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Case Report

Spinal subarachnoid and subdural hematoma presenting as a Brown-Séquard-like myelopathy following minor trauma in a patient on dabigatran etexilate

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ABSTRACT

Dabigatran etexilate is a relatively new anticoagulant from the class of direct thrombin inhibitors which is administered orally and does not require routine blood work monitoring. Dabigatran may be attractive to both clinicians and patients because of both its convenience and efficacy; however, clinical complications are still being elucidated. Here, we present a previously unreported case of spinal subarachnoid and subdural hematoma presenting as a Brown-Séquard-like myelopathy in a patient after minor trauma in the setting of Dabigatran anticoagulation.

Background

Patients on anticoagulant treatment carry an increased risk of developing spinal hematoma, possibly leading to unforeseen neurologic sequelae. The development of spontaneous spinal epidural hematoma secondary to warfarin use, the oldest anticoagulant used in clinical practice, is well known [1–3]. In the setting of spontaneous spinal epidural hematoma, however, only one case report identifies warfarin administration leading to an episode of Brown-Séquard syndrome (BSS) [4]. Although spinal hematoma is a known cause of BSS, anticoagulant use as the initial trigger is rarely reported.

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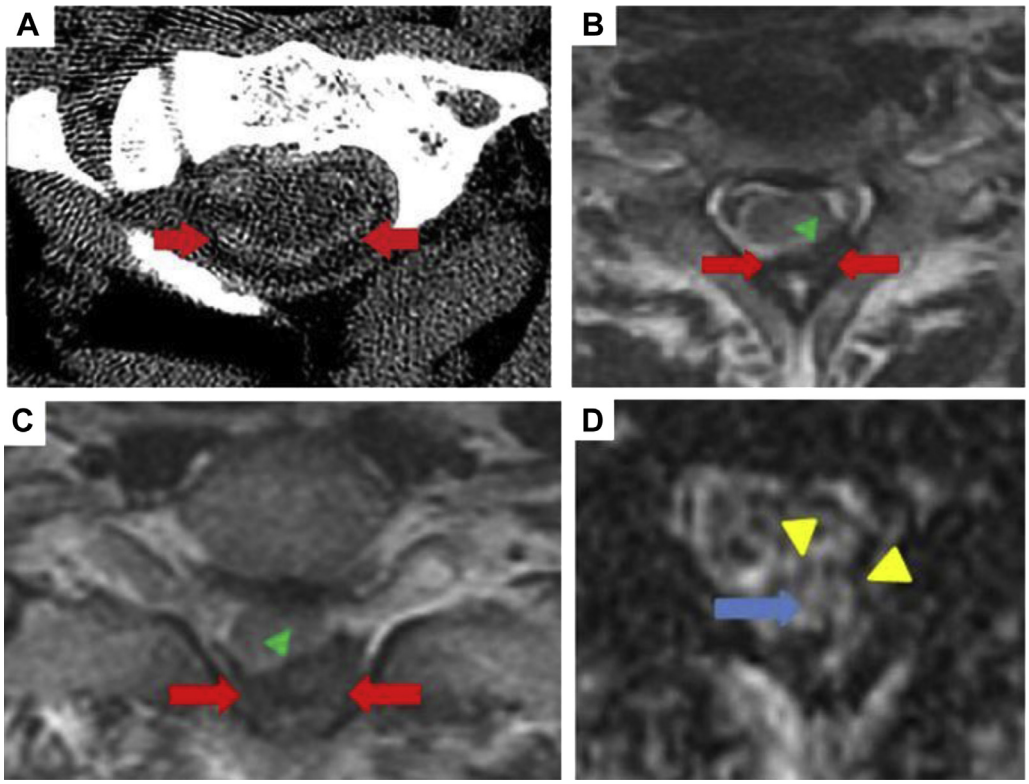

Fig. 1 – Axial CT image (A) demonstrates high-density material surrounding the cervical spine (red arrows), suspicious for subarachnoid hematoma. Two consecutive MR axial T2-weighted images (B and C) at the C6/C7 level demonstrate hypointense crescent-shaped signal (red arrows) compressing the cord posterolaterally (green arrows), consistent with subdural hematoma. GRE sequences of the lesion (D) show mixed signal intensity (blue arrow) with a hypointense rim (yellow arrows), indicating an early subacute hemorrhage with surrounding hemosiderin. CT, computed tomography; GRE, gradient echo.

