

Video Abstracts

The Clinical Course of a Drug-induced Acute Dystonic Reaction in the Emergency Room

Massimo Marano^{1,2*}, Lazzaro di Biase^{1,3}, Gaetano Salomone⁴, Alessandro Di Santo¹, Annalisa Montiroli⁵ & Vincenzo Di Luzzaro¹

¹ Parkinson's Disease and Movement Disorder Center, Neurology Unit, Campus Bio-Medico University of Rome, Rome, Italy, ² Mendel Institute of Human Genetics, IRCCS Casa Sollievo della Sofferenza Hospital, Rome, Italy, ³ Nuttfield Department of Clinical Neuroscience, University of Oxford, Oxford, England, ⁴ Neurological Rehabilitation Unit, Campolongo Hospital, Campolongo, Salerno, Italy, ⁵ Sapienza University of Rome, Rome, Italy

Abstract

Background: Acute dystonic reactions following the administration of safe, reliable drugs can occur and must be promptly recognized and treated in the emergency room.

Phenomenology Shown: The entire clinical course of an acute dystonic reaction due to metoclopramide, from early motor signs to full-blown clinical symptoms and resolution.

Educational Value: Providing elements for early recognition of a drug-induced movement disorder phenomenology.

Keywords: Dystonia, dyskinesias, drug-induced movement disorders, metoclopramide, anticholinergic

Citation: Marano M, di Biase L, Salomone G, et al. The clinical course of a drug-induced acute dystonic reaction in the emergency room. Tremor Other Hyperkinet Mov. 2016; 6. doi: 10.7916/D87P8ZS1

*To whom correspondence should be addressed. E-mail: masmarano@gmail.com

Editor: Elan D. Louis, Yale University, USA

Received: October 26, 2016 **Accepted:** November 14, 2016 **Published:** December 8, 2016

Copyright: © 2016 Marano et al. This is an open-access article distributed under the terms of the Creative Commons Attribution–Noncommercial–No Derivatives License, which permits the user to copy, distribute, and transmit the work provided that the original authors and source are credited; that no commercial use is made of the work; and that the work is not altered or transformed.

Funding: None.

Financial Disclosures: Dr. Massimo Marano, Dr. Gaetano Salomone, Dr. Lazzaro di Biase, Dr. Alessandro Di Santo, Dr. Annalisa Montiroli and Prof. Vincenzo Di Luzzaro report no disclosures; The study is not industry-sponsored.

Conflict of Interest: The authors report no conflict of interest.

Ethics Statements: This study was performed in accordance with the ethical standards detailed in the Declaration of Helsinki. The authors' institutional ethics committee has approved this study and all patients have provided written informed consent. All patients that appear on video have provided written informed consent; authorization for the videotaping and for publication of the videotape was provided.

A 23-year-old female with no personal or family history of movement disorders presented to the emergency department complaining of lower facial muscle tightness and mild difficulties in breathing due to a referred sensation of “swollen neck and tongue.” Multiple consultations were performed based on suspicion of anaphylaxis and temporomandibular joint pathology, both of which were excluded by a clinical ear, nose, and throat examination. Psychogenic movement disorders were initially considered due to the outbreak of anxiety, mild grimace, and blepharospasm reported as “uncontrolled smiling,” but this hypothesis was excluded based on the natural clinical progression of painful involuntary facial twitching with forced jaw opening and deviation, torticollis, and carpal spasm with thumb adduction (Video 1). In-depth anamnesis revealed that the patient had self-medicated with oral metoclopramide 10 mg every

8 hours for 1 day because of nausea; her symptoms began 24 hours after the first dose and worsened during the next 6–8 hours. The reported intake of a dopamine-receptor-blocking-agent, negative family history, and the absence of any other associated neurological sign supported the diagnosis of drug-induced movement disorder (DIMD; i.e., metoclopramide-induced acute dystonia) involving the cranial and neck areas with spread to the upper extremities.^{1,3,4} The patient was accordingly medicated with 5 mg intravenous biperiden, and remission occurred in a few hours.³ A large number of drugs have been described as causative for acute dystonia, which is more often associated with antipsychotics or antiemetics, often after a single dose, and more frequently in young males.^{2,3} The pathogenesis has not been completely elucidated, but the blockage of striatal D2-receptors with enhanced dopamine turnover and receptor super-sensitivity have putative roles.



