

ADVERSE REACTION OF COARTEM (ARTEMETHER-LUMEFANTRINE) RESULTING IN OCULOGYRIC CRISIS: A CASE REPORT

Amponsah Emmanuel .K.,¹, Anyetei-Anum A¹., Kim Soung.M¹.

¹.Department of Oral & Maxillofacial Surgery, Brong Ahafo Regional Hospital, P. O. Box 27, Sunyani, Ghana

*Corresponding Author: Dr. Dr. Emmanuel Kofi Amponsah' ampek2003@yahoo.co.uk

ABSTRACT

An oculogyric crisis is an acute dystonic reaction of the ocular muscles characterized by bilateral dystonic elevation of visual gaze lasting from seconds to hours. This reaction is most explained as an adverse reaction to drugs such as antimalarials, antiemetics, antipsychotics, antidepressants, and antiepileptics. It is important to recognize these ocular symptoms of adverse reaction to medications because, without a thorough patient history, symptoms can be confused with other diseases. Differential diagnoses can include aversive seizures, paroxysmal tonic upward gaze, and encephalopathy. In this paper, we report a case of oculogyric crisis induced by Artemether-lumefantrine (Antimalarial).

KEYWORDS: Antimalarials, Artemether-lumefantrine, Rapid Diagnostic Test, oculogyric crisis, dystonic reactions

INTRODUCTION

Artemether/lumefantrine, sold under the trade name Coartem, combines the two medications artemether and lumefantrine¹. It is used to treat malaria caused by Plasmodium falciparum since it became resistant to chloroquine¹. It is not typically used to prevent malaria¹.

Common side effects include muscle and joint pains, fever, loss of appetite, and headache¹. Serious side effects include prolongation of the QT interval on electrocardiogram (ECG)¹. While not well studied, it appears to be safe for use in pregnancy¹. In addition, the dose does not need changing in those with mild or moderate kidney or liver problems¹.

The combination came into medical use in 1992². They were both developed in China^{2,3}. It is on the World Health Organization's List of Essential Medicines⁴. It is not available as a generic medication⁵. Although the incidence of drug-induced acute dystonic reactions has been reported in other parts of the world, there have been no published cases on oculogyric crisis in Ghana. Our search in the literature during the incident of this case did not find any. This may be due to an oversight during the examination of patients who present with such symptoms or poor reporting of antimalaria medications' adverse drug reaction in endemic region of malaria; such as Ghana

Ethical issues

Written informed consent was obtained from the patient and his parents to use his photographs in this case report.

CASE REPORT

A 19-year-old male patient presented to the Oral & Maxillofacial department of Brong Ahafo Regional

Hospital in Sunyani, Ghana, with double vision and involuntary upward deviation, and inability to close both eyes. Two days prior to the presentation at our facility, he reported to a pharmacy shop with complaints of fever 37.90 Celcius, general bodily pains, and weakness. Rapid Diagnostic Test (RDT) conducted at the pharmacy was positive to plasmodium falciparum. Therefore, the client was put on antimalaria therapy (Artemether-lumefantrine) 80/480mg start and the same dosage after 8 hours for day one, the same dosage at 12 hourly twice daily for two days.

After initiating the treatment, the client started experiencing double vision and involuntary upward deviation, and inability to close both eyes (Picture. 1).



Picture. 1

At the presentation, he and his parents did not know what it was, so they were in severe distress. On neurological examination, his consciousness was clear. He had conjugate upward deviation and inability to close both eyes fully (oculogyric crisis).

Physical examination did not reveal any other dyskinetic movement. The patient could bring his eyes back to the primary position with difficulty,

but he could not sustain the effort, and the eyes resumed their upward position within seconds⁵.

On ophthalmic examination, he exhibited isocoria, with his pupils giving indirect and direct light reflexes. Ocular motility and visual acuity could not be evaluated due to the presence of an oculogyric crisis. Owing to the history and physical examination findings, a diagnosis of Coarterm-induced oculogyric crisis was made. The drug was discontinued, and the client was treated with intramuscular injection of Promethazine Hydrochloride (Phenergan) 25mg start. The symptoms of the oculogyric crisis reduced significantly one hour after the IM injection. The client was discharged home on the same day with oral Cetirizine 10mg daily for five days. He reported for a review a week later, with all the symptoms completely disappeared (Picture. 2).



