

Contrast-provoked myasthenic crisis: A case report and review of literature

David Kar Yue Ngan, Helen Hyemin Moon

ABSTRACT

Introduction: Myasthenia gravis is a disease of the neuromuscular junctions in which antibodies target the acetylcholine receptors of the postsynaptic membranes, causing skeletal muscle weakness and fatigability. Myasthenic crisis is an acute exacerbation of these symptoms that requires non-invasive ventilatory support or intubation. Only a few case reports exist of such episodes following administration of radiographic contrast for computed tomography. **Case Report:** A patient with poorly-controlled symptoms of myasthenia gravis was administered intravenous contrast during computed tomography (CT) pulmonary angiogram. Following contrast injection, the patient became nauseated and acutely hypoxic, followed by respiratory arrest and intubation. Clinical examination and nerve conduction studies were subsequently consistent with myasthenic crisis, which resolved completely with treatment. **Conclusion:** Our review of existing literature of contrast-precipitated myasthenic crisis finds no conclusive link between contrast type and severity of reaction, but is limited by inconsistencies in reporting. Further examination is required to determine

the risk to patients with myasthenia gravis from contrast exposure.

Keywords: Computed tomography, Myasthenia gravis, Myasthenic crisis

How to cite this article

Ngan DKY, Moon HH. Contrast-provoked myasthenic crisis: A case report and review of literature. Case Rep Int 2018;7:100049Z06DN2018.

Article ID: 100049Z06DN2018

doi: 10.5348/100048Z06DN2018CR

INTRODUCTION

Myasthenia gravis is a disease of the neuromuscular junctions in which antibodies target the acetylcholine receptors of the postsynaptic membranes. The resultant reduction in available receptors leads to skeletal muscle weakness and fatigability [1]. Myasthenic crisis is an acute exacerbation of these symptoms, of which multiple precipitating agents have been described; however only a few reports [2–11] exist of crisis precipitated by intravenous radiologic contrast. We present a case of myasthenic crisis following administration of intravenous contrast in a patient with poorly controlled symptoms who had previously been exposed to contrast without incident, and review the existing literature on this topic.

CASE REPORT

A 70-year-old female patient presented to the emergency department with a one-week history of dysphagia to solids and then liquids. No infective

David Kar Yue Ngan¹, Helen Hyemin Moon²

Affiliations: ¹Medical Officer, Royal Adelaide Hospital, Central Adelaide Local Health Network, Adelaide, SA, Australia; ²Registrar, Department of Radiology, Royal Adelaide Hospital, Central Adelaide Local Health Network, Adelaide, SA, Australia.

Corresponding Author: Dr. David Kar Yue Ngan, Royal Adelaide Hospital, Port Road, Adelaide, SA, Australia 5000; Email: David.ngan@sa.gov.au

Received: 28 April 2018

Accepted: 01 June 2018

Published: 14 July 2018

symptoms, limb weakness, ptosis, diplopia or other neurological symptoms were present at the time. She had been diagnosed with myasthenia gravis about eight months prior and was positive for acetylcholine receptor antibodies. This was her third such presentation that year; on two prior occasions she had been investigated for dysphagia attributed to oral candidiasis. She had also been treated for deep vein thrombosis and subsequent pulmonary embolism five months ago.

On the day of admission, she became tachycardic and anxious and complained of central chest pain impeding her breathing; serum troponin measurements were not elevated and no intervention was undertaken. Over the following two days, three Medical Emergency Team (MET) calls were made as per hospital protocol for tachycardia and hypertension. A CT pulmonary angiogram (CTPA) was thus requested over concerns of recurrence of pulmonary embolism. 70 ml of Ultravist® 370 (iopromide, Bayer HealthCare Pharmaceuticals, Germany) contrast solution was administered and the CTPA was completed with findings of bilateral lower lobe consolidation but no pulmonary emboli. Approximately, seven minutes following contrast administration, the patient became nauseated and acutely hypoxic, with saturations of 90% on six litres of oxygen by mask. About four minutes later, she became drowsy, and a minute later developed respiratory arrest and was intubated on the CT table. Haemodynamic stability was maintained throughout with pulse rate of 115 beats per minute and blood pressure of 160/70 mmHg. A further CT head did not find acute intracranial abnormality. No rashes or other skin changes were noted.

