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July 22, 2013

Fungal Meningitis Can Masquerade as Ischemic Stroke

IMNG Medical Media, 2013 Jul 22, MA Moon



The recent outbreak of fungal meningitis caused by spinal injections of contaminated methylprednisolone illustrates that the disease can present as ischemic stroke, according to a report published online July 22 in JAMA Neurology.

Three such cases occurred in elderly patients who had clear risk factors for stroke and no fever or meningeal signs; whose exposure to the contaminated injection was as remote as 4 weeks earlier; and whose early MRI scans indicated stroke rather than infection, said Dr. Kirk Kleinfeld and his associates at Vanderbilt University Medical Center, Nashville, Tenn.

The investigators described these cases in detail so as to alert clinicians to this confusing presentation, which would enable them to initiate antifungal therapy as soon as possible. In two of these cases, the diagnosis was delayed and the patients died. In the third case, once clinical suspicion of fungal meningitis had been aroused, empiric antifungal therapy appears to have saved the patient's life, they noted.

“An awareness of the presentation and vascular sequelae of fungal meningitis in immunocompetent patients should lead to earlier treatment and improved outcomes prior to a definitive diagnosis,” Dr. Kleinfeld and his colleagues wrote.

In the first case, a 78-year-old man presented with acute-onset, left-sided weakness and dysarthria. He was afebrile and had no meningeal signs, and his laboratory workup showed only mild leukocytosis. He had hyperlipidemia, hypertension, and atrial fibrillation, and an MRI scan showed a small-vessel ischemic infarct of the right anterior superior pons/lower midbrain.

The patient failed to improve with standard poststroke care. When his left-sided weakness worsened on day 3, another MRI showed that the infarct had extended and a new one had formed in the right thalamus. The next day he became unresponsive, and repeated imaging showed enlargement and evolution of those infarcts plus formation of an occlusion of

the right superior cerebellar artery. The patient died on day 6.

An autopsy was performed when it was noted that the patient had received an epidural steroid injection 2 weeks earlier to treat low-back pain. It “revealed small areas of focal cortical and pontine subarachnoid hemorrhage, as well as fungal cerebral vasculitis with aneurysm formation.” Infection with *Exserohilum* species was identified, the investigators reported (JAMA Neurol. 2013 July 22 [doi: 10.1001/jamaneurol.2013.3586]).

In the second case, a 78-year-old woman presented with subacute vertigo, nausea, and headache, and was found on examination to have one-sided dysmetria and mild ataxia. Her medical history included hypertension, hyperlipidemia, and coronary artery disease, and the initial laboratory workup revealed type 2 diabetes. The authors noted that an MRI scan showed “ischemic infarcts of the left lateral pons, superior cerebellar peduncle, and superior cerebellum suggestive of a large-vessel (superior cerebellar artery) etiology.”

A hypercoagulable panel revealed lupus anticoagulant and elevated antiphospholipid protein antibodies. Anticoagulation therapy was given. The patient failed to improve, and on day 4 she developed a low-grade fever and mild encephalopathy. A repeat MRI showed a new ischemic pontine stroke.

The patient’s mental status failed to improve, and it was noted that she had received an epidural steroid injection 2 weeks earlier to treat low-back pain. The patient underwent lumbar puncture to identify any fungal infection, and intravenous antibiotics and voriconazole were administered beginning on day 15. However, the patient died on day 50.

“An autopsy revealed a left superior cerebellar artery mycotic aneurysm with vascular infiltration of the arterial wall by hyphal fungal forms,” which were thought to represent *Exserohilum* species based on polymerase chain reaction studies, the investigators reported.

In the third case, a 70-year-old woman presented with headache, difficulty balancing, nuchal rigidity, and mild fever. She had hyperlipidemia, and physical examination showed mild dysarthria and bilateral dysmetria. An MRI scan revealed acute small-vessel strokes in the right thalamus and internal capsule.

Because the patient had chronic back pain and the clinicians’ suspicions were raised regarding fungal meningitis, it was found that she had undergone an epidural steroid injection 1 month earlier. A lumbar puncture was performed to identify possible fungal infection, and treatment with intravenous antibiotics and voriconazole was initiated.

The patient became encephalopathic on day 7, and a repeat MRI showed a new small-vessel stroke involving the left internal capsule. With continued voriconazole therapy, the patient’s mental status and her cerebrospinal fluid cell counts slowly improved. She survived and was discharged 37 days later.

“We suspect that [the early antifungal treatment] halted the further vascular progression of her infection,” Dr. Kleinfeld and his associates wrote.

All three patients received methylprednisolone from contaminated lots at medical facilities that were identified by the Centers for Disease Control and Prevention as recipients of contaminated lots.

These cases show that clinicians should consider an atypical pathogenesis when small-vessel infarctions expand locally or when new infarctions develop in the same vascular territory. They also demonstrate the angioinvasive nature of some fungal species such as *Exserohilum*, which can lead to progressive vascular occlusion, the investigators said.

No relevant financial conflicts of interest were reported.



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