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

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
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

<table>
<thead>
<tr>
<th>Author, Title, Year</th>
<th>Cases</th>
<th>Scan type</th>
<th>Agent, type</th>
<th>Reported effects, intervention</th>
</tr>
</thead>
</table>
| Canal et al. [2], Myasthenic crisis precipitated by iotthalamic acid, 1983 | 1 | CT mediastinum | 40 ml iotthalamic 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 iothalamate, 61.6g meglumineiothalamate (Telebrix 38®, Liebel-Flarsheim Canada Inc., Canada), ionic | Two scans performed, reported reaction occurring with second scan  
Polyynoia  
“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 iotthalamic acid, ionic | Dyspnoea  
Cyanosis  
Aphonia  
Intubation |
Omipaque™ 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® (gadobenatedimeglumine, 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


Abbreviations: DTPA: diethylenetriaminepentaacetic acid

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

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Conflict of Interest
Authors declare no conflict of interest.

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