Picture. 2

DISCUSSION

Acute dystonic reactions are extrapyramidal side effects due to alteration of the dopaminergic–cholinergic balance in the nigrostriatum.^{5,7} Medication-induced acute dystonia can be a side effect of treatment with antiemetics, antipsychotics, antidepressants, antiepileptics, antimalarials, and other drugs^{5,7,8}. Such drugs produce acute dystonic reactions through a nigrostriatal dopamine D2 receptor blockade, which results in excess of striatal cholinergic output^{5,6,9}. These drug-induced side effects are dose independent⁵⁻⁸. Artemether-lumefantrine, the most commonly prescribed antimalaria, may cause acute dystonic reactions at any age, even if it is used at therapeutic dosages. The incidence of these reactions secondary to Artemether-lumefantrine has not been reported much in the literature, but in old and young patients, this incidence exists in third world countries like Ghana, where malaria is endemic⁵⁻⁹. Coarterm-induced side effects are also known to appear more frequently in female patients, at high drug doses, in patients with a family history of neurological disease, in those who are treated with neuroleptics, and in patients whose family members have developed acute dystonic reactions due to Artemether-lumefantrine.^{5-7,10,11}

Acute dystonic reactions include contractions of the muscles, especially in the facial, trapezius, and dorsal levator scapulae and rhomboid muscles; opisthotonos; torticollis; dysarthria; trismus; and oculogyric crisis⁵⁻¹⁰.

An oculogyric crisis is characterized by a temporary period of frequent spasms of eye deviation, particularly upward, each spasm lasting from seconds to hours and the entire episode lasting from days to weeks⁵⁻¹². The spasm may be preceded or accompanied by disturbing emotional symptoms, including anxiety, restlessness, compulsive thinking, sensations of increased brightness, or distortions of visual background^{5,23}. Although oculogyric crisis usually occurs as a side effect of drugs, it can be seen in patients with post-encephalitic parkinsonism, brainstem encephalitis, Wilson's disease, and cystic glioma, for whom the onset of the crisis is positional^{5,23}. Versive seizures, paroxysmal tonic upward gaze, eye movement tics, and retinal disease must also be excluded from the differential diagnosis. Epilepsy can manifest as oculogyric seizures, also called versive seizures⁵. Wyllie et al. defined versive seizures as chronic or tonic head and eye deviations, unquestionably forced and involuntary, resulting in sustained unnatural positioning of the head and eyes²³. Versive seizures with upgazed deviation can simulate oculogyric crises, but they are associated with an alteration of consciousness and electroencephalogram abnormalities⁵. Paroxysmal tonic upward gaze is characterized by infantile or early childhood-onset, with episodes of sustained conjugate upward deviation of the eyes. It can be distinguished from an oculogyric crisis by the presence of neck flexion and concomitant episodic ataxia^{5,23}. Eye movement tics in children are seen between the ages of 6 and 12 years and are characterized by a stereotyped conjugate deviation of the eyes upward and outward. An oculogyric crisis is more sustained than eye movement tics²³. Differential diagnoses considered included Bilateral Bell's palsy involving the upper face, Bilateral ptosis. Based on the history and physical examination findings, a diagnosis of Artemether/lumefantrine (Coarterm)-induced oculogyric crisis was made

CONCLUSION

Although drug-induced acute dystonic reactions have been reported to be 25% in children, few cases have been published on the oculogyric crisis in general. It is, therefore, necessary for clinicians to recognize this ocular side effect in patients who presents with adverse drug reaction of antimalaria drugs. Since recognizing oculogyric crisis in these patients could help in our disease surveillance and reporting.

REFERENCES

1. Artemether and Lumefantrine. The American Society of Health-System Pharmacists. Archived from the original on 2015-12-08. Retrieved Dec 2, 2015.
2. Ravina, Enrique (2011). The evolution of drug discovery: from traditional medicines to modern drugs (1. Aufl. ed.). Weinheim: Wiley-VCH. p. 139. ISBN 9783527326693. Archived from the original on 2015-12-08.

