Posterior Circulation Stroke after C1–C2 Intraarticular Facet Steroid Injection: Evidence for Diffuse Microvascular Injury

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C ERVICAL pain is increasingly being treated with invasive procedures such as transforaminal and intraarticular facet steroid injections.[1] Most patients experience at least transient symptomatic benefit after transforaminal injection for cervical radicular pain,[2] but catastrophic complications, including stroke[3,4] and spinal cord infarction,[5,6] can occur. Although ischemic complications of facet injections have not been reported, their benefit has not been clearly demonstrated.[7] The overall incidence of complications with cervical steroid injections is unknown. However, a recent survey by American Pain Society physicians identified 78 ischemic neurologic events, including 13 fatalities.[8]

The mechanism of stroke after cervical steroid injection remains unclear. During cervical transforaminal and intraarticular facet injections, the needle tip comes into close proximity with the vertebral artery. Thus, potential stroke mechanisms include vertebral artery dissection, vasospasm, and intravascular injection of steroid suspension causing microvascular embolization of particulate macromolecules.

We describe a patient who became comatose immediately after an intraarticular cervical facet steroid injection (fig. 1) and discuss the implications of the clinical, radiologic, and histopathologic data. To our knowledge, this is the first reported case of posterior circulation stroke related to cervical intraarticular facet steroid injection. The pattern of tissue damage on serial magnetic resonance imaging and postmortem microscopy provides strong evidence for microvascular embolization of particulate macromolecules as the etiology of stroke.

CASE REPORT

A 64-yr-old man with chronic cervical pain consented to a C1–C2 intraarticular facet steroid injection. A 25-gauge needle was advanced using radiographic guidance. Iohexol contrast was injected, and anteroposterior and lateral radiographs were obtained to confirm needle placement (fig. 1A). Neither live fluoroscopy nor digital subtraction was used. Two milliliters of a 40-mg/ml triamcinolone acetonide suspension was then injected.

The patient immediately lost consciousness and developed extensor posturing in the limbs. He briefly became apneic, followed by a rapid increase in blood pressure from 144/85 to 219/110 mmHg and bradycardia with a heart rate of 46 beats/min. The patient was intubated before a videoconference with our stroke service, and the findings of the head and cervical spine computed tomography were unremarkable.

The patient arrived in our emergency department 3 h and 20 min after the injection. Blood pressure was 163/77 mmHg, and heart rate was 75 beats/min. The patient was breathing spontaneously and his eyes were open, but he was not following commands. Pupils were 3 mm and briskly reactive but without blink to threat. Corneal, gag, and cough reflexes were present, but the oculocephalic reflex was weak. Flexor posturing was present in the upper extremities, with triple flexion in the lower extremities and Babinski sign present bilaterally.
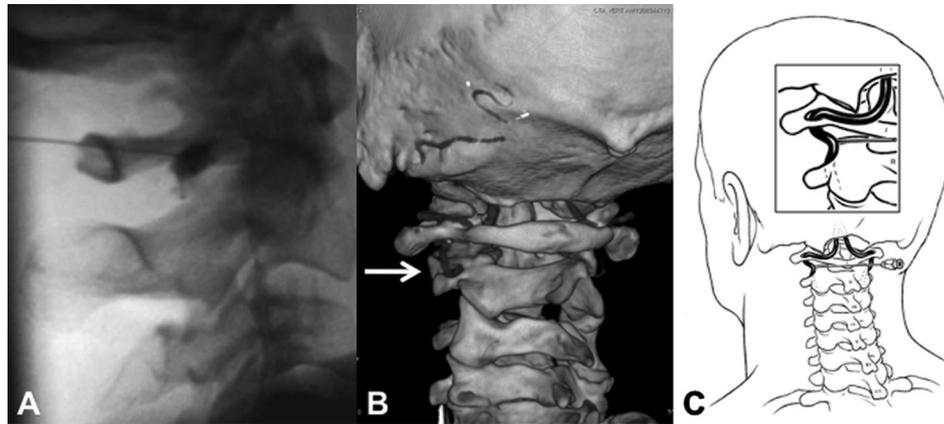
The findings of repeat head computed tomography were unremarkable. Computed tomography angiography of the head and neck showed no abnormality of the cervicocranial arteries (fig. 1B). Diffusion-weighted magnetic resonance imaging demonstrated multiple hyperintensities, reflecting infarction of the thalami, pons, occipital lobes, hippocampi, splenium of the corpus callosum, and cerebellum (fig. 2, A and B). T2-weighted fluid-attenuated inversion recovery (FLAIR) sequence revealed hyperintensities throughout the posterior circulation territory (fig. 2C). Apparent diffusion coefficient maps showed not only restricted diffusion in some affected areas but also increased diffusion in other regions (fig. 2B), a finding not typically seen in ischemic strokes.

