Transient encephalopathy and asterixis following metrizamide myelography

Case report

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A case is presented in which cervicolumbar myelography with metrizamide was followed by transient encephalopathy and asterixis. Metabolic etiology was excluded. A large degree of intracranial penetration of metrizamide was demonstrated by computerized tomography. Residual symptoms persisted for 10 days.

KEY WORDS □9 neuroradiology □9 metrizamide myelography □9 myelography complications □9 metrizamide encephalopathy

WITH the more frequent use of metrizamide for myelography, some potential side effects are becoming apparent. Cerebral irritability and seizures following metrizamide myelography have been documented.9,11,17,20 Rubin, et al.,18 recently reported two cases of encephalopathy associated with asterixis following metrizamide lumbar myelography. We report the clinical course and computerized tomography (CT) findings in a patient who suffered a marked, but transient, encephalopathic reaction following a cervicolumbar metrizamide myelogram. A brief review of the literature is presented.

Case Report

This 54-year-old right-handed housewife was admitted to Yale-New Haven Medical Center for evaluation of severe and progressive neck pain and cervical radiculitis of 2 years' duration and lower back and leg pain of several months' duration. The patient had suffered a right cerebral vascular accident 4 years ago, a myocardial infarction, and a gastric ulcer 5 years earlier, and chronic cystitis for many years. She had been maintained on Percocet (oxycodone) and Tylox (oxycodone and acetaminophen) for back pain, Tagamet (cimetidine) and Maalox antacid for abdominal discomfort, and Elavil (amitriptyline) and Seconal (secobarbital) for depression and insomnia. She had no history of alcohol abuse.

Routine laboratory tests on admission were normal. Following radiographs of cervical and lumbar spine, a combined cervicolumbar metrizamide myelogram was performed via a lumbar puncture in the prone position. A No. 22 spinal needle was used to instill 12 ml of metrizamide at 250 mg/cc, with a total of 3 gm of iodine under fluoroscopic control. After completion of the lumbar study, the contrast agent was directed into the cervical region for cervical myelography by tilting the fluoroscopic table to a 45° head-down position. Once sufficient pooling was achieved, the table was brought to the horizontal position for filming. The table was then tilted to a steep head-up position for collection of the contrast medium in the caudal sac. After the study, the patient was placed in a sitting position for 15 minutes before being transferred. She was maintained in bed with her head elevated for the next 24 hours. No premedication was given. The patient was comfortable and free of headache, nausea, and vomiting during the remainder of the day. During the night she complained of headache and insomnia. The nurse noted that she was stuttering and mildly agitated.

On the following morning, she became nauseated and vomited. She remained awake and alert, but confused, agitated, paranoid and dysphasic; she also had involuntary facial muscular twitches. She had ataxic writhing movements of the fingers on out-
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Fig. 1. Computerized tomography scans. Left: Scan performed 24 hours following myelography demonstrates marked cortical penetration. Dense collections of contrast material can be seen over the cortical sulci. Right: The scan performed at 48 hours is normal.

stretched hands, diffuse weakness, and marked asterixis. Complete blood count, erythrocyte sedimentation rate, electrolytes, calcium, phosphate, blood urea nitrogen, serum creatinine, and routine liver function tests were normal. Tests for antinuclear antibody, lupus erythematosus cells, rheumatoid factor, and serum protein electrophoresis were within normal limits. Electroencephalography (EEG) revealed marked generalized rhythmic slowing which was intermittent and included some minimal spike and wave discharges. A noncontrast CT scan performed that afternoon demonstrated no evidence of ventriculomegaly or intraventricular reflux. A large amount of metrizamide was present in the subarachnoid space over the convexities along with cortical penetration which extended deep into the white matter (Fig. 1 left). The patient was treated with bed rest and intravenous fluids, and started on a 3-day course of dexamethasone.

By the next day, her dysphasia and agitation had improved. She had no abnormal motor activity except for persistent asterixis. On the 3rd day after myelography, she had complete clearance of her symptoms except for malaise and subjective diffuse weakness. A CT scan at this time was completely normal (Fig. 1 right), and the patient was discharged home. She complained of malaise and weakness which gradually cleared over the next 10 days.

Discussion

Metrizamide is a non-ionic water-soluble contrast agent that is now regarded by many as the contrast agent of choice for myelography. In addition, its value in cisternography is now well established.5 The wide acceptance of this compound for myelography is predicated upon its low neurotoxicity based on experimental studies as compared to other water-soluble contrast agents.10

However, with increasing clinical use of this compound, information regarding its neurotoxicity is now emerging. Earlier reports on this subject have dealt with its more common side effects, such as headache, nausea, vomiting, back pain, neck stiffness, temperature elevation, and seizures.3,9,13,16,17 Electroencephalographic changes have been documented in patients after metrizamide myelography.1,11,12,17 Kaada12 reported a 16% incidence of EEG changes, while other studies1,11,17 have reported EEG abnormalities in as many as 35% of cases. These changes tend to occur 24 to 48 hours after intrathecal administration of metrizamide, coinciding with the arrival of the contrast material over the cerebral convexities. The pattern and time course of the EEG changes described are compatible with findings in our patient.

