Vertebral Artery Dissection Complicating Occipital Injection of Heparin for Treatment of Thoracic Outlet Syndrome

Judy Melinek, MD and Amy P. Hart, MD

Abstract: A 38-year-old woman with a 2-year history of chronic neck pain radiating down her right arm underwent radiological and neurological evaluations, which revealed no anatomical cause for her pain. She sought alternative therapies including intramuscular heparin injections. Following a right occipital injection of heparin, cyanocobalamin, and lidocaine, she had a sudden cardiorespiratory arrest and was successfully resuscitated, but did not regain consciousness.

Computed tomography of the head and neck and subsequent autopsy revealed a right vertebral artery dissection, but at autopsy, no significant subarachnoid hemorrhage was noted at the base of the brain. This is the first case report where heparin (a potent anticoagulant) used in an occipital injection was documented to cause a vertebral artery dissection. It is also the first reported case where radiographically and histologically documented vertebral artery dissection did not present with overwhelming subarachnoid hemorrhage at the base of the brain. The subtle gross anatomical findings in this case highlight the importance of evaluating the cervical spinal cord in any case of sudden cardiorespiratory arrest following even apparently minor neck injury.

Key Words: vertebral artery dissection, therapeutic complication, thoracic outlet syndrome, heparin injection, autopsy

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Thoracic outlet syndrome (TOS) was first described in 1956 by Peet to define compression of neurovascular structures in the interscalene triangle. Also known as scalenus anticus syndrome, costoclavicular syndrome, cervical rib or first rib syndrome, its diagnosis and best treatment modalities still elicit controversy.[1] It is generally accepted that TOS is caused by compression of the brachial plexus neurovascular structures as they pass from the cervical area to the arm. The compression may be caused by congenital bony structures such as cervical ribs, fibromuscular bands or anomalies, or even posture and physical movements.[2] Incidence is estimated at 3 to 80 cases per 1000 population and is more common in women than in men. Some diagnosticians advocate dividing patients into 3 groups: (1) neurogenic TOS—those with compression of the brachial plexus; (2) vascular TOS—those with compression of the subclavian vessels; and (3) nonspecific TOS—consisting of a poorly defined chronic pain syndrome with features suggestive of brachial plexus involvement.[3] The latter, nonspecific type of TOS refers to patients with unexplained pain in the arm, scapular region, and cervical region, with no anatomical cause for their physical findings. Diagnosis is made by history, physical examination, provocative tests, ultrasound, radiological evaluation, and electrodiagnostic evaluation.[4] Conservative treatments include behavior modification by avoiding provocative activities or arm positions and physical therapy programs that strengthen the pectoral girdle muscles to help restore normal posture. Conservative management can help improve the condition in 50% to 90% of patients.[3] Definitive treatment involves the surgical decompression of the interscalene triangle with removal of the offending muscle band or rib and possible reconstruction of the damaged vessel, but even then, there is a low recurrence rate, often because of secondary scar tissue formation.[5] In the absence of identifiable anatomical cause for the pain, regional steroid injections, heparin injections, and local anesthetic injections have been suggested, but there is little published information on the success rate of these modalities.

CASE REPORT

A 38-year-old woman with a 2-year history of chronic neck pain radiating down her right arm underwent radiological and neurological evaluations, which revealed no anatomical cause for her pain. She sought alternative therapies including herbal supplements, massage, Feldenkrais passive-motion techniques, and intramuscular heparin injections. She had recurrence of her symptoms with onset of an occipital headache, which she reported was typical of headaches she had had in the past. A few hours after a therapeutic right occipital injection of heparin, cyanocobalamin, and lidocaine at a doctor's office, she complained of weakness, nausea, and worsening occipital and neck pain. She was taken to the hospital by ambulance because she was too weak to walk. At the emergency room, she was admitted and treated with first 2 mg, then 4 mg morphine sulfate for her severe pain. She received pain relief but did not appear somnolent, and approximately 4 hours later, she had an acute cardiorespiratory arrest. Before arrest, she appeared to be breathing normally, but she became tachycardic to 180, with her rhythm subsequently degenerating from sinus tachycardia to ventricular tachycardia. She was successfully intubated for a secondary respiratory arrest, and normal cardiac rhythm returned with a single defibrillator shock and administration of dopamine. However, she did not regain consciousness. Computed tomography scans of the head and neck were diagnostic of global anoxic-ischemic encephalopathy, but one scan of the neck (Fig. 1) showed an "irregularity" of the extracranial right vertebral artery, which was "suspicious for a right vertebral artery dissection." Two days later, she was removed from life support and died. The unexpected arrest of this young woman was initially clinically attributed to be possibly secondary to the therapeutic administration of pain medication in the emergency room, which prompted notification of the Office of the Chief Medical Examiner.