The patient was admitted to the neurologic intensive care unit. Repeat magnetic resonance imaging on day 3 demonstrated interval progression of diffusion-weighted

Fig. 1. Anatomic considerations: cervical spine and vertebral artery. (*A*) Lateral x-ray shows iohexol contrast injection for confirmation of needle placement. (*B*) Reformatted computed tomography angiography of the left vertebral artery (*white arrow*, posterior view) performed approximately 5 h after cervical injection does not reveal evidence of arterial dissection, vasospasm, or occlusion. (*C*) Schematic illustration with inset highlighting the anatomic area of interest demonstrates proximity of the superior cervical portion of the vertebral artery to the injection site (illustration by Gary Nelson, Medical Illustrator, retired from the University of Vermont College of Medicine, Burlington, Vermont).
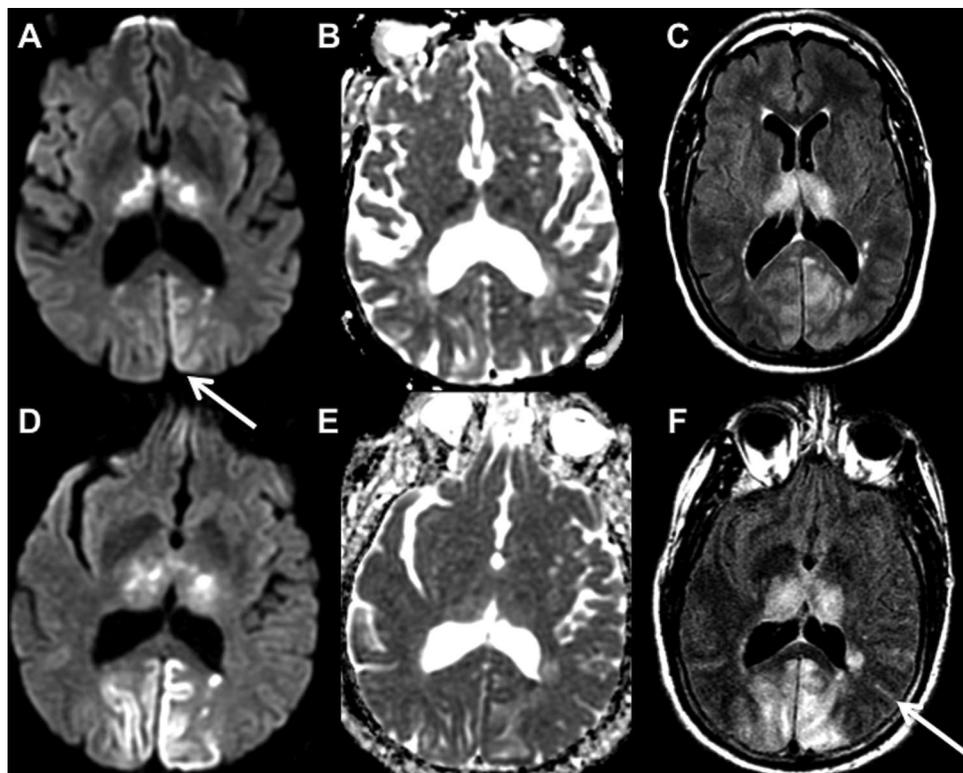
Fig. 2. Brain magnetic resonance imaging (MRI) performed acutely and on day 3 after steroid injection. (*A*) Axial diffusion-weighted imaging sequence and (*B*) apparent diffusion coefficient maps from MRI performed approximately 6 h after injection demonstrate diffusion restriction, suggestive of acute infarction, in the bilateral thalami and occipital lobes. The region of infarction predominantly involves the cortex, as evidenced by the "cortical ribbon" of diffusion-weighted imaging hyperintensity (*white arrow*, fig. 2A) and apparent diffusion coefficient hypointensity in the occipital lobes. (*C*) Axial T2-weighted fluid attenuated inversion recovery sequence from the acute MRI reveals diffuse posterior circulation hyperintensity out of proportion to the diffusion restriction, suggesting concurrent vasogenic and cytotoxic edema. (*D*) Axial diffusion-weighted imaging