In a clinical trial of 6000 patients, seven developed seizures.9 This incidence is in keeping with our experience in 1000 cases. We have seen two patients with generalized seizures following cervical myelography; both patients had had seizures in the past. Neither had received anticonvulsant premedication, since their seizure history was not known prior to myelography. We now regard a positive seizure history as a moderate contraindication to metrizamide myelography. Recently, a case of seizure was reported in a patient on phenothiazine therapy.11 Phenothiazine was thought to lower the seizure threshold to metrizamide. Barbiturates and diazepam premedication may help reduce the risk of seizures, especially in patients with previous seizure history.

Gelmers8 recently drew attention to another side effect of metrizamide myelography which he called “acute psycho-organic reaction.” In 439 patients so studied, 12 developed this reaction consisting of anxiety, perception disorder, and difficulty in maintaining attention. It is noteworthy that all these patients had cervical myelography with a dosage far exceeding that recommended by the manufacturer. A controlled clinical trial performed by Schmidt19 included psychological pretesting followed by tests conducted after myelography. Moderate to severe changes in mentation were noted in 16% to 33% of patients. Our patient demonstrated marked distortions of mentation. She was confused, paranoid, and suffered from delusions. Rubin, et al.,18 reported two cases of asterixis following lumbar myelography; however, the diffuse facial twitches and muscular incoordinated movements seen in our patient have not been reported previously.

The mechanism of clearance of this compound after intrathecal administration into the lumbar region is not well understood. Schmidt10 demonstrated individual variability in blood concentration following subarachnoid administration, with the maximum level reached in a few hours. Presumably the bulk of the contrast agent is absorbed in the spinal theca, while the intracranial meninges, the brain, and the intracranial arachnoid granulations play a secondary role. The rostral passage after lumbar instillation can be demonstrated by CT; the agent reaches the basal cisterns in 3 to 4 hours, and the intracranial subarach-
noid spaces and the cerebral cortex in 24 hours.\textsuperscript{4,6,21} By 48 hours, it can no longer be detected by CT, but its presence in the blood continues for several days.\textsuperscript{2} These observations are compatible with the delayed onset of symptoms and the CT findings in our patient. Prolonged presence of detectable drug levels in blood may relate to the subjective residual symptoms that lasted up to 10 days in this patient.

Inflammatory reaction in the leptomeninges, arachnoid granulations, and brain has been demonstrated in response to metrizamide in laboratory animals.\textsuperscript{14} The resultant cerebral edema is dependent on the dosage of contrast media.\textsuperscript{14} Schmidt\textsuperscript{10} hypothesized that the cortical penetration is accountable for encephalopathic reaction and may be related to patient positioning and dose of iodine. Cortical penetration is usually not demonstrated after lumbar myelography when less than 1.6 gm of iodine is used. It is interesting that the patients reported by Rubin, \textit{et al.},\textsuperscript{18} developed asterixis after what should have been low-dose myelography. This seems to be out of keeping with the generally accepted low incidence of complications associated with lumbar myelography. Rubin did not indicate the dosage used.

The proposed preventive measures for side effects involving the central nervous system (CNS) include aspiration of the contrast material, ambulating patients after myelography, appropriate patient positioning, and adequate hydration.\textsuperscript{6,7,20} The main objective is to limit the amount of contrast medium reaching the brain and facilitating its clearance via the spinal theca. The frequency and severity of side effects may be decreased by limiting the metrizamide dose to below 3 gm of iodine. However, this will usually result in an inadequate cervical myelogram when instilled by lumbar injection, in part because the contrast material is diluted as it moves to the cervical region. Some of the diluted iodine not contributing to the myelogram will ultimately reach the cranial cavity. Utilization of a lower dose of iodine administered by a C1–2 puncture for cervical myelography should result in a decrease in the incidence of CNS side effects; however, Rolfe and Maguire\textsuperscript{16} have reported a higher incidence of side effects with this approach than with the higher-dose lumbar approach.

Certain important considerations should be borne in mind during metrizamide cervical myelography by the lumbar approach. Since the rostral aspect of the moving metrizamide column, unlike Pantopaque, is poorly visualized fluoroscopically when it is directed from the lumbar to the cervical region by the downward tilt of the head of the fluoroscopic table, the patient’s neck is kept well extended to provide for pooling of the contrast material and prevent intracranial spillage. Failure to do so may result in severe intracranial spillage and a poor study. Once adequate pooling in the cervical region has occurred, the table is brought back to the horizontal position to minimize intracranial spillage during filming. Immediately after filming is completed, the table head is tilted up to direct the contrast material back toward the caudal sac to maximize its absorption from the spinal region. In the case presented here, the cervical myelogram was performed following completion of the lumbar study without any difficulty, with scrupulous technique, and without any intracranial spill.

This case illustrates a severe side effect of metrizamide myelography. With the increasing use of metrizamide, encephalopathic reactions are to be anticipated in more cases. Only judicious use and meticulous technique will prevent such complications by minimizing the exposure of the brain to this contrast agent.

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