Autopsy Findings

A needle puncture mark was not identified at the back of the neck in the reported location. The 1450-g brain had diffuse edema and vascular congestion, but no grossly visualized subarachnoid hemorrhage at the base of the brain. The cervical

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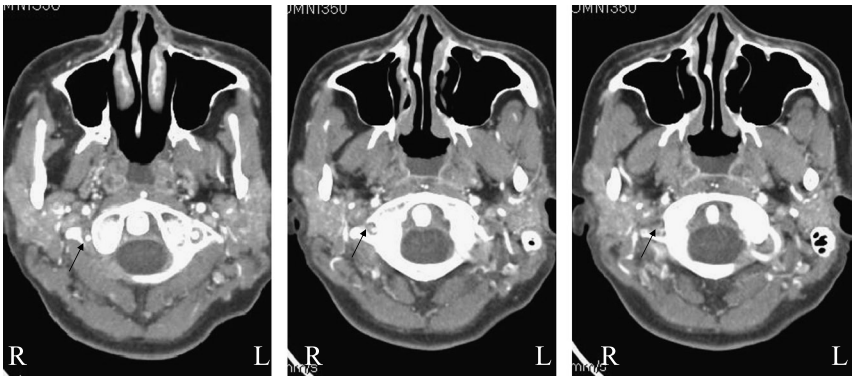

FIGURE 1. Radiographic findings. Computed tomography scan of the base of the skull and upper cervical vertebrae. Serial sections of computer tomography scan with contrast at the upper cervical levels indicate an irregular and poorly visualized right vertebral artery from transverse foramen of C1 to the origin of basilar artery, raising the possibility of dissection.

spinal cord demonstrated no external abnormality, but there was a thin layer of acute subarachnoid hemorrhage at the thoracic and lumbar levels, behind the dorsal columns (Fig. 2A). Transverse sections of the cord at 0.5-cm intervals were remarkable for an 8.0-cm-long area of central gray matter hemorrhage along the upper cervical spinal cord, without grossly apparent subarachnoid hemorrhage or discernible white matter damage (Fig. 2B). Microscopic sections of the cervical cord were remarkable for central cord perivascular acute hemorrhage and necrosis in association with very scant acute subarachnoid hemorrhage. Sections of the intracranial vertebral arteries confirmed the presence of an acute dissection (Fig. 3). Toxicologic testing of antemortem blood specimens collected on admission and after the cardiorespiratory arrest showed promethazine and morphine in the urine, but not in the blood at the time of cardiorespiratory arrest.

Based on these findings, the cause of death was determined to be anoxic-ischemic encephalopathy due to upper cervical spinal cord infarct due to right vertebral artery dissection due to complications of therapy for chronic neck pain.

Comment

The extracranial vertebral artery originates from the subclavian artery, courses through the spine within the intervertebral foramina, and is tethered by the dura at the point of intracranial penetration at the foramen magnum. The extracranial segments are common sites of traumatic dissection, as they are vulnerable to longitudinal stretching, whereas flexion and extension in the atlanto-occipital joint increase the risk of stretching at the intracranial segment. Unlike the internal carotid artery, which enters the skull through the narrow carotid foramen, which can stop the upward extension of the dissection, extracranial vertebral artery dissection extends intracranially in about 10% of cases.[6]

Localized cervical injections have been previously implicated in causing acute vertebral artery dissections, as have chiropractic manipulations and low-velocity trauma.[7,8] Typically, acute vertebral artery dissections due to manipulations or trauma have basilar subarachnoid hemorrhage. Reported iatrogenic complications can occur after transforaminal epidural steroid injections but can also occur complicating cerebral angiographic procedures.[9,10] However, spontaneous dissections can also occur in the absence of trauma, and these present with signs of neck pain or occipital headaches.[11] By definition, spontaneous dissections have no history of a predisposing traumatic incident, such as invasive procedures or manipulations. The incidence of spontaneous dissections ranges from 2.5 to 3 per 100,000 in the United States.[12] Spontaneous cervical arterial dissections