sequence and (*E*) apparent diffusion coefficient maps from repeat MRI performed approximately 64 h after the injection demonstrate expected evolution of the regions of diffusion restriction. (*F*) Axial T2-weighted fluid-attenuated inversion recovery sequence from the repeat MRI reveals interval increase in the degree and distribution of signal hyperintensity within the posterior circulation territory. There are scattered sulcal T2 hyperintensities (*white arrow*, fig. 2F), suggesting inflammation and protein exudation.
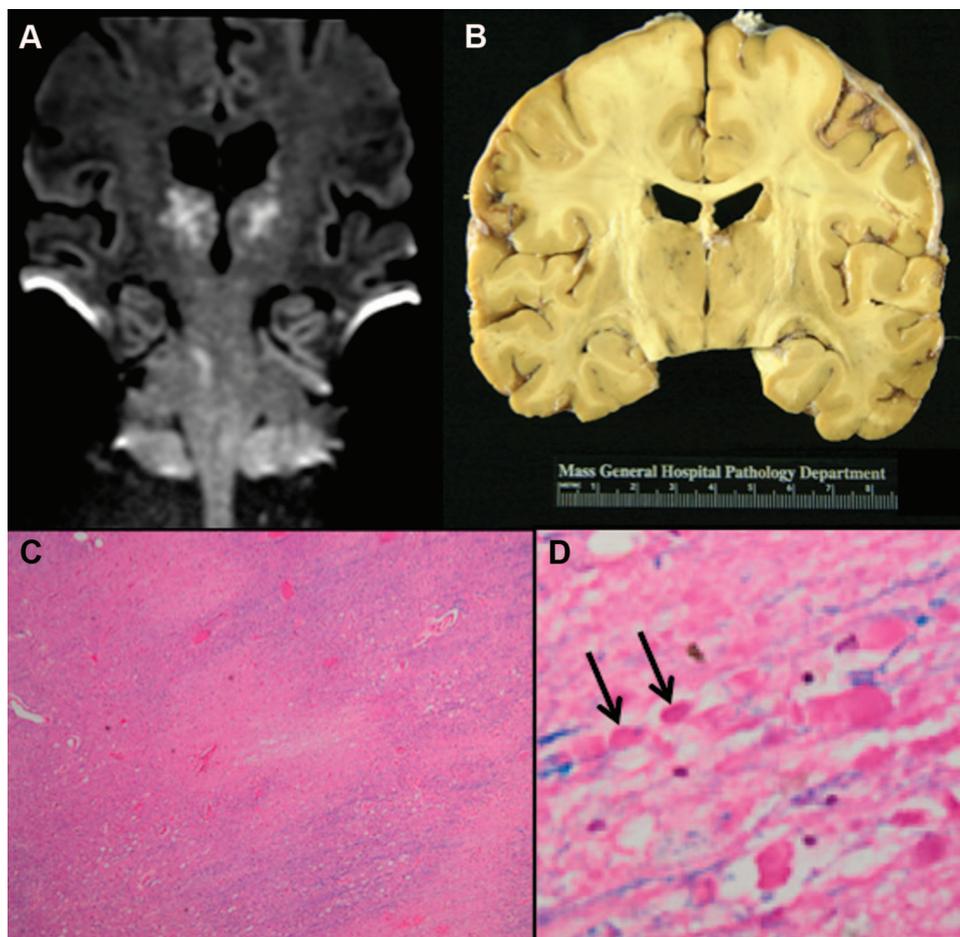
Fig. 3. Radiologic and histopathologic analysis of bithalamic infarcts. (*A*) Coronal diffusion-weighted imaging sequence through the thalami demonstrates bithalamic diffusion restriction as well as right pontine infarct (apparent diffusion coefficient map not shown). (*B*) Fixed brain demonstrates gross evidence of bithalamic necrosis and microhemorrhages. (*C*) Luxol fast blue with hematoxylin and eosin staining of thalamic section demonstrates small, irregular discrete areas of acute infarction. (*D*) Axonal spheroids are present in the surrounding thalamus adjacent to the lesions, consistent with ischemic injury (*black arrows*). The combination of small, distinct regions of infarction in (*C*) with axonal spheroids in (*D*) confirms that the ischemic lesions occurred because of occlusion of distal vascular beds, consistent with the hypothesis of microembolization.

imaging hyperintensities and apparent diffusion coefficient hypointensities in the posterior circulation territory (fig. 2, D and E). FLAIR imaging revealed more prominent gyral T2 hyperintensity (fig. 2F). On day 4, the patient remained comatose. Given the poor prognosis, the family withdrew life support, and the patient died shortly thereafter.