Myasthenic exacerbation was suspected, and subsequent assessment by the neurology team in the intensive care unit found mild bilateral fatigable ptosis with full preservation of extraocular movements, as well as mild to moderate neck flexion weakness. No limb weakness was present. Nerve conduction studies were performed and induced an approximate 20% early decrement in compound muscle action potential, consistent with myasthenia crisis. Her serum azathioprine level was found to be subtherapeutic and she was instead prescribed mycophenolate mofetil with improvement. She remained intubated for six days. Her ptosis resolved completely during admission, and she was discharged with outpatient follow-up.

DISCUSSION

Myasthenia gravis is a disease characterised by weakness of the skeletal muscles due to antibody-mediated antagonism of receptors or structures in the postsynaptic membranes of neuromuscular junctions. The antibodies may target acetylcholine receptors (AChR), Muscle-Specific Kinase (MuSK) or lipoprotein receptor-related peptide 4 (LRP4) [12]. AChR antibodies cause damage to the postsynaptic membrane by activating complement

and causing formation of membrane attack complexes [1], while MuSK and LRP4 antibodies are thought to interfere with creation of the agrin-LRP4-MuSK complex that is required for MuSK signaling. These effects manifest as a failure to maintain muscular contracture for a prolonged period. Acetylcholinesterase inhibitors and immunosuppressants are used to treat the condition. Acetylcholinesterase inhibitors ameliorate the symptoms of myasthenia gravis, while immunosuppressants are used with intent to suppress underlying pathophysiological mechanisms.

The ocular muscles are most commonly affected, with around 15% of patients showing weakness restricted to this group [12]. The weakness may also be generalised to affect bulbar and proximal limb muscles. This generalised weakness can occur in a sufficiently severe state to cause respiratory compromise, either due to bulbar dysfunction or ventilatory dysfunction; when this requires non-invasive ventilation or intubation this is termed a myasthenic crisis [13].

Multiple precipitants are known to trigger this situation and can be roughly grouped into stressors such as surgery and infections, and into medications [14]. Included in precipitating medications are various antibiotics, antiepileptic medications, beta-adrenergic antagonists and calcium-channel antagonists [14].

Radiographic contrast media has also been reported to cause crisis [14]. The mechanism by which this occurs is unknown. Precipitation of crisis by intravenous contrast has been reported in various case reports, with literature search of English publications finding seven such reported cases following a strict definition of myasthenic crisis requiring non-invasive ventilation or intubation [2, 3, 6, 7, 9–11], with one additional case reporting crisis following gadolinium injection [8]. A further four case reports describe various episodes of acute symptom exacerbation following contrast injection, but not to the extent that ventilatory support was required [4, 5, 8, 15]. These reports are summarized in Table 1. It should be noted that both ionic and non-ionic agents have been reported in association with crisis, and that severity requiring intubation is not limited to either group. All agents except gadolinium are iodinated, as is standard in intravenous radiographic contrast used in computed tomography.

There have been additionally two retrospective studies examining the association between symptom exacerbation and contrast injection. Mehrizi et al. conducted a study to determine safety of intravenous contrast in patients with myasthenia gravis [16]. The authors retrospectively reviewed 432 patient reports over 11 years examining patients with myasthenia gravis documented in the radiology request who underwent either CT or MRI. Exclusion criteria were patients with only suspected myasthenia gravis, repeat investigations on the same patient, CT-guided biopsies and CT 2 or 3D reconstruction studies. The contrasts used for CT were Isovue® 370 (iopamidol, Bracco S.p.A, Italy) and

Table 1: Reported cases of contrast-provoked myasthenia gravis symptom exacerbation comparing contrast agent, effects and intervention