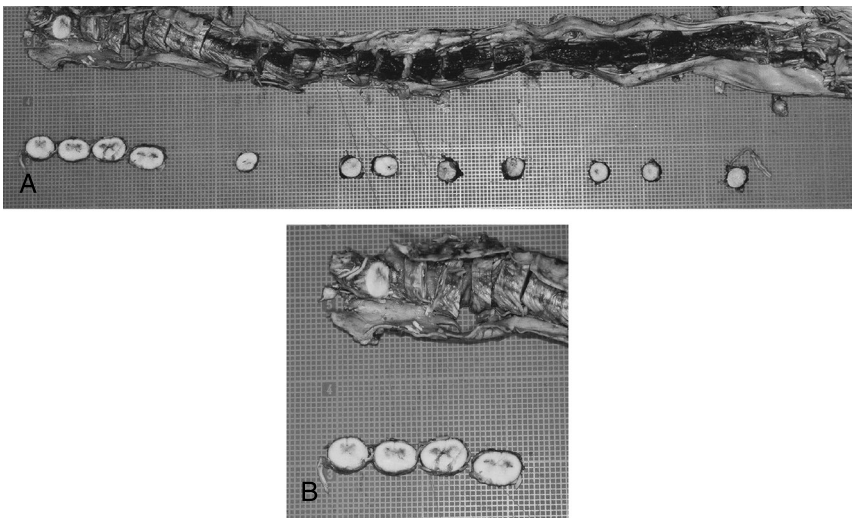

FIGURE 2. Gross pathological findings. A, Subarachnoid hemorrhage at midthoracic spinal cord. B, Cervical cord cross-sections demonstrate central necrosis.

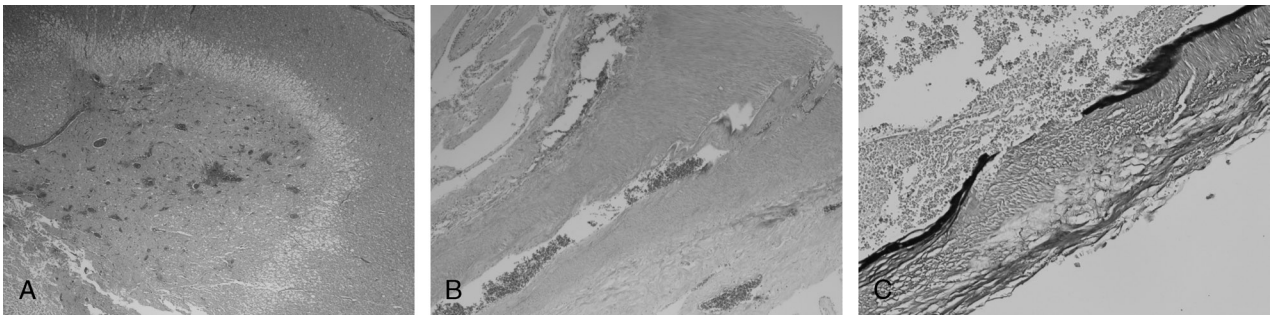

FIGURE 3. Microscopic findings. A, Hematoxylin-eosin stain of cervical spinal cord demonstrates central edema and necrosis. B, Hematoxylin-eosin stain of intracranial vertebral artery showing hemorrhage in arterial media. C, Elastic van Gieson stain highlights disruption of elastica.

account for about 25% of strokes in patients younger than 45 years.[6,13] They have no sex predilection, but appear to peak in the fifth decade, although women, on average, present 5 years earlier than men.[12] In several studies, hypertension appears to be a risk factor.[14] Seasonal increases in the presentation of spontaneous vertebral artery dissections during winter months have raised concerns of a possible infectious etiology, although this is not substantiated by the absence of inflammation on histopathology.[15] A family history of collagen vascular disease also appears to be a risk factor.[6,12] Half of patients with spontaneous vertebral dissections present with neck pain, and two thirds present with an occipital headache, and the median interval between the onset of neck pain to the appearance of other symptoms is 2 weeks.[16] Because symptoms may be interpreted as musculoskeletal in nature, diagnosis may be delayed, and it is sometimes unclear whether therapeutic modalities (such as cervical manipulations or injections) caused the dissection or were being used to treat a preexisting, undiagnosed dissection.