At autopsy, dissection of the posterior neck revealed soft tissue hemorrhage overlying the left C1–C2 facet joint. The cervical dura mater was intact. The vertebral arteries were patent, with no macroscopic evidence of injury to the cervical portions of the vertebral arteries. There was no atherosclerosis, dissection, or other vascular abnormality in the intracranial cerebral arteries.

Examination of the brain revealed diffuse tissue softening throughout the posterior circulation territory, including the pons, inferomedial left temporal lobe, left occipital lobe, cerebellar hemispheres, and bilateral thalami (fig. 3). Microscopic examination of paraffin-embedded sections revealed that the gross alterations (fig. 3B) corresponded to well-circumscribed areas of microvacuoliza-

tion of the neuropil and white matter, scattered red neurons, and axonal retraction balls—all indicative of acute infarction (fig. 3, C and D). Vascular congestion and petechial hemorrhages were present in the regions of ischemic injury. Attempts to identify intravascular embolic material with frozen sections from the formalin-fixed brain were not successful, reflecting the capacity of the material to dissolve during the postinjection, premortem period or during the 2-week period of fixation.

Discussion

The clinical, radiologic, and histopathologic data from this case provide new insights into the mechanism of stroke in cervical steroid injection. A needle advanced toward the C1–C2 facet joint may enter the vertebral artery with slight lateral deviation (fig. 1C). The absence of vertebral artery abnormality on computed tomography angiography or pathologic analysis rules out pseudoaneurysm or dissection.

The diffuse posterior circulation involvement is inconsistent with thromboembolism or vasospasm. Rather, the hyperacute, extensive FLAIR hyperintensity, cortical predominance of diffusion restriction, and histologic evidence of widespread posterior circulation infarction all support microvascular embolization of particulate macromolecules as the etiology of these infarcts.

The signal characteristics and evolution of signal changes on serial diffusion-weighted imaging, apparent diffusion coefficient maps, and T2-FLAIR imaging provide strong evidence for diffuse microvascular injury. FLAIR hyperintensity developed hyperacutely (fig. 2C) and involved a significantly larger volume of tissue than the diffusion-weighted imaging abnormality. Furthermore, much of the affected brain tissue exhibited increased, rather than decreased, signal on the apparent diffusion coefficient maps, just a few hours postictus. These signal changes are not characteristic of ischemic strokes and could be due to vasogenic edema. In addition, the cortical (fig. 2, A and B) and nuclear (fig. 3A) predominance of the lesions suggest that diffuse microvascular occlusion caused a greater ischemic burden on the more metabolically active neurons.

The postmortem microscopic analysis further supports the mechanism of diffuse microvascular injury. Vascular congestion identified throughout the posterior circulation territory is consistent with microvascular occlusion by particulate macromolecules in the steroid suspension. The water solubility of these particulate macromolecules may explain how they acted temporarily as microembolic agents but were later dissolved from the tissue and not identified after fixation and tissue processing.

The frequency of intravascular injection during cervical transforaminal injection may be as high as 63%, with approximately 15% of cases involving intraarterial injection.[9] Relying on aspiration to detect intravascular needle position is insufficient, given a reported sensitivity of less than 50% for intraarterial needle placement.[10] Alternative safety measures include injection of a test dose of contrast during continuous fluoroscopy with or without digital subtraction[11] and use of a flexible catheter extension to limit needle manipulation.[3]

The use of nonparticulate corticosteroid solutions has also been recommended[12] because particulate steroid suspensions contain particles (including the steroid itself and benzyl alcohol, carboxymethylcellulose sodium, and polysorbate 80 in the case of triamcinolone acetonide) that may aggregate into or promote aggregation of macromolecules with diameters greater than 100 μm.[12,13] The exact composition of these particulate macromolecules is not known, but they can occlude distal cerebral arteries whose diameters are as small as 50 μm. In contrast, nonparticulate steroid solutions do not carry the same risk of particles coalescing into macromolecules and, therefore, are less likely to occlude the distal cerebrovasculature. The danger of vertebral artery injection of particulate steroids has been confirmed in an animal study, in which stroke was caused by injection of particulate as opposed to nonparticulate steroids.[14]

It is clear that devastating neurologic injury can occur during cervical transforaminal or facet injection because of particulate steroid entering the posterior cerebral circulation. We call on all practitioners to perform cervical procedures only when the benefits clearly outweigh the risks, to provide adequate explanation of these risks during the informed consent process, and to adopt safety measures to minimize risk. In the specific case of cervical intraarticular facet injections, the benefit of this treatment is unclear; thus, practitioners should stop performing these injections altogether until further scientific evidence is available.

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