Video 1. The dystonic reaction from subtle onset to the full-blown presentation. In the first segment, the patient presents with involuntary grimacing, slight jaw opening dystonia and blepharospasm, and dystonic posturing of the right hand with involuntary adduction and opposition of the thumb. In the second segment, the patient lays down with a painful left torticollis, jaw opening and jaw-deviating dystonia, head movements are still possible, and left hand dystonia with thumb adduction and opposition is observed; in the last segment, the patient gradually recovers to complete resolution following biperiden injection.

Cholinergic hyperactivity due to dopamine antagonism has also been proposed. This justifies the prevalence of dystonic reactions in young patients, since compensatory mechanisms decrease with age,^{3,4} and it supports our choice to prescribe an anticholinergic drug (i.e., biperiden) instead of other available medications. Onset is generally characterized by painful dystonia preceded by generalized and sensory discomfort, anxiety, and restlessness. In the present case, subtle facial tightness and breathing difficulties were initially misleading for the emergency physicians. The diagnostic cue is the anamnestic

relationship with drug intake: 50% and 90% occur within 48 hours and 5 days, respectively.² However, in the emergency setting, patients may not spontaneously report the consumption of over-the-counter antiemetic drugs. Metoclopramide is a widely prescribed antiemetic agent that can induce the entire DIMD spectrum,^{1,2} with acute dystonic reaction or acute akathisia seen in about 6% of cases. Alternatively, the prevalence of dystonic reactions has been estimated as 2.3–60% with conventional neuroleptics, while it is 2–3% with atypical ones.³ Given the known risk of DIMD, particularly with chronic use or in young people, the Food and Drug Administration and European Medicines Agency restricted the indications for metoclopramide to short-term use (up to 12 weeks or 5 days, respectively), and to cases with sufficient evidence of efficacy (e.g., serious gastrointestinal discomfort due to organic conditions when other treatments fail).² These disorders remain grossly underestimated. Early recognition would avoid serious patient distress, possible dangerous consequences, and malpractice suits. The most common dystonic pattern involves neck and craniofacial areas, but life-threatening laryngeal dystonia and respiratory dyskinesia have also been reported.³ Anticholinergics lead to relief, and diphenhydramine and benzodiazepines could be considered although they are less effective. While discontinuation of the causative agent is recommended, prophylaxis should be considered when an antipsychotic is continued.^{3,4} Other authors propose a role for botulinum toxin for safer resolution of drug-induced stridor with laryngeal dystonia,³ although it would be more suitable in patients with a relapse risk or in the context of a chronic disorder such as tardive syndrome.

Acknowledgments

We thank the LIRH foundation ONLUS for support, Michela Marano and Dr. Francesco Tibuzzi for their help in preparing the manuscript.

References

1. Miller LG, Jankovic J. Metoclopramide-induced movement disorders. Clinical findings with a review of the literature. *Arch Intern Med.* 1989;149:2486–2492. doi: 10.1001/archinte.1989.00390110070015.
2. Pasricha PJ, Pehlivanov N, Sugumar A, Jankovic J. Drug Insight: from disturbed motility to disordered movement--a review of the clinical benefits and medicolegal risks of metoclopramide. *Nat Clin Pract Gastroenterol Hepatol.* 2006;3:138–148. doi: 10.1038/ncpgasthep0442.
3. Burkhard PR. Acute and subacute drug-induced movement disorders. *Parkinsonism Relat Disord.* 2014;20 Suppl 1:S108–S112. doi: 10.1016/S1353-8020(13)70027-0.
4. van Harten PN, Hoek HW, Kahn RS. Acute dystonia induced by drug treatment. *BMJ* 1999;319:623–626. doi: 10.1136/bmj.319.7210.623.