In this case, the delay between her presentation and autopsy (2 days) made it impossible to identify the needle track, either visually or radiographically. Thus, there was no way to definitively address whether a needle of the size the doctor reported he used could reach the vertebral artery from the point of injection. During subsequent investigations, discrepancies were identified between the length of the needle the doctor reportedly used (5/8 inch) and receipts from his office indicating what needle size he routinely orders and was noted to use by others (1.5 inches). Anatomical studies of this region in the orthopedic literature (to establish ideal size and angle of approach for cervical screw fixation) have demonstrated significant variability in the size and shape of the foramina and the depth of the vertebral artery among individuals.[17] The distance from surface of the skin to the vertebral artery is not a routine measurement noted at autopsy. Clearly, it would not represent the actual depth a needle could reach because gentle pressure could easily indent the skin and plunge a needle deeper than its length. However, this measurement should be considered by pathologists conducting autopsies in cases of vertebral artery dissection that are lacking antemortem radiological studies that would allow such a measurement.

Complicating the picture in this case investigation was the patient's utilization of alternative therapies including herbal medication, acupuncture, and Feldenkrais method passive-motion techniques. The herbal medications she used included chamomile, wild garlic, sandalwood, cumin, cardamom, *Terminalia chebula*, *Terminalia belerica*, and lavender. Although wild garlic is reported to have antiplatelet effects,[18] none of these have reported associations with coagulopathy or vascular injury. Acupuncture was last performed 9 days before she underwent injection and hospitalization. Acupuncture needles were placed on the legs, hand and on top of the shoulders, and at the proximal humerus; none were in the neck. Feldenkrais was last done 2 days before the occipital injection and admission to the hospital. Feldenkrais is a series of stretching maneuvers developed by Moshe Feldenkrais, DSc, and promoted by the Feldenkrais Educational Foundation of North America.[19,20] The method consists of slow, passive stretching exercises without high-velocity manipulations. All these were deemed unlikely sources of vertebral artery dissection. The most compelling association remains the temporal link between the occipital injection of heparin and her subsequent clinical exacerbation and the lack of subarachnoid hemorrhage at the base of the brain.

Heparin, besides being a potent anticoagulant, also has anti-inflammatory properties. It has been used to alleviate inflammation in asthma, adult respiratory distress syndrome, burns, ulcerative colitis, rheumatoid arthritis, and myocardial infarction.[21,22] However, there is little reported information on the efficacy of heparin in treating chronic pain syndromes, and the only report in the medical literature of heparin being used in injections for nerve entrapments was written by this patient's doctor, in a small cohort of patients from his clinical practice.[23]

In this case, the patient reported a 5-day history of a gradually worsening severe headache, getting worse over the last couple of days, and according to her physician, it was "typical" of the type of headache she would get with TOS. The patient had no family history or evidence at autopsy of a collagen vascular disease. In addition, the autopsy showed no evidence of localized infection or inflammation. The subarachnoid hemorrhage suspected on the computed tomography scan was not visualized at autopsy, but there was subarachnoid hemorrhage seen at the thoracolumbar segment of the spinal cord, suggesting that during the survival interval it may have drained down the cord. Although it is not possible to completely rule out that a contained, minimally symptomatic spontaneous dissection occurred before the injection, the clinical picture in this case showed a dramatic exacerbation with weakness starting immediately upon injection and progressing to nausea, vomiting, and cardiac arrest in the hours following the injection. These are indicative of progressive cerebral edema and impending herniation. Thus, the combination of the clinical history, reported location of the injection site, the radiographic findings of the right vertebral irregularity in the extracranial vertebral artery, and the microscopic dissection in the intracranial portions of the vertebral artery in the absence of subarachnoid hemorrhage at the base of the brain supports that idea that the starting point

of the dissection was in the cervical area and the dissection reentered the lumen in the intracranial portion sampled histologically.

