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AJNR Am J Neuroradiol 2009, 30 (5) 1074-1075

doi: <https://doi.org/10.3174/ajnr.A1365>

<http://www.ajnr.org/content/30/5/1074>

This information is current as
of April 19, 2024.

Aseptic Meningoencephalitis after Iohexol CT Myelography

CASE REPORT

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SUMMARY: We describe the case of a patient with aseptic meningoencephalitis after intrathecal iohexol injection for myelography and review the previous literature on similar cases of contrast-induced neurotoxicity.

Aseptic meningoencephalitis is a rare complication of myelography with nonionic, iodinated, water-soluble contrast agents. We describe a case of a 69-year-old woman in whom aseptic meningoencephalitis developed after she underwent iohexol myelography.

Case Report

A 69-year-old white woman underwent a technically successful outpatient CT myelogram with 10 mL of iohexol (Omnipaque 300; GE Healthcare, Cork, Ireland). The CSF was clear and colorless, and myelogram revealed degenerative osteoarthritis and severe central canal stenosis at L3–L4 secondary to short pedicles, facet and ligamentum flavum hypertrophy, and diffuse disk bulging. Approximately 12 hours after the injection, she experienced fever, headache, confusion, agitation, and aphasia. She was brought to the emergency department 20 hours after the myelogram.

In the emergency department, her initial temperature was 102.5°F, and she was agitated and unable to speak, though she could shake and nod her head for “yes” or “no” responses. She complained of a severe headache and low back pain but denied incontinence or lower extremity numbness. On physical examination, she had mild symmetric lower extremity weakness that measured 4 of 5 bilaterally. Her serum white blood cell count (WBC) was 24,300 cells/ μ L (90% neutrophils). Head CT revealed moderate to severe, chronic, small-vessel ischemic disease. Lumbar puncture and CSF analysis approximately 30 hours after the iohexol injection revealed turbid-appearing fluid with 300 white cells/ μ L (61% polymorphonuclear cells and 1% monocytes), 5200 red cells/ μ L, glucose level of 63 mg/dL, and elevated total protein level of 624 mg/dL. A second tube of CSF from the same lumbar puncture revealed 220 white cells/ μ L (94% polymorphonuclear cells and 2% lymphocytes) and 1545 red cells/ μ L. Results of CSF bacterial and cryptococcal antigens were negative. CSF culture revealed no growth at 5 days.

She was initially started on intravenous ceftriaxone (2000 mg) and vancomycin (1000 mg) every 12 hours. The following day, approximately 48 hours after the myelogram, she was afebrile, and her mental status and neurologic examination had returned to near baseline with fluent speech. She was alert and oriented, with no recollection of the previous day, and complained only of a bandlike headache. An infectious disease consultation was obtained, and the patient was diagnosed with an allergic reaction to the iohexol. Diagnosis was based on the negative Gram stain result, negative culture result, and rapid res-

olution. Antibiotics were discontinued after results of CSF tests, blood tests, and urine cultures remained negative.

Discussion

Intrathecal injection of ionic, water-soluble contrast agents, first used in the United States in 1931, was associated with significant meningeal irritation and therefore was never popularized.¹ Metrizamide, developed in the late 1960s, was the first of a newer generation of nonionic, water-soluble contrast agents that were better tolerated.² Aseptic meningitis was still reported in approximately 5% of these myelograms.³ Newer agents such as iohexol and iopamidol replaced metrizamide, as comparative trials showed a decreased incidence of severe adverse neurologic effects with these agents.^{4,5} Iohexol is a popular nonionic, water-soluble, radiographic contrast medium for myelography with an iodine content of 46.36%. Omnipaque 240, 300, and 350 contain 240 mg, 300 mg, and 350 mg of organic iodine per milliliter, respectively. The osmolarity of Omnipaque 240, 300, and 350 is 391 mOsm/L, 465 mOsm/L, and 541 mOsm/L, respectively, compared with 285 mOsm/L of plasma and 301 mOsm/L of CSF.

The most common minor adverse effects after iohexol myelography are headache (11% to 21%),^{5,6} nausea (10%), vomiting (3%), and dizziness (3%).⁵ Mild neckache and backache are also not unusual. Complications of myelography include seizure, aseptic meningitis,⁷⁻¹⁰ meningoencephalitis,¹¹⁻¹³ bacterial meningitis,¹⁴ intracranial hemorrhage,¹⁵ spinal hematoma,¹⁶ encephalopathy,¹⁷ transient confusion,^{18,19} and paraplegia.²⁰

Aseptic meningitis or meningoencephalitis after iohexol myelography is very rare. In a 1986 review of the literature by Elkin et al,⁴ they found no cases of serious neurologic adverse effects (defined as mental status changes or seizure) in 248 patients who underwent myelography with iohexol. In 1988, Nestvold and Sortland²¹ also found no severe neurologic complications in the 331 patients reviewed who underwent iohexol myelography. Also in 1988, Skalpe and Nakstad²² reported a study of 1000 iohexol myelographies with no serious neurologic adverse effects. To our knowledge, there are only 2 case reports of aseptic meningitis^{9,10} and 1 case of aseptic meningoencephalitis¹³ after iohexol myelography. In the case of meningoencephalitis, the patient received 18 mL of iohexol 180. The patient's mental status improved 72 hours after the myelogram, and his fever resolved by 120 hours. Two cases of aseptic meningitis with iotrolan myelography^{7,8} and 2 cases of aseptic meningoencephalitis with iopamidol myelography^{11,12} have also been described.

Previous reports of patients with chemical aseptic meningoencephalitis from myelography describe headaches, nausea, fevers, and mental status changes within 24 hours of the my-

Received September 7, 2008; accepted September 12.

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DOI 10.3174/ajnr.A1365

eologram. Serum leukocytosis and CSF pleocytosis (with polymorphonuclear cell predominance) may be seen. Negative results on CSF cultures are a requisite. Bender et al⁷ proposed measuring serum procalcitonin levels as a guide to help differentiate between bacterial and aseptic chemical meningitis because procalcitonin levels are higher in bacterial infections.

Iomeprol is a newer agent that also seems to have a safety profile similar to that of iohexol, iotrolan, and iopamidol.²³ It is a nonionic iodinated contrast medium that has a lower osmolarity and higher water solubility than older agents.²⁴ It is also the first contrast medium to be formulated without edetic acid.²³ These factors may reduce its potential to cause adverse events,²³ and comparative studies with iohexol and iomeprol with regard to neurologic complications may be useful.

The pathophysiology and predisposing factors for the development of aseptic meningitis or meningoencephalitis after intrathecal injection of these mentioned contrast agents are not well understood. The neurotoxicity of contrast agents has been linked to the osmolarity, presence of sodium ions, and lipid solubility of the agent.²⁵ Some authors hypothesize that osmolarity disturbances¹⁷ or direct toxicity¹¹ cause meningeal irritation. In addition, an immune-mediated cause has not been excluded. If immune related, steroids could play a role in early treatment and possibly hasten recovery. However, most reported patients experienced no serious sequelae without steroid treatment.

Conclusions

In general, iohexol is a safe and effective contrast agent for CT myelography. Clinicians should be aware of the rare occurrence of aseptic meningoencephalitis related to myelography. The clinical symptoms, timeline, and CSF analysis are helpful to differentiate aseptic meningoencephalitis from other complications of myelography.

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