Case Report

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Pharmaceutical-Induced Dyskinesia: A Case Study of Thoracotomy Treated with Amantadine

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ABSTRACT

Dyskinesia, marked by involuntary and irregular movements, can result from various pharmaceutical agents. The case presented features a patient undergoing thoracotomy, experiencing dyskinesia, likely attributed to antipsychotics, antiemetics, and antibiotics, and subsequently treated with amantadine.

Introduction

The majority of movement disorders, indicative of degenerative conditions, typically exhibit a gradual and progressive course. Nevertheless, certain movement disorders may present with an abrupt onset [1]. Dyskinesia is an extrapyramidal movement disorder marked by involuntary, repetitive, and irregular movements impacting either the oral and facial regions or the limbs and trunk [2].

Numerous pharmaceutical agents have the potential to induce movement disorders as adverse reactions, with dopamine-receptor blockers (DRB), commonly employed as antipsychotics (neuroleptics) and antiemetics, being among the most prevalent culprits [1]. Metoclopramide, employed as a dopamine-2 receptor antagonist for diverse gastrointestinal issues, has the potential to induce or worsen several extrapyramidal movement disorders [3, 4]. Approximately 0.2% of individuals taking 30–40 mg of metoclopramide daily may experience extrapyramidal symptoms (EPS) [5, 6].

Neuroleptic Malignant Syndrome (NMS), characterized by a distinctive clinical syndrome of mental status change, fever, altered consciousness, rigidity, and dysautonomia, constitutes EPS and autonomic symptoms, a rare yet perilous adverse

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response to neuroleptic medications. Its occurrence has been reported in 0.2% of individuals exposed to neuroleptics, including haloperidol. Moreover, isolated instances of NMS have been documented following the administration of metoclopramide. The initiation of NMS can also be prompted by the swift withdrawal of dopamine agonists [7-11].

It is imperative to note that, in certain instances, the documented potential for antibiotics-induced neurotoxicity serves as a contributing factor to specific aspects of dyskinesia [12-14].

We present a case of dyskinesia reaction in a patient undergoing treatment for a mediastinal mass (thoracotomy) due to the use of antipsychotics, antiemetics, and antibiotics. This highlights the heightened impact of metoclopramide-induced movement disorders in specific cases, considering other potential drugs and conditions, and underscores the effectiveness of amantadine in addressing these reactions.

Case presentation

An 88-year-old woman, with a medical background of ischemic heart disease (IHD), hypertension (HTN), and chronic obstructive pulmonary disease (COPD) managed with Losartan, Salbutamol, and Seroflo® for several years, was referred to Sina Hospital on December 11, 2023. The patient presented with a Glasgow Coma Scale (GCS) score of 14, oxygen saturation (O2Sat) ranging between 83-88%, and blood pressure (BP) of 152/84 mmHg. This referral was prompted by an escalation in the severity of her dyspnea, and a mediastinal mass was detected during a CT scan. On the day of admission, the patient underwent thoracotomy surgery, during which the mass was successfully removed. Three days later, the patient required intubation due to respiratory depression. In managing the patient, Medication Management Services employed heparin at a rate of 1000 units per hour to address atrial fibrillation-related rhythm issues. Positive sepsis biomarkers prompted the administration of broad-spectrum antibiotics, including ciprofloxacin at an intravenous dosage of 400 mg as a stat dose, and this was subsequently repeated every 8 hours for several days. To manage gastrointestinal bleeding, Octreotide and pantoprazole were incorporated into the treatment plan. It should be emphasized that during drug management, the patient received haloperidol at a dosage of 2.5 mg as needed for agitation whenever necessary. Considering the patient's oral intolerance, a one-week as-needed regimen of metoclopramide as a prokinetic was initiated. Subsequently, the patient transitioned to a 10 mg metoclopramide regimen twice daily for 24 hours, followed by a dose of 10 mg metoclopramide three times a day for the next 48 hours. The onset of dyskinesia symptoms occurred when the patient was receiving metoclopramide, and even upon discontinuation of the medication, these abnormal movements persisted. Neurology and anesthesia consultations ruled out any underlying disease, confirming the presence of abnormal dyskinesia. Considering the limitations on anticholinergic administration in the intensive care unit (ICU), diphenhydramine was initially prescribed and demonstrated a positive response. However, due to its safety profile and effectiveness as a dopamine agonist, amantadine was ultimately prescribed. It is noteworthy that tetrabenazine was considered a treatment option, but its unavailability in the hospital precluded its use at that time. The patient exhibited symptom control 24 hours after initiating oral amantadine at a dosage of 100 mg twice daily, and this regimen was maintained for one week. Following this period, amantadine was gradually tapered over another 6 days until complete discontinuation, and remarkably, the dyskinesia symptoms did not reoccur post-cessation of the drug.

