Brainstem Stroke Following Uncomplicated Cervical Epidural Steroid Injection

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Background: Cervical epidural steroid injection treatment of radicular pain has become a common procedure.

Objectives: To describe the clinical, radiologic, and autopsy findings of a 41-year-old patient treated with methylprednisolone acetate cervical epidural steroid injection, who developed a fatal hemorrhagic brainstem infarction and to discuss the possible mechanisms involved.

Design: Case report.

Setting: Pain management center and tertiary care hospital.

Results: Immediately following a seemingly uncomplicated epidural steroid injection at C5-6, the patient developed progressive symptoms of extensive brainstem and thalamic infarction (documented by magnetic resonance imaging and autopsy) with hemorrhagic conversion and hydrocephalus. Hemorrhage within the adventitia of the left vertebral artery, but no dissection, was found at the C5 vertebral level at necropsy.

Conclusions: This case report shows the possibility of serious intracranial pathology resulting from cervical epidural steroid injection despite use of fluoroscopic guidance. Vascular spasm distant to the site of injection is a possible mechanism.

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Cervical epidural steroid injections (CESIs) are often used to treat cervical radiculopathy secondary to cervical disc pathology or spinal stenosis and refractory occipital headaches. Transforaminal epidural steroid injection is a nerve root block that involves placement of a needle into the epidural space surrounding the spinal cord and nerve root to deliver medication. Reduction of inflammation and swelling due to mechanical or inflammatory nerve root irritation is posited to result in long-term pain relief, although placebo-controlled blinded studies are lacking. Transforaminal nerve root blocks require imaging guidance, either fluoroscopy or computed tomography, to allow direct visualization of the epidural space and closely proximate vertebral artery. The procedure is performed on an outpatient basis with a low complication rate; most complications are self-limited.

This report examines a death associated with a CESI procedure. It is also the first known documented case of an isolated fatal hemorrhagic-ischemic brainstem injury without vertebral artery dissection related to this procedure.

The patient was a 41-year-old African American man with a history of left-side neck pain radiating into the arm. Medical history included distant intravenous drug abuse (15 years in recovery), hepatitis C, cervical spondylitis, and having completed 11 months of viral suppression therapy (bacillus Calmette-Guérin vaccine and ribavirin). He reported no tobacco or alcohol use and took no medications. Magnetic resonance imaging (MRI) showed a left lateral disk herniation with severe left neural foraminal narrowing at C3-4, and cervical spondylitis at C4-5 and C5-6. There was no cord compression.

He had 3 CESI procedures at the C5-6 level, 1 week apart. The injection was performed by an experienced anesthesiologist under fluoroscopic guidance and without sedation. A test injection was performed with nonionic contrast prior to steroid injection, confirming proper needle placement in the posterior epidural space. There was no arterial flashback during the test injection. This was followed by injection of 40 mg of methylprednisolone acetate.
and 1.0 cm³ of preservative-free saline. No anesthetic was injected, either locally or epidurally. During the third procedure, within minutes of injection (at 3:30 PM), the patient developed nausea, vomiting, and headache. He had no respiratory distress and no focal neurologic deficits. He was observed for 2 hours with some improvement in his symptoms and then discharged. At approximately 11 PM he telephoned for help and had slurred speech and progressive weakness in all 4 extremities. Within a half hour his level of consciousness deteriorated and he was taken to a local emergency department where he was intubated. His blood pressure was 150/80 mm Hg; pulse rate was 110/min; and respiratory rate was 30/min. Pupils were sluggish at 2 to 3 mm. He had minimal spontaneous movement of his right side and no movement on the left. His symptoms progressed to unresponsiveness with nonreactive pupils, extensor posturing in the left arm, and triple flexion responses in the lower extremities. Initial MRI showed diffuse ischemic infarction of the midbrain, pons, medulla, and left thalamus. There was no abnormal signal within the spinal cord. Results of a cranial-cervical magnetic resonance angiography (MRA) were normal and showed patency of both vertebral arteries and basilar artery. No thrombus, hematoma, or dissection were seen.

The patient was transferred to our hospital approximately 18 hours after injection and arrived hemodynamically normal and afebrile. Neck was supple. Pupils were ovoid and nonreactive (left, 3 mm; right, 4 mm). He was comatose with no corneal reflexes, and no cervicococular or vestibulo-ocular responses. A weak cough and gag reflex were present. There was no apparent respiratory effort. The right lower extremity showed weak flexion response; motor response was otherwise absent. Deep tendon reflexes were 2+ in the upper extremities, 3+ in the knees with crossed adductors on the left, and 1+ for bilateral ankle jerks. Plantar response was extensor on the left and equivocal on the right with no clonus. A cardiovascular examination revealed no murmur or carotid bruit.

Because of an absence of thrombus on MRA and the patient’s poor neurologic status, angiography and thrombolysis were not indicated. Both MRI and MRA were repeated within 24 hours and showed progression of ischemia with extensive edema throughout the midbrain, pons, brachium pontis, medulla, right thalamus, right internal capsule, and medial aspect of the right temporal lobe (Figure). An intraventricular catheter was inserted for management of intracranial pressure due to development of noncommunicating hydrocephalus on MRI. Intracranial pressure was normal at all

Figure. Magnetic resonance imaging at approximately 24 hours after epidural steroid injection. Axial fluid-attenuated inversion recovery sequence showing stroke within the right thalamus (A), bilateral midbrain (B), bilateral pons (C), and medulla (D and E). Axial diffusion-weighted magnetic resonance image reveals intense brightness in the brainstem, confirming suspicion of stroke. Apparent diffusion coefficient map (not shown) was consistent with infarction, not edema.