Author, Title, Year	Cases	Scan type	Agent, type	Reported effects, intervention
Canal et al. [2], Myasthenic crisis precipitated by iohalamic acid, 1983	1	CT mediastinum	40 ml iohalamic acid, ionic	Dyspnoea Cyanosis Divergent strabismus Palpebral ptosis Aphonia "Assisted respiration" Resolution after 2 hours
Chagnac et al. [3], Myasthenic crisis after intravenous administration of iodinated contrast agent, 1985	2	CT chest	Meglumine diatrizoate, ionic	Laryngospasm Apnoea Intubation Bilateral ptosis Weakness of all limbs
		CT brain	Meglumine diatrizoate, ionic	Apnoea "Mechanical ventilation" Weakness of all limbs Bilateral ptosis Diplopia Respirator
Anzola et al. [4], Myasthenic crisis during intravenous iodinated contrast medium injection, 1986	1	CT chest (mediastinum)	60 ml iopamidol (Iopamiro®, Bracco S.p.A., Italy), non-ionic	Respiratory distress "Fast breathing" Slurred speech Spontaneous divergent strabismus Weakness of both arms Resolution after three minutes No intubation or non-invasive ventilation
Van den Bergh et al. [5], Intravascular contrast media and neuromuscular junction disorders, 1986	1	Mediastinal and abdominal CT	Meglumine diatrizoate 30% (Reno-M-DIP®; Bristol-Myers Squibb, United States), ionic	Eaton-Lambert myasthenic syndrome Weakness lasting 2 hours Dyspnoea No intubation
Bonmarchand et al. [6], Myasthenic crisis following the injection of an iodinated contrast medium, 1987	1	Thoracic CT	30.8g sodium iohalamate, 61.6g meglumineiothalamate (Telebrix 38®, Liebel-Flarsheim Canada Inc., Canada), ionic	Two scans performed, reported reaction occurring with second scan Polypnoea "Impossibility of speech" Deglutition Hypersalivation Diffuse muscular weakness Intubation
Eliashiv et al. [7], Aggravation of Human and Experimental Myasthenia-Gravis by Contrast-Media, 1990	1	CT of mediastinum	180ml sodium diatrizoate and melamine diatrizoate (Urografin®, Bayer AG, Germany), ionic	Apnoea Paralysis
Nordenbo et al. [8], Acute deterioration of myasthenia gravis after intravenous administration of gadolinium-DTPA, 1992	1	MRI brain	Gadolinium DTPA (Magnevist®, Schering AG, Germany)	Bilateral ptosis Severe ophthalmoplegia Dysarthria Difficulties in chewing and swallowing Proximal weakness of upper and lower extremities Dyspnoea No intubation or non-invasive ventilation
Rocha Mde et al. [9], Exacerbation of myasthenia gravis by contrast media, 1994	2	Not stated	100ml iohalamic acid, ionic	Dyspnoea Cyanosis Aphonia Intubation

		Not stated	150ml iothalamic acid, ionic	Ptosis Aphonia Dyspnoea No intubation
Bonanni et al[10], Myasthenia Gravis following Low-Osmolality Iodinated Contrast Media, 2014	1	Total body CT	200ml low-osmolality iodinate contrast (Iohexol, concentration 300mgI/ml), non-ionic	“Acute respiratory failure requiring orotracheal intubation and mechanical ventilation” Post-extubation: Dysphagia Dysarthria Hypophonia Proximal muscle hyposthenia
Khandelwal et al[11], Low - osmolality contrast agents - A risk for myasthenics, 2016	1	CT thorax	50ml iodinated contrast agent (Ultravist® 370, Bayer HealthCare Pharmaceuticals, Germany), non-ionic	Acute respiratory distress Stridor Restlessness Tachycardia Desaturation Intubation

Abbreviations: DTPA: diethylenetriaminepentaacetic acid

Omnipaque™ 300 (iohexol, GE Healthcare, United States), both non-ionic contrasts, and the contrasts used for MRI were ProHance® (gadoteridol, Bracco S.p.A, Italy) MultiHance® (gadobenedimeglumine, Bracco S.p.A, Italy). The authors found no reports of increasing myasthenic weakness, and only one reported adverse reaction of nausea and vomiting post CT with contrast. No adverse reactions were reported following MRI. Mehrizi et al. concluded that there was no immediate increase of risk of myasthenic weakness examination following injection of intravenous contrast [16]. In contrast, Somashekar et al. conducted a retrospective cohort study examining symptom progression rather than crisis association in patients with myasthenia gravis with the use of low-osmolality iodinated intravenous contrast [17]. Patients included were both paediatric and adult patients with myasthenia gravis who underwent CT at a single centre. Only the first CT of each patient was studied. A total of 112 cases of contrast-enhanced CTs and 155 unenhanced CTs were studied after exclusion criteria were applied. The contrasts used were iohexol, iopamidol and iopromide. The authors found that within 45 days of the scan, 5.8% of patients who had undergone an unenhanced scan and 12.5% of patients who had received contrast experienced a symptom progression. Somashekar et al also found patients exposed to contrast also experienced progression sooner than those without contrast, and that symptom exacerbation occurred more frequently in the first day following CT scan in patients given contrast than those who did not receive contrast [17].

