Spinal Epidural Hematoma Following Epidural Steroid Injection in a Patient Treated with Dabigatran

A Case Report

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Lumbar epidural steroid injections are commonly employed in the treatment of degenerative lumbar conditions. The procedure is generally accepted as safe, and few complications have been reported in the literature. An exceedingly rare complication of epidural steroid injection is a spinal epidural hematoma. Although millions of epidural steroid injections have been completed since 1960[1-3], to our knowledge, there have been no more than fifteen reported cases of epidural hematoma related to epidural steroid injections[4-16]. A review of these reports reveals that nearly all of the patients involved were taking anticoagulants near the time of injection. In October 2010, the U.S. Food and Drug Administration (FDA) approved the use of a novel anticoagulant called *dabigatran* (Pradaxa; Boehringer Ingelheim Pharmaceuticals, Ridgefield, Connecticut) for the prevention of stroke in patients with atrial fibrillation. In Europe and Canada, the drug also has been approved for the prevention of thromboembolism in patients undergoing total joint arthroplasty.

Dabigatran has experienced a rapid increase in popularity in the orthopaedic community because it has several benefits over enoxaparin and warfarin. Unlike enoxaparin, dabigatran is administered orally. Unlike warfarin, dabigatran has minimal monitoring requirements and few drug-drug and drug-food interactions, and it becomes therapeutic within hours instead of days[17].

Currently, to the best of our knowledge, there are no known cases in the literature of dabigatran-associated complications after epidural steroid injections. Recent clinical trials involving over 20,000 patients treated with dabigatran did not identify a single case of spinal epidural hematoma[17,18]. The patient was informed that data concerning the case would be submitted for publicaton, and he provided consent.

Case Report

History

A seventy-year-old man presented with ongoing symptoms of lower back pain and bilateral leg pain for four months. Neurological examination revealed full motor strength in the bilateral lower extremities and no sensory deficits. The symptoms had developed insidiously, and he had no history of trauma. Magnetic resonance imaging (MRI) of the lumbar spine revealed severe canal and foraminal stenosis at L4-L5 (Fig. 1-A).

Notably, the patient had a history of atrial fibrillation for which he was being treated with dabigatran (150 mg twice daily). The patient previously had taken warfarin for this condition;

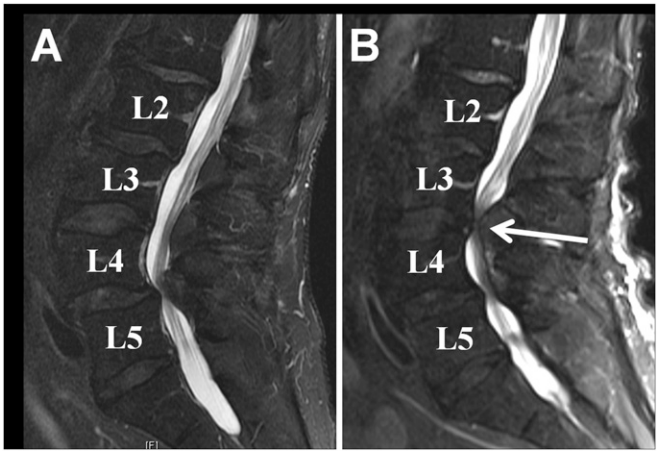

Fig. 1

Sagittal T2-weighted MRI of the lumbar spine taken prior to (**Fig. 1-A**) and after (**Fig. 1-B**) the epidural steroid injection. The development of an acute stenotic lesion (arrow) after the injection is apparent at L3-L4.

Disclosure: None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. None of the authors, or their institution(s), have had any financial relationship, in the thirty-six months prior to submission of this work, with any entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. Also, no author has had any other relationships, or has engaged in any other activities, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

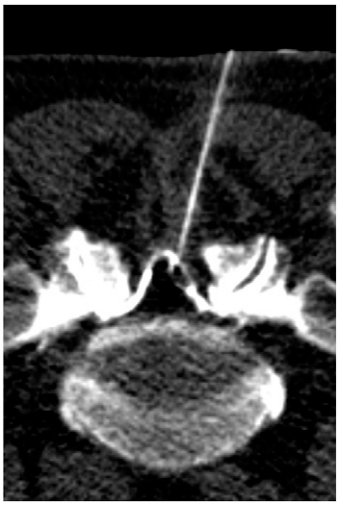

Fig. 2
Axial CT imaging shows the needle placement during an epidural steroid injection. Contrast can be seen filling the epidural space at L4-L5.

he had been converted to dabigatran six months earlier under the recommendation of the cardiologist.

