



INADVERTENT INTRAOPERATIVE MYELOGRAPHY WITH HYPAQUE: CASE REPORT AND DISCUSSION

James A. Killeffer, M.D., and Howard H. Kaufman, M.D.

Department of Neurosurgery, West Virginia University School of Medicine, Morgantown, West Virginia

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BACKGROUND

Myelography is routinely performed safely using non-ionic water-soluble radiographic contrast media. However, inadvertent introduction of ionic contrast media into the thecal space can result in a syndrome of spasms and convulsions, which can lead to death if not recognized and dealt with in a timely manner.

METHODS

We report a case of inadvertent use of the ionic diatrizoate meglumine, an ionic contrast agent, instead of a non-ionic contrast agent during intraoperative myelography.

RESULTS

The patient developed a stereotypical syndrome of ascending myoclonic spasms, resulting in rhabdomyolysis. Treatment included elevation of the head, removal of cerebrospinal fluid, administration of anticonvulsants, diuresis and sedation, and neuromuscular blockade. The patient recovered well, and there were no long-term sequelae.

CONCLUSIONS

Intrathecal introduction of ionic contrast media and the resultant syndrome must be recognized promptly and treated with aggressive medical management to address rhabdomyolysis and seizures. Ionic contrast media should be stored and marked in such a way as to avoid inadvertent use in myelography. © 1997 by Elsevier Science Inc.

KEY WORDS

Hypaque, myelography, rhabdomyolysis, ionic contrast media.

Many radiographic contrast agents have significant neurotoxicity and therefore should not be introduced into the thecal sac. We report a case in which there was inadvertent introduction of an

ionic contrast medium for intraoperative myelography. Recognition and appropriate management of such an event are essential to avoiding a catastrophe.

Radiographic contrast agents that have been used intrathecally include oil-based compounds, water-soluble ionic compounds, and water-soluble nonionic compounds. Oil-based compounds, such as Pantopaque (iopendylate), were the agent of choice for many years; but lack of fine imaging detail, due to their cohesiveness and the need for removal because of their propensity to cause arachnoiditis, make these agents suboptimal [6,10,11,13]. Water-soluble ionic media, such as Conray (iothalamate meglumine) and Abrodil (methiodal sodium), are soluble in cerebrospinal fluid (CSF) and are metabolized from the thecal space. Their propensity to cause spasms and convulsions when introduced intrathecally, however, make them unsuitable for such applications [1,4,8,9,21].

Over the last 2 decades, nonionic water-soluble contrast agents have been developed and are now favored for myelography. The two agents of choice are metrizamide and iohexol. Both have high miscibility with spinal fluid, are metabolized and excreted, and have significantly less neurotoxicity than the ionic water-soluble agents [7].

Ionic agents continue to be stocked by hospitals for angiographic and urographic procedures. The ionic contrast media are clear, colorless solutions, and impossible to distinguish visually from non-ionic media in solution. Several case reports document inadvertent introduction of ionic water-soluble contrast media into the thecal space, with significant morbidity and mortality. Awareness of the possibility of confusing these agents and of the possibility of substitution of ionic contrast media for nonionic compounds is essential to avoid this problem. In addition, physicians involved in my-

Address reprint requests to: James Killeffer, M.D., Department of Neurosurgery, West Virginia School of Medicine, Morgantown, West Virginia 26506-9183.

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elography should be aware of, and be prepared to deal with, the deleterious effects of intrathecal administration of ionic contrast media, if they occur.

We report and discuss a case of the use of Hypaque (diatrizoate meglumine, 60%), an ionic contrast medium, during intraoperative myelography. At least seven other cases of administration of a similar intrathecal dose of Hypaque have resulted in fatal outcomes. Our case demonstrates that prompt recognition and appropriate management of inadvertent intrathecal administration of ionic water-soluble contrast may prevent a fatal outcome.

CASE REPORT

A 65-year-old man presented with new onset of leg pain and weakness. Iohexol myelography demonstrated complete block of contrast flow at L3-L4, and a hemilaminectomy with removal of a large disc fragment was performed. Because of the extent of the lesion on the preoperative study, intraoperative myelography was performed to confirm complete decompression. Ten mL of Hypaque was inadvertently substituted for iohexol, due to a mental lapse on the part of the surgeon and a lack of secondary safety checks. The error was not recognized intraoperatively. Immediately postoperatively the patient was awake, alert, and recovering normally.