CONCLUSION

Evidence of the ability of contrast to provoke a myasthenic crisis is largely confined to case reports, and

studies have produced conflicting results with limitations of poor documentation. In addition, the mechanism by which this may occur is unknown. Further investigation is required to elucidate this association, and to assess the risk of administering contrast to patients with myasthenia gravis.

REFERENCES

1. Phillips WD, Vincent A. Pathogenesis of myasthenia gravis: Update on disease types, models, and mechanisms. *F1000Res* 2016 Jun 27;5.
2. Canal N, Franceschi M. Myasthenic crisis precipitated by iothalamic acid. *Lancet* 1983 Jun 4;1(8336):1288.
3. Chagnac Y, Hadani M, Goldhammer Y. Myasthenic crisis after intravenous administration of iodinated contrast agent. *Neurology* 1985 Aug;35(8):1219–20.
4. Anzola GP, Capra R, Magoni M, Vignolo LA. Myasthenic crisis during intravenous iodinated contrast medium injection. *Ital J Neurol Sci* 1986 Apr;7(2):273.
5. Van den Bergh P, Kelly JJ Jr, Carter B, Munsat TL. Intravascular contrast media and neuromuscular junction disorders. *Ann Neurol* 1986 Feb;19(2):206–7.
6. Bonmarchand G, Weiss P, Clavier E, Lerebours-Pigeonniere G, Massari P, Leroy J. Myasthenic crisis following the injection of an iodinated contrast medium. *Intensive Care Med* 1987;13(5):365.
7. Eliashiv S, Wirguin I, Brenner T, Argov Z. Aggravation of human and experimental myasthenia gravis by contrast media. *Neurology* 1990 Oct;40(10):1623–5.
8. Nordenbo AM, Somnier FE. Acute deterioration of myasthenia gravis after intravenous administration of gadolinium-DTPA. *Lancet* 1992 Nov 7;340(8828):1168.
9. Rocha Mde S, Bacheschi LA. Exacerbation of myasthenia gravis by contrast media. *Am J Roentgenol* 1994 Apr;162(4):997.

10. Bonanni L, Dalla Vestra M, Zancanaro A, Presotto F. Myasthenia gravis following low-osmolality iodinated contrast media. *Case Rep Radiol* 2014;2014:963461.
11. Khandelwal A, Shamim R, Supriya. Low - osmolality contrast agents - A risk for myasthenics. *Neurol India* 2016 May-Jun;64(3):558-9.
12. Gilhus NE. Myasthenia gravis. *N Engl J Med* 2016 Dec 29;375(26):2570-81.
13. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology* 2016 Jul 26;87(4):419-25.
14. Wendell LC, Levine JM. Myasthenic crisis. *Neurohospitalist* 2011 Jan;1(1):16-22.
15. Frank JH, Cooper GW, Black WC, Phillips LH 2nd. Iodinated contrast agents in myasthenia gravis. *Neurology* 1987 Aug;37(8):1400-2.
16. Mehrizi M, Pascuzzi RM. Complications of radiologic contrast in patients with myasthenia gravis. *Muscle Nerve* 2014 Sep;50(3):443-4.
17. Somashekar DK, Davenport MS, Cohan RH, Dillman JR, Ellis JH. Effect of intravenous low-osmolality iodinated contrast media on patients with myasthenia gravis. *Radiology* 2013 Jun;267(3):727-34.

Author Contributions

David Kar Yue Ngan – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Helen Hyemin Moon – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None

Consent Statement

The protocol of the hospital does not require consent for case studies; therefore consent was not obtained for this report.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© 2018 David Kar Yue Ngan et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

Access full text article on other devices



Access PDF of article on other devices