Procedure
The patient was referred for a lumbar computed tomography (CT)-guided epidural steroid injection. Prior to proceeding with the injection, the patient discontinued the dabigatran for seven days. During the procedure, a twenty-two gauge spinal needle was inserted into the central epidural space at L4-L5 (Fig. 2). The position of the needle in the central epidural space was confirmed with the injection of 0.2 mL of iopamidol contrast media. Also injected was a mixture of 1.5 mL of triamcinolone (40 mg/mL) and 1.0 mL of bupivacaine (0.5%). The needle was withdrawn, and hemostasis was achieved with use of direct pressure at the injection site. The patient tolerated the procedure well and immediately noted substantial improvement in the pain.

Postoperative Course
The patient restarted the dabigatran twenty-four hours after the injection. At that time, he had nearly complete resolution of the symptoms. Forty-eight hours after the injection, he began to develop numbness in the bilateral lower extremities. Upon initial examination, he had nearly complete paraplegia of the bilateral lower extremities. An emergency MRI (Fig. 1-B) was obtained; it revealed an acute stenotic lesion centered at L3-L4, which had not been present on the previous MRI. The patient was immediately taken to the operating room for decompression.

Because the patient had restarted dabigatran, hematology was consulted for evaluation of the clotting status and reversal of anticoagulation. Preoperative laboratory values revealed a normal prothrombin and partial thromboplastin time, as would be expected with dabigatran. A thrombin clotting time test was ordered; it revealed a markedly elevated value of more than 120 seconds (normal, 16.6 to 24.3 seconds), consistent with therapeutic dabigatran. Although the patient was being treated at a major academic medical center, no appropriate reversal factors were immediately available for administration. Given his rapidly deteriorating neurological status, the decision was made to proceed with emergency surgery despite the increased risk of bleeding. Multiple units of packed red blood cells were made readily available in anticipation of substantial blood loss. Midway through the case, 1100 IU of Profilnine (Factor IX, Factor II, Factor X, and Factor VII concentrate) was transfused after it arrived via emergency courier from an outside facility. A laminectomy from L3 to L5 was completed. Upon exposure of the epidural space, a large hematoma from L3 to L5 was identified. The hematoma was evacuated, and the wound was inspected for sites of active hemorrhage. Although no large bleeding vessels were identified, there was extensive venous oozing. Hemostasis was achieved with use of Gelfoam and bipolar electrocautery. A single subfascial drain was placed during closure.

Postoperatively, the patient's neurological status improved. He was deemed to have made a full neurological recovery six months after surgery. At fifteen months postsurgery, he had not experienced any complications.

Discussion

Epidural steroid injections are among the most common medical procedures performed in the United States. It is estimated that 6.8 million epidural injections were completed in 2005, representing a 121% increase from 1998[3]. The procedure is widely accepted as safe, with a low risk of serious complications.

Among the complications reported, spinal epidural hematomas are exceedingly rare. Since the first description of an epidural steroid injection in the United States in 1960[1,5], to our knowledge, there has been a total of only fifteen reports of associated spinal epidural hematoma (Table I)[4-16]. In several large series of epidural steroid injections, there was not a single case of spinal epidural hematoma[19-25]. Given the exceedingly rare frequency with which this complication occurs, it is difficult to make any conclusions regarding the incidence or risk. The best estimates come from an extrapolation of the anesthesia literature, which includes several large studies of epidural procedures in obstetrical and perioperative settings. The largest of these studies cite an incidence of spinal epidural hematoma in the range of 1 in 150,000 to 1 in 250,000[26-29]. However, the actual risk for epidural steroid injections may be substantially lower than these values because these steroid injections use small needles and do not involve the placement of indwelling catheters.

With such a small number of reported cases, it is also difficult to identify definite risk factors for epidural hematoma formation after epidural steroid injection. However, a review of the literature reveals that nearly all of the reported cases involved patients who were being treated with medical anticoagulation (Table I).