Three hours later, he began having painful myoclonic spasms in his lower extremities, occurring approximately every 90 seconds. The spasms became gradually more frequent over the next hour and ascended to involve the trunk, upper extremities, and face. The patient became obtunded and was intubated. He was noted to be hyperthermic (T 39.0 C), and the serum creatinine phosphokinase was elevated at 17,000 IU. The operative record was reviewed, and the inadvertent administration of Hypaque was recognized.

The head of the bed was immediately elevated, and 20 mL of spinal fluid were removed via lumbar puncture. Over the next 3 days, the patient was kept intubated with continuous neuromuscular blockade and benzodiazepine sedation. Severe rhabdomyolysis, with serum creatinine kinase (CK) values consistently greater than 10,000 IU and urinalysis demonstrating the presence of urine myoglobin, was evident on the first 3 postoperative days. To maintain adequate renal perfusion and mitigate the renotoxic effects associated with rhabdomyolysis, crystalloid was administered to maintain a central venous pressure between 12 and 15 cm H₂O. Intravenous mannitol and Lasix were used to sustain

high urine output, and intravenous sodium bicarbonate was used to maintain high urine pH.

Serial CK values indicated that the rhabdomyolysis began to subside 3 days after surgery and resolved 2 days later. Renal function, as indicated by serial blood urea nitrogen and creatinine analysis, remained normal. Phenytoin was given for 3 days, and periodic electroencephalographic monitoring revealed no evidence of seizure activity. On postoperative day 3, the neuromuscular blockade and benzodiazepines were withdrawn, and the patient was extubated. By postoperative day 5, the patient was awake and alert and had returned to his baseline neurologic exam. No further effects of the intrathecal Hypaque were recognized, and the patient was eventually discharged, with resolution of his presenting symptoms and no obvious sequelae from the Hypaque myelogram.

DISCUSSION

The clinical manifestations of lumbar intrathecal administration of ionic contrast material are a result of their tendency to facilitate spinal cord activity and, as the medium ascends in the CSF, abnormal brain stem and cortical activity.

An intact blood-brain barrier appears to protect the nervous system when ionic agents are given intravenously [12,22,23]. However, the ionic agents may cause limited disruption of the blood-brain barrier, particularly when administered in high concentrations, and can irritate neural tissue [13]. This may account for occasional neurologic complications associated with their intravenous use [28]. These effects are uncommon, and a variety of ionic water-soluble compounds are considered safe for intravenous use in appropriate doses [22].

Direct contact with nervous tissue is generally necessary for the ionic contrast agents to exert their neurotoxic effects. Spasms are caused by direct effects on the spinal cord [3,8]. The onset of these spasms occurs several hours after application of the agents to the spinal cords of laboratory animals [8]. These effects parallel the clinical course of patients with ionic medium myelography who have a several-hour delay in the initiation of extremity spasms.

Epileptiform activity occurs in animals after direct application of ionic contrast media to the cerebral cortex [19]. In humans, ventriculography and myelography with ionic contrast media have been noted to cause seizures [4,9]. No studies have demonstrated the optimal agent to prevent these seizures.

Seizure prophylaxis could be carried out using phenytoin or phenobarbital and benzodiazepine, which causes sedation as well. We maintained a benzodiazepine drip and periodic electroencephalographic monitoring in our patient for 3 days and found no evidence of epileptiform activity. It is possible that raising the head of the bed and draining spinal fluid shortly after the patient became obtunded prevented the contrast medium from reaching sufficient concentration over the cortex to significantly increase cortical excitability.

Our patient demonstrated a typical sequence of events that paralleled several other documented cases of intrathecal ionic contrast media [2,17,24]. A latent period of 1 to 6 hours is followed by the onset of periodic painful lower extremity spasms lasting a few seconds, which may be elicited by lightly touching the lower extremities. The spasms ascend to involve the upper extremities, and the previously alert patient subsequently becomes obtunded and may manifest tonic-clonic seizures. Uncontrolled muscular activity results in severe rhabdomyolysis. Death may result from acute renal failure, cardiac arrest, and multiorgan failure.

Treatment should address the physical properties of the contrast in the CSF and the pathophysiologic effects. Elevating the head of the bed may help prevent the contrast media, which is denser than CSF, from ascending in the thecal space. After the patient has been in a head-up position, drainage of spinal fluid via lumbar puncture and lavage of the thecal space may also be considered. Experimental work has shown the effects of ionic contrast media on the spinal cord may be reversed by saline lavage [3]. Several published reports mention the use of lumbar and cisterna magna puncture to drain the CSF and replace it with saline, sometimes with good outcome [2,14,15].

