

Pearls & Oy-sters: Reversible Postpartum Pseudocoma State Associated With Magnesium Therapy

A Report of 2 Cases

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Abstract

Magnesium (Mg) competes with calcium in normal synaptic transmission, inhibiting neurotransmitter release. As a drug, it is usually given as a treatment for eclampsia and preeclampsia. Two eclamptic pregnant women treated with Mg developed a pseudocoma state immediately after emergency Caesarian section. The clinical presentation was flaccid quadriparesis, areflexia, absent respiratory effort and vestibular-ocular reflexes, but with preserved pupillary responses. Decremental responses on repetitive nerve stimulation were found in both women. Recovery was obtained after cessation of Mg. The persistence of pupillary reflexes in the absence of reflexes involving striated muscles was an important clinical clue, indicating neuromuscular junction dysfunction.

Pearls

- Neuromuscular junction (NMJ) dysfunction should be suspected when a patient treated with magnesium (Mg) develops flaccid paralysis with ophthalmoplegia.
- Pseudocoma due to Mg is usually due to overdose.

Oy-sters

- Mg therapy, even at therapeutic doses, can result in a severe pseudocomatose state in people with preexisting NMJ dysfunction.
- When assessing brainstem function in the context of Mg therapy, special attention must be given to assessing pupillary responses; their presence despite the absence of vestibulo-ocular reflexes is an important clinical clue, suggesting NMJ dysfunction.

Magnesium (Mg) competes with calcium in normal synaptic transmission, inhibiting neurotransmitter release.¹ As a drug, it is usually given as a treatment for eclampsia and preeclampsia.² We describe 2 women treated with Mg who developed a pseudocoma state immediately after emergency Caesarian section (CS).

Case Reports

Case 1

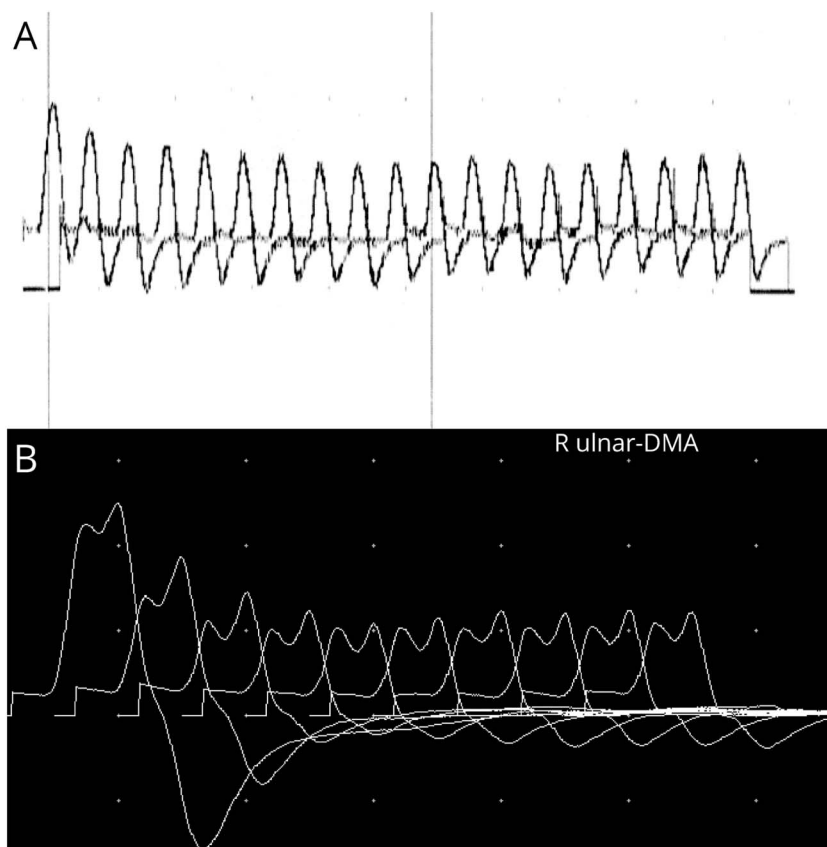
A 34-year-old woman in her first pregnancy presented for delivery at term with hypertension and proteinuria, suggesting preeclampsia. She was given IV Mg and underwent emergency CS. Postoperative course was complicated by hemorrhage and hypovolemic shock, requiring surgical hemostasis and blood transfusion. Immediately after the second surgery, she was

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Decremental response of 22% in patient 1 (A) and 48% in patient 2 (B) on repetitive nerve stimulation (RNS) during symptomatic weakness. RNS was performed in patient 1 after 1 dose of calcium gluconate and in patient 2 after resolution of magnesium toxicity, but before initiating treatment for myasthenia gravis. Testing was performed at 3 Hz in both cases, and first and fourth responses were compared with obtained percentage of decrement.

found to be unresponsive with absent respiratory effort. The clinical suspicion was of severe hypoxic-ischemic encephalopathy, and a neurologic consultation was requested.