Discussion

Pharmaceutical agents belonging to various categories have the potential to induce Drug-Induced Movement Disorders (DIMDs). Key groups of implicated drugs encompass antidepressants, antipsychotics, antiepileptics, antimicrobials, antiarrhythmics, mood stabilizers, and gastrointestinal medications, among others [15].

The findings of the study conducted by Boyer et al. revealed an exceptionally high incidence of dystonia (94%) among young patients aged 19 to 32 who were administered haloperidol [16]. These data were consistent with several recent reports. Moleman et al. observed a heightened likelihood of dystonic reactions in males under the age of 34 treated with neuroleptics [17]. In another study by Chiles, a 64% incidence of dystonia was reported in 11 adolescents aged 13 to 18 receiving potent neuroleptics [18]. Keepers and associates documented a 45% incidence of dystonic reactions in individuals aged 20 to 29 (65% in those aged 10 to 19) [19].

The study conducted by Host et al. reported that, while infrequent, levofloxacin has been associated with rare central nervous system (CNS) toxicities, notably orofacial dyskinesia. The study suggests a vigilant monitoring approach for patients of advanced age and those with renal insufficiency who are prescribed

fluoroquinolones, aiming to promptly identify and address potential toxicities [12]. Similar case reports have been documented, highlighting various facets of fluoroquinolone-induced dyskinesia [13, 14].

Metoclopramide, renowned for its antiemetic and prokinetic properties, stands as the most widely prescribed antiemetic. Extrapyramidal reactions, constituting the most common acute side effect of metoclopramide, are reported at a frequency of 0.2%. However, this incidence can escalate significantly, reaching up to 25% in the elderly and young populations. Despite the high prescription rates in the developing world, there is a notable dearth of research on metoclopramide-induced acute dystonic reactions or extrapyramidal side effects [20]. The under-reporting of the incidence of this condition in these settings can be attributed to inadequate data collection practices and a lower frequency of case reporting. Identified risk factors for developing a metoclopramide-induced dystonic reaction include long-term use, female sex, older age, diabetes mellitus, and polypharmacy [21].

NMS is a rare and life-threatening adverse reaction to neuroleptic medications, initially described in 1960. Occurring in approximately 0.2% of patients exposed to neuroleptics, the risk is higher with potent neuroleptics like haloperidol or fluphenazine, and depot intramuscular preparations. All antipsychotics, including atypical ones, have the potential to trigger NMS, and rare cases have been reported after the use of metoclopramide, amoxapine, and lithium. The pathophysiology of NMS is believed to involve D2-receptor dysfunction in the hypothalamus and striatum, though understanding remains incomplete. NMS occurrence is unpredictable, with symptoms emerging at any point during neuroleptic treatment. Key features include rigidity, hyperthermia, reduced consciousness, and autonomic failure. Management of NMS necessitates early intervention and immediate withdrawal of the offending agent, accompanied by intensive medical care addressing fluid and metabolic imbalances. Amantadine and other dopamine agonists, while slightly less effective, may offer therapeutic benefits in managing NMS [1].

L-DOPA-induced dyskinesias (LIDs) can affect up to 40% of Parkinson's disease (PD) patients, negatively impacting their quality of life. Amantadine, available in various forms, including oral immediate-release (IR), extended-release (ER), and intravenous infusion (IV), has demonstrated substantial antidyskinetic effects in both animal PD models and randomized controlled trials (RCTs) involving PD patients. The mechanisms involve NMDA receptor blockade, influencing cortico-striatal glutamatergic–dopaminergic interactions contributing to LIDs. Additionally, amantadine may address other PD symptoms like apathy or fatigue and significantly reduce daily OFF-time. Common adverse reactions encompass constipation, cardiovascular issues, neuropsychiatric symptoms, nausea, and livedo reticularis. While corneal degeneration is rare, it remains a critical concern [22].

Conclusion

Polypharmacy stands out as a recognized risk factor for the development of dyskinesia reactions. The prompt discontinuation of the implicated agents, coupled with the potential utilization of amantadine, may contribute to the resolution of the issue.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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