3. Nightingale, Charles H. (2007). *Antimicrobial pharmacodynamics in theory and clinical practice* (2nd ed.). New York: Informa Healthcare. p. 380. ISBN 9781420017137. Archived from the original on 2015-12-08.
4. World Health Organization (2019). *World Health Organization model list of essential medicines: 21st list 2019*. Geneva: World Health Organization. hdl:10665/325771. WHO/MVP/EMP/IAU/2019.06. License: CC BY-NC-SA 3.0 IGO. Hamilton, Richard (2015). *Tarascon Pocket Pharmacopoeia 2015 Deluxe Lab-Coat Edition*. Jones & Bartlett Learning. p. 45. ISBN 9781284057560.
5. Oculogyric crisis in a patient taking metoclopramide Yaran Koban, Metin Ekinci, Halil Huseyin Cagatay, and Zeliha Yazar *Clin Ophthalmol*. 2014; 8: 567–569. Published online 2014 Mar 19. doi: 10.2147/OPHTH.S60041, PMID: PMC3964159, PMID: 24672222
6. Hibbs AM, Lorch SA. Metoclopramide for the treatment of gastroesophageal reflux disease in infants: a systematic review. *Pediatrics*. 2006;118(2):746–752. [PubMed] [Google Scholar]
7. Batts KF, Munter DW. Metoclopramide toxicity in an infant. *Pediatr Emerg Care*. 1998;14(1):39–41. [PubMed] [Google Scholar]
8. Carey MJ, Aitken ME. Diverse effects of antiemetics in children. *N Z Med J*. 1994;107(989):452–453. [PubMed] [Google Scholar]
9. Low LC, Goel KM. Metoclopramide poisoning in children. *Arch Dis Child*. 1980;55(4):310–312. [PMC free article] [PubMed] [Google Scholar]
10. Yis U, Ozdemir D, Duman M, Unal N. Metoclopramide induced dystonia in children: two case reports. *Eur J Emerg Med*. 2005;12(3):117–119. [PubMed] [Google Scholar]
11. Lou E, Abou-Zeid N. A case of metoclopramide-induced oculogyric crisis in a 16-year-old girl with cystic fibrosis. *South Med J*. 2006;99(11):1290–1291. [PubMed] [Google Scholar]
12. Bateman DN, Rawlins MD, Simpson JM. Extrapyramidal reactions with metoclopramide. *Br Med J (Clin Res Ed)* 1985;291(6500):930–932. [PMC free article] [PubMed] [Google Scholar]
13. Bhachech JT. Aripiprazole-induced oculogyric crisis (acute dystonia) *J Pharmacol Pharmacother*. 2012;3(3):279–281. [PMC free article] [PubMed] [Google Scholar]
14. Busari OA, Fadare J, Agboola S, Gabriel O, Elegbede O, Oladosu Y. Chloroquine-induced acute dystonic reactions after a standard therapeutic dose for uncomplicated malaria. *Sultan Qaboos Univ Med J*. 2013;13(3): E476–E478. [PMC free article] [PubMed] [Google Scholar]
15. van der Padt A, van Schaik RH, Sonneveld P. Acute dystonic reaction to metoclopramide in patients carrying homozygous cytochrome P450 2D6 genetic polymorphisms. *Neth J Med*. 2006;64(5):160–162. [PubMed] [Google Scholar]
16. Silfeler I, Arica V, Arica S, Dogan M. Development of acute dystonia in three brothers due to metoclopramide. *J Res Med Sci*. 2012;17(3):308–309. [PMC free article] [PubMed] [Google Scholar]
17. Liu GT, Carrazana EJ, Macklis JD, Mikati MA. Delayed oculogyric crises associated with striatocapsular infarction. *J Clin Neuroophthalmol*. 1991;11(3):198–201. [PubMed] [Google Scholar]
18. Lavin PJM, Donahue S. Neuro-ophthalmology: the efferent visual system. Gaze mechanisms and disorders. In: Daroff RB, Fenichel GM, Marsden CD, Bradley WG, editors. *Neurology in Clinical Practice*. 3rd ed. Boston, MA: Butterworth Publishing; 2000. pp. 699–720. [Google Scholar]
19. Onuaguluchi G. Crises in post-encephalitic parkinsonism. *Brain*. 1961;84(3):395–414. [PubMed] [Google Scholar]
20. Matsumura K, Sakuta M. Oculogyric crisis in acute herpetic brainstem encephalitis. *J Neurol Neurosurg Psychiatry*. 1987;50(3):365–366. [PMC free article] [PubMed] [Google Scholar]
21. Lee MS, Kim YD, Lyoo CH. Oculogyric crisis as an initial manifestation of Wilson's disease. *Neurology*. 1999;52(8):1714–1715. [PubMed] [Google Scholar]
22. Stechison MT. Cystic glioma with positional oculogyric crisis. *J Neurosurg*. 1989;71(6):955–957. [PubMed] [Google Scholar]
23. Wyllie E, Lüders H, Morris HH, Lesser RP, Dinner DS. The lateralizing significance of versive head and eye movements during epileptic seizures. *Neurology*. 1986;36:606–611. [PubMed] [Google Scholar]