Examination revealed a Glasgow Coma Scale of 3 with absent vestibulo-ocular reflexes (VOR) and flaccid paralysis with absent tendon reflexes. Surprisingly, pupillary responses to light were present. The anesthesiologist reported absent respiratory effort and was unable to evoke a muscle twitch using a peripheral nerve stimulator. At this point, it was noted that her Mg infusion had accidentally been continued throughout the procedure—having been mistaken for saline—and had been given at a rapid rate during the hypovolemic state, resulting in overdose.

Mg was stopped and IV calcium gluconate was administered. Motor responses returned within 15 minutes, and she fully recovered within 24 hours. A bedside repetitive nerve stimulation (RNS) test performed in intensive care unit after the first calcium dose showed a decremental response at 3 Hz (Figure, A).

She later reported being fully conscious throughout the initial evaluation, even reporting that she had overheard discussion of posthumous organ donation. Unfortunately, serum Mg levels were not measured during the period of toxicity.

Case 2

A 39-year-old woman in the 36th week of her ninth pregnancy presented with a loss of consciousness. One month before admission, she complained of general weakness and dysphagia; however, neurologic examination was reported as normal. On the day of admission, she was found unresponsive and cyanotic. She received emergency intubation in the field and was transported to the emergency department. On arrival, her blood pressure was 170/68. She had proteinuria with impaired renal and hepatic function. A presumptive diagnosis of seizures as a manifestation of eclampsia was made, and she underwent emergency CS. IV Mg was given perioperatively and continued in the recovery room.

Eighteen hours postsurgery, she was still unresponsive with no respiratory effort. Examination revealed ophthalmoplegia with absent VOR and corneal reflexes, and a flaccid quadriplegia with areflexia and absent plantar responses. However, pupils were round, mid-sized, and responsive to light—a finding which reminded one of the authors of case 1. As such, NMJ dysfunction due to Mg was suspected, and the Mg infusion was stopped. Nevertheless, she was sent for brain MRI, which was normal.

Mg levels at the time of Mg infusion cessation was 4.1 mmol/L. An hour later, voluntary eye movements returned. Over the

Table Pupillary Responses Previously Reported at a Range of Serum Magnesium Levels

Peak serum magnesium levels	Pupillary response	Somatic muscles
1.96–3.08 mmol/L (4.7–7.4 mg/dL) ⁵	Present (normal or slightly reduced, average reduction from 1.1 to 0.5 mm ³)	Presumable normal but not mentioned explicitly (therapeutic dose)
4.1 mmol/L (case 2 presented here)	Present (magnitude not evaluated)	Complete paralysis including absent brainstem reflexes ^b
5.73 mmol/L ²	Present (magnitude not evaluated)	Failure to wake up, no explicit mention of somatic evaluation
9.5 mmol/L ⁶	Present, estimated as reduction from 5 to 3 mm	Complete paralysis including absent brainstem reflexes
9.85 mmol/L ⁴	Absent, no response—pupils fixed and dilated (6 mm)	Complete paralysis including absent brainstem reflexes

^a This is the only study where the response was measured by neuro-ophthalmologists. The others are bedside evaluations by neurologists.

^b Combined effect of Mg with myasthenia gravis (case 2 presented above).

next few days, she regained limb movement but remained extremely weak. The RNS test performed at 3 Hz demonstrated a decremental response (Figure, B), and elevated serum anti-acetylcholine receptor antibodies were found. She made a full recovery after treatment for MG with plasmapheresis, immunosuppressive treatment, and thymectomy.

Discussion

These 2 cases of NMJ dysfunction associated with peripartum Mg treatment are strikingly similar. In both cases, the presentation was of complete quadriplegia, respiratory muscle paralysis with ophthalmoplegia, but with preserved pupillary reflexes. The first woman had been erroneously given Mg at a dose expected to cause toxicity, presumably resulting in pure presynaptic failure, in the absence of additional postsynaptic dysfunction. By contrast, the second woman—who received Mg at therapeutic levels—developed complete NMJ block because of combined presynaptic and postsynaptic processes, due to Mg and myasthenia gravis, respectively. This case demonstrates that undiagnosed MG may become unmasked because of Mg therapy, in the form of pseudocoma.

In both cases, the pupillary responses suggested a peripheral etiology rather than brainstem dysfunction. A pseudocoma state caused by severe hypermagnesemia has been reported before, with pupillary reflexes reported variably as present,^{2,5} sluggish,^{5,6} or completely absent⁴ (Table). The only case reported with a complete loss of the pupillary reflex was with Mg levels as high as 9.85 mmol/L, approximately 2.5 times higher than the target level in eclampsia treatment⁴; this

suggests that parasympathetic ACh release is susceptible, but less sensitive to high Mg levels when compared with somatic motor terminals. It is of interest that pupillary responses are often lost in other presynaptic NMJ disorders, such as botulism⁷ and Lambert-Eaton myasthenic syndrome.⁸ In case 2, the preserved pupillary responses were to be expected, given that Mg was given at therapeutic doses, and the additional effect of the ACh-receptor antibodies is limited to skeletal muscle.

NMJ dysfunction should be suspected in peripartum women treated with Mg, who develop flaccid paralysis mimicking coma. Although extremely high Mg levels may abolish pupillary responses, their presence, even if somewhat reduced, in the absence of VOR, is an important clinical clue.

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Continued

Appendix (continued)

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