthcare models combine physical and mental healthcare in a seamless system. Patients experiencing DSH receive immediate psychological support in the emergency room, with follow-ups integrated into the primary care system. This holistic approach has

proven effective in continuity of care but may face limitations in rural areas. In **low-resource settings**, such as some parts of **Africa and Asia**, mental health services are often limited, relying on non-governmental organizations (NGOs) and community-based care. While these models ensure some level of support, they lack the infrastructure and comprehensive care available in wealthier nations. Each model has strengths in crisis response but faces challenges in providing consistent, accessible follow-up care, highlighting the global disparity in mental health resources.

In addition, this case highlights that oral antipsychotic use can lead to rhabdomyolysis without the rest of the clinical findings associated with NMS. Therefore, prompt recognition of this adverse effect is crucial to improve patient outcomes and prevent long-term renal impairment. This case report highlights the significance of managing chlorpromazine-induced rhabdomyolysis. CK elevation should be rigorously investigated bearing in mind factors known to modulate CK levels before making any precipitate decisions.

Neuroleptic malignant syndrome (NMS) is a life-threatening complication of treatment with dopamine antagonists, or occasionally abrupt withdrawal of dopamine agonists. The patient was at risk of developing NMS by virtue of the overdose of medications. Since there were no episodes of hyperthermia >38.0°C on at least two occasions or altered mental status, sympathetic nervous system lability, and hypermetabolism there was no heightened suspicion of NMS. However, as creatine kinase was elevated it could not be excluded. Generalized rigidity, described as 'lead pipe' in its most severe form and usually unresponsive to antiparkinsonian agents, is a cardinal feature and may be associated with other neurological symptoms [24]. In addition, alternative differential diagnoses including sepsis and drug reactions should be excluded before a diagnosis of NMS is considered. It is imperative that episodes of NMS be documented in the medical records for safe prescribing in the future.

Ananth J, Aduri K, Prameswaran J, et al. [22] succinctly state several lines of evidence that provide support for the involvement of dopamine. Most of the drugs implicated in NMS are D2 dopamine receptor antagonists. Central noradrenergic activity is also possibly related to the disorder, as sympathetic hyperactivity is associated with the active phase of NMS. A high degree of suspicion and the discontinuation of antipsychotic agents even if the diagnosis is not established are essential for the safety of the patient. The clinical conclusion of rhabdomyolysis is supported by the clinical information (significantly elevated CK). The findings of this case are clinically correlated and the possible causal association has been ruled out.

Using Diazepam together with citalopram may increase side effects such as dizziness, drowsiness, confusion, and difficulty concentrating. Of note elderly patients, may also experience impairment in thinking, judgment, and motor coordination. Both Chlorpromazine and Citalopram prolong the QT interval [25]. Most manufacturers advise avoiding the use of two or more drugs that are associated with QT prolongation. The patient's ECG was negative for any QTc prolongation.

The diagnosis of NMS is based on history and the presence of certain physical examinations and laboratory findings[26] Although NMS has classically

been characterized by the presence of the triad of fever, muscle rigidity, and altered mental status, its presentation can be quite heterogeneous, as reflected

in the current Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition [*DSM-IV*]) criteria (see **Table 1**) [27].

Table 1.

Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition [*DSM-IV*]) Research Criteria for Neuroleptic Malignant Syndrome [8]

A.	Development of severe muscle rigidity and elevated temperature associated with the use of neuroleptic medication.
B.	Two (or more) of the following:
	(1) Diaphoresis
	(2) Dysphagia
	(3) Tremor
	(4) Incontinence
	(5) Changes in level of consciousness ranging from confusion to coma
	(6) Mutism
	(7) Tachycardia
	(8) Elevated or labile blood pressure
	(9) Leucocytosis
	(10) Laboratory evidence of muscle injury (eg, elevated CPK)
C.	The symptoms in criteria A and B are not due to another substance or a neurological or other general medical condition.
D.	The symptoms in criteria A and B are not better accounted for by a mental disorder.

Abbreviation: CPK, creatinine phosphokinase

The clinical course typically begins with muscle rigidity followed by fever within several hours of onset and mental status changes that can range from mild drowsiness, agitation, or confusion to severe delirium or coma [2].

The primary trigger of NMS is dopamine receptor blockade, and the standard causative agent is an antipsychotic. Potent typical neuroleptics such as haloperidol, fluphenazine, chlorpromazine, trifluoperazine, and prochlorperazine have been most frequently associated with NMS and are thought to confer the greatest risk [2]. Neuroleptic malignant syndrome in hospitalized patients is considered a neurologic emergency as a delay in treatment or withholding of therapeutic measures can potentially lead to serious morbidity or death. As such, some consider it prudent to treat for NMS even if there is doubt about the diagnosis [28].

Patients with NMS can have high morbidity due to renal failure and disseminated intravascular coagulation (DIC) secondary to rhabdomyolysis [23]. Chlorpromazine is considered a higher risk medication for NMS in contrast to the newer 2nd generation antipsychotics, thereby this patient being at higher risk of both complications namely NMS and rhabdomyolysis. The risk of rhabdomyolysis increases, especially when ingested at high doses or when combined with certain other medications (such as mixed overdoses). The latter succinctly being the case in this patient's presentation precepting an increased risk as they had taken a mixed overdose of including said medication.

Rhabdomyolysis is not a well-understood adverse effect of antipsychotic use. The proposed mechanism is the involvement of serotonergic and/or dopaminergic blockade [5]. Another proposed mechanism is the increased release of calcium from the sarcoplasmic reticulum of muscle cells leading to increased muscle contractility and rigidity, breakdown of muscle, and hyperthermia [2].

Learning Points/Take-Home Messages

- Antipsychotic agents are commonly employed to manage behavioral changes linked to various disorders. However, their severe side effects necessitate a high degree of vigilance, the cessation of all medications, and the implementation of supportive care measures.
- A prompt and accurate diagnosis of NMS is crucial to alleviating the severe, prolonged morbidity and potential mortality associated with this syndrome [29].
- Being aware of acute rises in CK in the presence of anti-psychotic overdose is crucial to aid in prompt diagnosis of such presentations. This patient was swiftly worked up for chlorpromazine-induced rhabdomyolysis and was initiated on the appropriate treatment regimen. Early recognition of this adverse effect is crucial to improve patient outcomes.
- Neuroleptic malignant syndrome (NMS) is a life-threatening complication of treatment with dopamine antagonists, or occasionally abrupt withdrawal of dopamine agonists.
- Early recognition of the potential adverse effects of NMS is crucial to improve patient outcomes. The clinical findings in this case are consistent with the presented diagnosis and supported by literature.
- The conclusion reached was that the patient presented with drug-induced rhabdomyolysis secondary to 1st generation antipsychotic drug overdoses this conclusion is supported by the clinical information described.
- Proactive involvement of mental health services is essential for effectively mitigating risks in high-risk patient groups.

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