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Iopamidol-induced meningoencephalopathy in an HIV-seropositive patient

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Central nervous system infectious and metabolic abnormalities are common in HIV-positive patients. Drug therapy, opportunistic infections, the clinical course of HIV disease itself, and very rarely iodinated radiographic contrast agents can all be linked to these abnormalities. The following case describes an HIV-seropositive patient who developed encephalopathy after undergoing a cervical myelogram that utilized iopamidol dye (Isovue-M 300 mg/mL).

Central nervous system (CNS) infections and metabolic abnormalities are frequent complications in HIV-positive patients (1). Diagnostic tests such as computed tomography (CT) or magnetic resonance imaging (MRI) scans are utilized to assess these conditions. The use of nonionic contrast media for radiological procedures has led to a significant decrease in allergic reactions during these tests. Iopamidol, a nonionic, water-soluble contrast medium, is often used for CT myelograms because of its nontoxic profile (2). Despite the use of nonionic contrast media to decrease toxicities, rare case reports have identified adverse reactions such as seizures, inappropriate antidiuretic hormone (ADH) secretion, meningoencephalitis, meningoencephalopathy, and paraplegia (3–9).

The possibility that HIV itself may alter the blood-brain barrier and predispose patients to severe contrast dye reactions has been considered (10), although this relationship has never been demonstrated in the literature. We present a case of an HIV-infected patient with iopamidol-induced meningoencephalopathy after a CT cervical myelogram.

CASE PRESENTATION

A 45-year-old African American HIV-seropositive man presented to an acute care institution with an acute mental status change that deteriorated into acute respiratory failure. His past medical history was significant for HIV diagnosed 12 years earlier, depression, and intracranial aneurysm with repair. His baseline neurological status was normal. His home medications included acyclovir 800 mg twice daily, sertraline 100 mg daily, lopinavir 133.3 mg/ritonavir 33.3 mg (Kaletra) 3 capsules twice daily, emtricitabine 200 mg/tenofovir 300 mg (Truvada) 1 tablet daily, clopidogrel 75 mg daily, and atorvastatin 80 mg daily. One month prior to admission, his $CD4^+$ count was 504 cells/μL and viral load was 380 copies/mL.

On the morning of admission, the patient had an outpatient CT myelogram of his cervical spine to assess severe neck pain; 15 mL of iopamidol dye (Isovue-M 300 mg/mL, Bracco Diagnostics, Princeton, NJ) was utilized. The patient tolerated the procedure well with no complications, and he was instructed to avoid heavy lifting and to sleep semierect to avoid intracranial spread of contrast. An MRI could not be performed because the patient had clips from an aneurysm repair. The myelogram showed multilevel cervical degenerative changes resulting in disk protrusion.

That afternoon his partner noticed that the patient was disoriented and angry. Several hours after these symptoms, the patient fell into a deep sleep and had a seizure. He was intubated by emergency services and brought to the emergency department. A CT scan of the brain was ordered to rule out any intracranial bleeding but was inconclusive due to the contrast dye already given to the patient earlier in the day *(Figure).*

The patient was transferred to the intensive care unit, and a lumbar puncture was performed. Analysis of the cerebrospinal fluid revealed a clear appearance with no evidence of xanthochromia, 5 white blood cells/mm^3 (90% mononuclear/10% polymorphonuclear), 200 red blood cells/mm^3, a glucose level of 82 mg/dL (reference range, 50–75), and a protein level of 50 mg/dL (reference range, 15–45). The increase in red cells was suspected to be secondary to a traumatic lumbar puncture. Results of the following cerebrospinal fluid tests were negative: bacterial culture, VDRL, histoplasmosis, cryptococcal antigen, acid-fast stain and culture, cytomegalovirus, and herpes simplex virus 1 and 2 by polymerase chain reaction. A complete blood count, comprehensive metabolic profile, and urinalysis were also performed. The patient's urine had a specific gravity of >1.030, tested positive for blood (3+) and protein (2+), and tested positive for marijuana. His last reported use of marijuana

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was more than a week earlier. Other laboratory results were unremarkable at baseline with a white blood cell count of 10.1×10^3 cells/μL (reference range, 4–12) with 1% bands. His serum glucose level at the time of the lumbar puncture was 93 mg/dL.