F, Magnetic resonance angiogram shows normal circle of Willis.
times. The patient received 1 g of intravenous methylprednisolone acetate for 5 days for the possibility of an inflammatory process, with no improvement. Cerebrospinal fluid analysis on day 1 postinjection yielded slightly bloody fluid with 8 white blood cells per cubic millimeter (97% polymorphonuclear cells), 5235 red blood cells per cubic millimeter, protein level of 23 mg/dL (normal, 15-45 mg/dL), and a glucose level of 100 mg/dL (5.6 mmol/L) (normal, 50-75 mg/dL [2.8-4.2 mmol/L]). Myelina basic protein was 77.3 µg/L (normal, 0.0-4.0 µg/L). Test results were normal for the following: prothrombin time, partial thromboplastin time, international normalized ratio, C3, C4, vitamin B12, liver function, electrolytes, and hematology panel. Westergen erythrocyte sedimentation rate was 46 mm/h. Anti–hepatitis B surface and hepatitis C virus antibody screens were positive. Screens were negative for hepatitis B surface antigen. Transcranial Doppler examination of the posterior circulation on day 1 postinjection showed normal cerebral blood flow velocities in the basilar artery and both vertebral arteries. Transthoracic echocardiogram showed normal left ventricular systolic function and no cardiac source of embolus. Brainstem auditory evoked response study showed absence of waves IV and V on the left and waves III through V on the right. Median nerve somatosensory evoked potential study revealed absent cortical responses bilaterally (N20 and P23). Repeated MRI and MRA on day 7 showed transtentorial herniation and hemorrhagic transformation of infarcts in the thalamus, midbrain, and pons. Because of the patient's progressive clinical and radiological deterioration, comfort care measures were instituted on day 7 after injection.

On autopsy, gross examination of the brain demonstrated edema and hemorrhage within the brainstem. Microscopic analysis revealed hemorrhagic necrosis of the basal thalamus, hypothalamus, midbrain, pons, and medulla bilaterally, consistent with infarction. There was no evidence of atherosclerosis of intracranial arteries, which were normal and patent.

Examination of the soft tissues and vasculature of the neck showed a small area of hemorrhage within the adventitia of the left vertebral artery at the level of the C5-6 vertebrae. There was no evidence of dissection or vasospasm of the vertebral arteries. The spinal cord, dura, and anterior spinal artery were normal.

Examination of the heart and great vessels revealed no cardiac sources of emboli, no patent ductus arteriosus, and no atherosclerotic change.

**COMMENT**

Neurologic sequelae following CESI are usually limited to increased neck pain (7%), transient nonpositional headache (5%), vasovagal reactions (2%), facial flushing (1.5%), and dural puncture (0.3%). There is only 1 previous report of intracranial sequelae following CESI. Rozin et al described a patient who had translaminar epidural steroid injection at C7 and died of massive cerebral edema, brainstem hemorrhage, and hydrocephalus, secondary to dissection of the left vertebral artery. Reports of neurologic injury involving the spinal cord are also rare and include the following: an anterior subdural hematoma after CESI at C4-5; a fatal cervical spinal cord infarction caused by impaired perfusion of the major-feeding anterior radicular artery following C6 nerve root block; 2 cases of permanent intrinsic cervical cord damage at the time of steroid injection; and several cases of neuropathic pain consistent with nerve injury.

Considering the onset of the patient's symptoms several minutes after CESI, it is most likely that the procedure caused the symptoms. In the absence of vertebral artery dissection, we hypothesize that the procedure triggered an event such as vascular spasm of the vertebral and basilar arteries or brainstem perforators, which resulted in decreased cerebral blood flow and subsequent brainstem ischemic infarct. The spasm may have been transient, as it was not observed on MRA, transcranial Doppler ultrasound, or autopsy. Reperfusion injury likely contributed to edema and hemorrhagic conversion. Vasospasm may have been caused by inadvertent intravascular needle entry, despite the use of fluoroscopic guidance with instillation of contrast, an accepted method to confirm epidural location of the needle tip. Alternatively, intradural needle entry may have occurred. An estimated 2.5% of epidural injections reach the subarachnoid space, presumably via transudation across dura mater and arachnoid through the arachnoid villi. Methylprednisolone acetate within the cerebral intravascular or subarachnoid space could have produced intracranial vascular spasm. Methylprednisolone acetate contains ethylene glycol, which can cause sterile meningitis and arachnoiditis, but acute vasospasm has not been reported. Myelina basic protein in the cerebrospinal fluid, significantly elevated in our patient, is a reported indicator of severity of brain damage due to vasospasm associated with subarachnoid hemorrhage, although it is nonspecific. Alternative explanations for this patient's pathology, such as allergic reaction or encephalomyelitis resulting from intradural injection, are unlikely to have caused the acute focal posterior cerebrovascular process observed.

This case illustrates the possibility of serious intracranial complications following CESI, even when performed according to accepted standard technique. During any procedure involving the insertion of a needle in close proximity to the vertebral arteries, symptoms suggestive of brainstem ischemia should be fully investigated to evaluate the possibility of arterial injury or other pathology compromising cerebral blood flow.

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