The patient described in this case report was being treated with the novel anticoagulant dabigatran. Dabigatran is a direct thrombin inhibitor that is administered orally; it was approved by the FDA in October 2010 for patients with atrial fibrillation. It reaches peak plasma concentration within two hours of administration and has a half-life of twelve to seventeen

TABLE I Summary of Cases of Spinal Epidural Hematoma Associated with Epidural Steroid Injection Previously Reported in the Literature

Author	Anticoagulant	Time to Symptoms
Swerdlow (1982)[16]	Unknown	Unknown
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Williams et al. (1990)[13]	Indomethacin	1 Hour
Horlocker and Wedel (1998)[10]	Enoxaparin	3 Days
Horlocker and Wedel (1998)[10]	Enoxaparin, ibuprofen	2 Days
Yagi et al. (1998)[9]	None	2 Hours
Benzon et al. (1999)[15]	Diclofenac, clopidogrel, aspirin	14 Hours
Ghaly (2001)[14]	Diclofenac	2 Hours
Siddiqui et al. (2001)[6]	Pentosan polysulfate sodium	8 Hours
Stoll and Sanchez (2002)[7]	Ibuprofen	8 Days
Ain and Vance (2005)[11]	Warfarin, enoxaparin	2 Days
Snarr (2007)[12]	Warfarin	7 Days
Yoo et al. (2009)[8]	None (idiopathic thrombocytopenic purpura)	1 Day
Xu et al. (2009)[5]	Aspirin, warfarin, enoxaparin	2 Days
Shanthanna and Park (2011)[4]	Warfarin	20 Minutes

hours[30]. Beyond its cardiac use, dabigatran is rapidly increasing in popularity among orthopaedic surgeons. It was recently approved in Canada and Europe for routine prophylaxis of thromboembolic disease following hip or knee replacement. Perceived benefits of dabigatran over enoxaparin or warfarin include its oral administration, minimal drug-drug and drug-food interactions, rapid therapeutic effect, and lack of monitoring requirements.

As part of the FDA approval process, two large multicenter studies of dabigatran were conducted in the United States[17,18]. A review of the data from these studies reveals no reported cases of spinal epidural hematoma in over 20,000 studied patients. Although use of the drug continues to increase, in December 2011 the FDA launched an investigation in response to 260 bleeding deaths worldwide between 2008 and 2011[31]. It is unclear at this time what the results of that investigation will reveal.

To date, there is no consensus regarding how long to hold administration of dabigatran prior to epidural steroid injections or how long to wait before restarting the medication after the injection. The Mayo Pharmaceutical Formulary Committee advises that dabigatran be discontinued for one to five days before invasive or surgical procedures[32]. Although there are no official recommendations on when to restart dabigatran after injections, recent publications advise waiting twenty-four hours[31].

At the time of emergency decompression, our patient had been therapeutically anticoagulated with dabigatran. In evaluating coagulation status, it is important to note that prothrombin time and partial thromboplastin time do not accurately assess the effects that dabigatran has on clotting. The most accurate laboratory tests for a direct thrombin inhibitor are thrombin time and ecarin clotting time, both of which are specialized laboratory studies that are only available at a limited number of institutions.

Currently, there is no established reversal protocol for dabigatran. In patients with renal insufficiency, dialysis may be effective[30]. However, this is often impractical in emergency settings. Established reversal agents such as protamine sulfate (heparin reversal) and vitamin K (warfarin reversal) have no substantial effect on the anticoagulant activity of dabigatran[33]. Furthermore, there is no evidence that systemic hemostatics (e.g., desmopressin, aprotinin, tranexamic acid, or aminocaproic acid) or plasma products (e.g., fresh-frozen plasma) have any reversal effect[34]. There are several anecdotal reports and nonclinical studies describing the use of recombinant activated factor VII and prothrombin complex concentrate for reversal[35,36]. However, the use of these agents is based on sparse data, and their effectiveness cannot be validated at this time[34]. Based on our experience with this case, we advise that clinicians investigate the availability of specialized laboratory studies and experimental reversal agents at their institutions before considering interventions in patients who are on dabigatran therapy. ■

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