After reviewing results of the history, physical examination, CT scan, and lumbar puncture, the neurosurgeon ruled out an intracranial bleed and agreed that the findings were consistent with contrast-induced meningoencephalopathy. A neurologist was consulted, and he agreed with the diagnosis and started the patient on phenytoin 100 mg intravenously every 8 hours and diazepam 5 mg intravenously every 8 hours.

The patient was extubated 5 days after admission and on day 6 was transferred to the general medical floor. He did not receive another lumbar puncture. He was released 9 days after his admission with no neurological sequelae, and he resumed only his admission medications on discharge from the hospital.

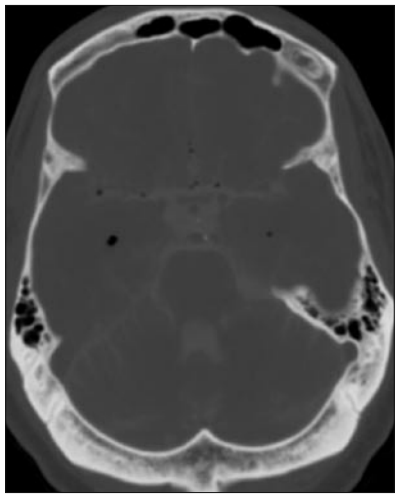

Figure. CT scan of the brain at the level of the basal cisterns reveals myelographic contrast material filling the fourth ventricle, basal cisterns, and surrounding subarachnoid spaces. This volume of contrast would preclude detection of any underlying subarachnoid hemorrhage. Note is made of incidental air in the subarachnoid space related to the myelographic procedure.

DISCUSSION

The differential diagnosis of an acute mental status change in an HIV-infected patient would include infection, neoplasm, metabolic causes, seizures, and drug reactions (1). Contrast dye reactions should be included also if a patient had a recent intravenous or intrathecal dye exposure. All of these possibilities need to be considered when evaluating these patients. Temporary or permanent disturbances in brain function such as encephalopathy are confusing to diagnose and can occur from four main causes: depletion of oxidative energy, nutritional deprivation, disturbances of neurotransmission, or altered ion balance (11). HIV infection may potentially affect all four of these factors. Despite this hypothesis, there have been no increased reports of dye reactions in HIV-infected patients.

Compared with cases reported in the literature of encephalopathy associated with iopamidol in non–HIV-infected patients, our patient did not have fever, pronounced encephalitis with increased white blood cells in the cerebrospinal fluid, or inappropriate ADH secretion (3, 4, 6). He did experience seizure activity, respiratory collapse, and severe mental status change within 12 hours of the myelogram, symptoms that were observed in some case reports (3, 4). Paraplegia has been described in the literature with iopamidol and iohexol dye formulations, and this occurs immediately after the infusion of the dye (7, 9). Unlike patients with reactions to older dye formulations such as metrizamide, most patients with reactions to iopamidol recover rapidly without any neurological sequelae, as seen in this case (2, 4).

In our patient case, the dose of iopamidol may have also contributed to the encephalopathy. Our patient was given 15 mL of the 300 mg/mL strength of iopamidol for the cervical myelogram. The manufacturer recommends that 10 mL of the 300 mg/mL strength or 15 mL of the 200 mg/mL strength be utilized for this procedure (12). A case report utilizing the dose administered to our patient also reported an outcome of generalized tonic-clonic seizure in a patient with no history of seizure disorder (13).

Although this case is not the first reported case of meningoencephalopathy associated with iopamidol, it appears to be the first case reported in an HIV-infected patient. Our patient had a very controlled HIV status, with a $CD4^+$ count of 504 cells/μL and a viral load of 380 copies/mL. Therefore, we do not feel that HIV itself contributed to this reaction, but it is important to include contrast dye reactions in the differential diagnosis in an HIV-infected or non–HIV-infected patient with mental status change after a radiologic procedure involving contrast material of any kind.

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