This is the first case report where heparin (a potent anticoagulant) was used in an occipital injection implicated in causing a vertebral artery dissection. Furthermore, this is the first reported case where a radiographically and histologically documented acute vertebral artery dissection did not present with significant subarachnoid hemorrhage at the base of the brain. The subtle gross anatomical findings in this case highlight the importance of evaluating the cervical spinal cord and vertebral arteries, using either the anterior or posterior approach,[24] in any case of sudden cardiorespiratory arrest following even apparently minor neck injury or following a cervical therapeutic procedure.

REFERENCES

1. Talu GK. Thoracic outlet syndrome. *Ağri*. 2005;17(2):5–9.
2. Cooke RA. Thoracic outlet syndrome—aspects of diagnosis. *Occup Med*. 2003;53:331–336.
3. Vanti C, Natalini L, Romeo A, et al. Conservative treatment of thoracic outlet syndrome: a review of the literature. *Eura Medicophys*. 2007;43:55–70.
4. Ruckley CV. Thoracic outlet syndrome. *Br Med J*. 1983;287(13): 447–448.
5. Urschel H, Razzuk MA. Neurovascular compression in the thoracic outlet: changing management over 50 years. *Ann Surg*. 1998;228(4):609–617.
6. Campos-Herrera CR, Scaff M, Yamamoto FI, et al. Spontaneous cervical artery dissection: an update on clinical and diagnostic aspects. *Arq Neuropsiquiatr*. 2008;66(4):922–927.
7. Rubinstein SM, Peerdeman SM, van Tulder MW, et al. A systematic review of the risk factors for cervical artery dissection. *Stroke*. 2005;36:1575–1580.
8. Katz M. Arterial dissections after cervical manipulation. *CMAJ*. 2002;166(10):1253.
9. Inamasu J, Guiot BH. Iatrogenic vertebral artery injury. *Acta Neurol Scand*. 2005;112(6):349–357.
10. Scanlon GC. Cervical transforaminal epidural steroid injections: more dangerous than we think? *Spine*. 2007;32(23):2638.
11. Iizuka T. Headaches and spontaneous vertebral artery dissections. *Intern Med*. 2002;41:1094–1095.
12. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. *NEJM*. 2001;344(12):898–906.
13. Thanvi B, Munshi SK, Dawson SL, et al. Carotid and vertebral artery dissection syndromes. *Postgrad Med J*. 2005;81:383–388.
14. Arnold M, Kappeler L, Georgiadis D, et al. Gender differences in spontaneous cervical artery dissection. *Neurology*. 2006;67(6):1050–1052.
15. Paciaroni M, Georgiadis D, Arnold M, et al. Seasonal variability in spontaneous cervical artery dissection. *J Neurol Neurosurg Psychiatry*. 2006;77:677–679.
16. Silbert PL, et al. Headache and neck pain in spontaneous internal carotid and vertebral artery dissections. *Neurology*. 1995;45:1517–1522.
17. Ebraheim NA, Reader D, Xu R, et al. Location of the vertebral artery foramen on the anterior aspect of the lower cervical spine by computed tomography. *J Spinal Disord*. 1997;10(4):304–307.
18. Cupp MJ. ed. *Toxicology and Clinical Pharmacology of Herbal Products*. Totowa, NJ: Humana Press; 2000:118.
19. The Feldenkrais Method of Somatic Education, Research Bibliography. Available at: http://www.feldenkrais.com/resources/bibliography/. Accessed June 29, 2010.
20. Buchanan PA, Ulrich BD. The Feldenkrais method: a dynamic approach to changing motor behavior. *Res Q Exerc Sport*. 2001;72(4):315–323.
21. Tyrell DJ, Kilfeather S, Page CP, et al. Heparin in Inflammation: potential therapeutic applications beyond anticoagulation. *Adv Pharmacol*. 1999;46:151–208.
22. Dotan I, Hallak A, Arber N, et al. Low dose molecular weight heparin (enoxaparin) is effective as adjuvant treatment in active ulcerative colitis: an open trial. *Dig Dis Sci*. 2001;46(10):2239–2244.
23. Ellis W. Heparin alleviates pain in nerve entrapments. *AJPM*. 2003;13(2):54–59.
24. Aggrawal A, Setia P. Vertebral artery dissection revisited. *J Clin Pathol*. 2006;59:1000–1002.

