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Gadopentetate-Induced Status Epilepticus

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Gadopentetate dimeglumine (gadolinium) is the most commonly used magnetic resonance imaging contrast medium. This medium has an excellent safety record, although it has been associated with occasional serious adverse events, including seizures. We present the first reported case of gadopentetate-induced status epilepticus, and discuss some of the possible risk factors for gadopentetate-associated reactions. **Key Words:** Adverse events—Contrast—Gadopentetate—Magnetic resonance imaging—Seizure.

The paramagnetic contrast agent gadopentetate dimeglumine (gadolinium) (Gd) was approved for use in cranial and spinal magnetic resonance imaging (MRI) in 1988 (1). It has an excellent safety profile and can be utilized in renally impaired patients (1,2) and pediatric patients (1,3). The magnitude of adverse events (AEs) after intravenous administration of Gd is considered to be on the order of 1–2% and the incidence of Gd-induced seizures is even lower (1). Because of this low complication rate, there is a tendency to become complacent in its use. We present a case where a patient receiving intravenous Gd went into status epilepticus, a potentially life-threatening situation.

Case Report

This 35-year-old man presented to the emergency room (ER) with a 5-day history of excruciating back pain radiating posteriorly down his left leg in the L5 distribution. On examination there was weakness in the left foot dorsiflexion and extensor hallucis longus, and decreased sensation in the L5 dermatomal distribution. He was unable to walk because of the severe discomfort. Reflexes and rectal tone were normal.

The patient's past medical history was significant for generalized seizures during a hospitalization for a closed head injury sustained during a fall from a three-story window 8 years previously. He had received phenytoin therapy (Dilantin) for 6 months and had been seizure free for 7.5 years.

The patient's surgical history was significant for a previous L4-5 laminotomy and discectomy performed at another institution 1 year prior to admission. The patient reported an allergic reaction to intravenous iodinated contrast that was given at the time of that hospitalization. The reaction was characterized by respiratory arrest requiring ventilatory support. He also reported developing a rash after Gd administration and was given diphenhydramine hydrochloride (Benadryl) for relief of the symptoms. After discharge, he did well and was relatively pain free until the recent exacerbation.

The patient was admitted from the ER and an MRI was obtained. Because of technical difficulties, a noncontrast examination was performed

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and, based on radiographic findings and clinical examination, the patient underwent L4–5 re-exploration surgery. A large extruded fragment was found and removed.

There was immediate postoperative relief of pain and improvement of the left-sided foot drop. However, 2 days later, the patient experienced lower back pain radiating into his right hip with ipsilateral hip flexor weakness. Plain radiographs of the hip and lumbosacral spine were unremarkable. The pain persisted despite bed rest.

An MRI with and without intravenous Gd was attempted to exclude recurrent disk herniation. The patient received the standard dose of Gd at our institution (0.1 mmol/kg infused at approximately 10 ml/min). Within 30 s of receiving Gd intravenously, his O_2 saturation level decreased to 90% and he became unresponsive; the study was aborted.

The patient had a blood pressure of 180/90 mm Hg and his pulse was 90/min. He remained unresponsive, and was gurgling and foaming at the mouth. His respirations were irregular and deep. The close temporal proximity of this event to Gd administration suggested an allergic phenomenon. His examination was consistent with a respiratory arrest or a postictal condition.

Resuscitative measures were initiated: 50% O_2 via face mask and intravenous diphenhydramine hydrochloride. The patient's respirations normalized and he became responsive to noxious stimuli. Nevertheless, within 10 min he again became unresponsive; right-sided tonic-clonic movements were observed, and his O_2 saturation level dropped. This seizure lasted approximately 2 min. Four minutes after termination of the second seizure, the patient suffered another generalized tonic-clonic seizure of 1-min duration. He did not regain consciousness between the seizures.

Because the MRI facility did not have either lorazepam (Ativan) or diazepam (Valium) available, the patient was returned to the ER for treatment. During transport he had a fourth seizure, and upon arrival in the ER, a fifth one. Seizures 4 and 5 were spaced approximately 10 min apart and each lasted approximately 2 min. Between seizures, the patient remained in a postictal state.

Intravenous lorazepam (4 mg) and a loading dose of phenytoin (13 mg/kg) were administered and no further seizures were noted. Cranial computed tomography (CT), performed once the patient was stable, was normal.

The patient was transferred to a monitored bed where he was observed and continued to receive phenytoin. Laboratory tests, including magnesium, calcium, sodium, and glucose, were within normal limits. He remained neurologically intact and seizure free during the remainder of his hospitalization. He was discharged with satisfactory resolution of his back pain and motor function on a maintenance dose of phenytoin.

Discussion

Gadopentetate was first described as a possible contrast agent for MRI in 1984 (4). Since its approval in 1988, Gd has proven remarkably safe and effective. In the large European pre- and post-marketing studies (phase IIIb–IV) prior to its approval, the incidence of AEs was documented to be only 1–2%. Post-marketing voluntary surveillance of 2,000,000 intravenous administrations of Gd reported only 672 AEs (1). Other studies cite AE rates of 5–21%, but with only 5–50% of those thought to be highly probable/probably related to Gd administration (5–9). In addition, studies with normal saline controls document no significant difference in AE rates (6,8,10). Adverse events, in order of frequency, are headache, injection site coldness, and nausea (1,5,6). There have been rare cases of true anaphylactic reactions, estimated at a frequency of 1/200,000 doses (8,11,12). Clinically significant changes in vital signs, hemodynamics, electrocardiogram, or electroencephalogram are not associated with Gd administration (6,13). Higher doses of Gd (to three times the standard amount) (14) and rapid infusion rates to four times recommended (1,15) have been shown to be safe.

Seizures are a serious but uncommon complication of Gd administration (1,6,7,16). The estimated incidence of Gd-induced seizures is 1/1,000 and was believed to be secondary to anxiety and hyperventilation (17). Most cases of seizures after Gd administration were thought to be unrelated to the medication. Almost all seizures occurred in patients at risk. In one report, all 4 patients had intracranial tumors (1); other patients had a history of chronic seizures while receiving anticonvulsants (6); 1 patient had his anticonvulsant medications abruptly discontinued (7).

To our knowledge, there is no previous report of status epilepticus after Gd administration and only one report of a patient suffering a generalized tonic-clonic seizure after receiving intravenous Gd. That 14-year-old boy had a negative brain MRI, no history of seizures or contrast allergies, and a nor-

mal postevent electroencephalogram (16). On the other hand, our patient had a past history of a post-traumatic seizure. In addition, he had a history of allergy to ionic CT contrast. It has been observed that the number of AEs is increased by a factor of 3.7 in patients with known allergies (1).

Generalized convulsive status epilepticus in the adult can be defined as continuous clinical and/or electrical activity lasting for >30 min, or recurrent generalized tonic-clonic seizures without full recovery of consciousness over 30 min (18). By the latter definition, our patient suffered a Gd-induced status epilepticus emergency. The mortality rate of untreated status epilepticus is approximately 10% (19).

It is easy to become complacent when using Gd enhancement because of its exemplary safety record. However, vigilance is required and seizures should always be considered as a possible complication, especially in patients with a history of past seizures and/or contrast allergy. In the case of status epilepticus, the complication may involve a life-threatening emergency. We recommend that anticonvulsants be available at all MRI facilities for just such events.

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