Intubation and mechanical ventilation are important for two reasons. First, declining mental status and seizures might threaten airway patency. Second, intubation allows maintenance of neuromuscular blockade to prevent continuing spasms and progressive rhabdomyolysis and acidosis.

Rhabdomyolysis and subsequent multisystem organ failure is a frequently cited cause of death in these patients. The presence of urine myoglobin, an increase in serum CK greater than five times the normal value, and a history of muscle trauma are diagnostic features of rhabdomyolysis [17]. Hyperkalemia, hypophosphatemia, and hypocalcemia may also result from extensive muscle damage. The consequences of rhabdomyolysis are multiorgan failure, especially cardiac and renal failure. Diffuse intravascular coagulopathy has also been associ-

ated with rhabdomyolysis [17]. Hyperkalemia is of particular concern and may lead to fatal dysrhythmias. Significant hyperkalemia may be treated with a potassium exchange resin.

Renal failure is the most commonly reported complication of rhabdomyolysis [17]. Treatment involves maintaining adequate circulating blood volume and urine output [17]. In addition to intravenous fluids, diuretics (including mannitol and furosemide) have been used to maintain high urine output [13,20], with one author administering mannitol when urine output fell lower than 300 mL/hour [20]. Alkalinization of the urine has been advocated in order to prevent dissociation of myoglobin into its nephrotoxic metabolite, ferriheme [19]. Sodium bicarbonate has been administered intravenously to maintain high urine pH (i.e., pH > 6.5) [5,20].

There have been few long-term sequelae of ionic contrast myelography, and our patient appears to have none. Headaches, possibly due to a CSF leak after lumbar puncture and head elevation of the bed, have been reported several days after the procedure. One report describes persistent lower extremity weakness of uncertain origin [2].

Prevention of inadvertent administration is of paramount importance. Physicians and ancillary personnel involved in myelography must be aware of the potential dangers of using inappropriate contrast media. Vials must be stored in a segregated manner and labeled appropriately. Subsequent to our reporting this incident, we received correspondence from the manufacturer of Hypaque stating that the Food and Drug Administration has asked all manufacturers of ionic contrast media and other media not approved for intrathecal use to clearly label cartons, vials, and package inserts "not for intrathecal use" or "not for myelography" (Berlex, Mellinckrodt, Sanofi, Squibb, 9/93).

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COMMENTARY

This case report summarizes the terrifying complications that can occur from the inadvertent installation of Hypaque into the cerebrospinal fluid. It also is a good summary of the development and evolution of various contrast agents used for myelography. The ultimate survival and absence of permanent sequelae testify to the correct manage-

ment of the complication and provide a management formula if this would ever happen again.

Joseph C. Maroon, M.D.
*Department of Neurosurgery
Allegheny General Hospital
Pittsburgh, Pennsylvania*

This article by Killeffer and Kaufman addresses a frequently fatal complication of the intrathecal injection of Hypaque. This syndrome, which has been called by some authors the "ascending tonic-clonic syndrome" [2], has a mortality rate of 50% in reported cases. It has been reported with many ionic contrast media, diatrizoate meglumine most prominently among them.

It is noteworthy that in a review of many of the cases by Bohn et al [1], the chart recorded iohexol, a nonionic contrast medium, as having been given; but when spinal fluid specimens, brain slices, or blood specimens were tested in a number of different cases with chromatography, there is not identified iohexol. Instead, it was diatrizoate or other ionic media. It would appear that the problem was the substitution of the inappropriate drug for the requested appropriate drug during the course of the performance of myelography.

The rapid recognition of the problem as described by the authors, its treatment with tracheal intubation, neuromuscular blockade, high-volume fluid, anticonvulsants, and treatment of the profound metabolic acidosis that occurs in these patients undoubtedly saved this patient's life.

Every neurosurgeon who does his own myelography needs to be aware of this complication and its appropriate treatment. More importantly, these medications need to be clearly identified prior to their use and not placed in an unmarked container in the back of the operating table where it might be confused for some other clear and colorless liquid.

John L. Seymour, M.D.
*Practicing Neurosurgeon
Minneapolis, Minnesota*

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