Low-molecular-weight heparin, such as enoxaparin, has also been reported to cause spontaneous spinal hematomas, but not BSS [5]. Rivaroxaban and apixaban, gaining approval by the Food and Drug Administration in 2011 and 2012, respectively, carry a lower risk of bleeding complications. However, both oral anticoagulants have been implicated in cases of traumatic spinal epidural hematoma [6,7] and nontraumatic spinal subdural hematoma [8–10]. Dabigatran etexilate is a novel oral anticoagulant, from the class of univalent direct thrombin inhibitors, initially approved by the Food and Drug Administration in 2010. Dabigatran has a standard dosing based on creatinine clearance and does not require any routine bloodwork monitoring [11]. However, the true clinical risks and complications of dabigatran anticoagulation therapy are still being elucidated [12]. Here, we present a previously unreported case of spinal subarachnoid and subdural hematoma, presenting as a Brown-Séquard-like myelopathy, in the setting of dabigatran etexilate anticoagulation therapy and minor trauma.

Case report

A 67-year-old man, taking dabigatran for paroxysmal atrial fibrillation, presented to the emergency department with a 1-day history of left lower extremity weakness and urinary retention. The patient reported having had minor trauma 1 day prior, described as being “shoved in the back” without fall or loss of balance. He denied any pain at the time of the incident. However, he subsequently developed pain in his neck and upper back within approximately 1 hour. Later that day, the patient's pain worsened and he began experiencing unilateral weakness in his left lower extremity and difficulty urinating. He also reported general fatigue. He denied any weakness in his other extremities, headache, numbness, or any perceived changes in mental status. The patient also denied any recent history of gingival bleeding, hemoptysis, hematuria, or melena. The patient reported to the emergency department the following day because of persisting symptoms.

The patient's past medical history was significant for atrial fibrillation, endocarditis, polycystic kidney disease with renal transplant, hypertension, benign prostate hyperplasia treated with transurethral resection of the prostate, osteoarthritis, obstructive sleep apnea, and melanoma. His home medications included dabigatran, metoprolol, sotalol, alendronate, atorvastatin, cholecalciferol, coenzyme q10, dutasteride, mycophenolate mofetil, prednisone, tamsulosin, and trazodone. Patient was also taking tacrolimus, a prostaglandin-p inhibitor, which may increase dabigatran bioavailability [11,13,14]. Otherwise, the patient was not taking any other prostaglandin-p inducers or inhibitors. Finally, he had no significant history of smoking or alcohol usage.

On presentation, patient's vital signs were remarkable only for some borderline hypertension (154/85 mm Hg). Physical examination was remarkable for diminished power with absent proprioception and vibratory sensation in his left lower extremity in addition to absent pain and temperature sensation in his right lower extremity. His deep tendon reflexes were absent in the left lower extremity. There was no topical evidence of injury at the site of trauma including no evidence of skin bruising or edema. Coagulation profile yielded a slightly elevated prothrombin time (PT) of 13.7s and a partial thromboplastin time (PTT) within normal limits at 31.5 seconds. The international normalized ratio was 1.33. The patient's creatinine was 1.0, and estimated glomerular filtration rate was 74.5 mL/min. The patient's hemoglobin (15.8 gm/dL), hematocrit (49.1%), and platelets (176 k/uL) were all within normal limits. The patient's urine exam was also unremarkable, with no evidence of gross or microscopic hematuria.

Based on patient's alarming neurologic signs and symptoms, consistent with BSS, imaging studies were ordered including non-contrast–enhanced computed tomography of the head, cervical spine, thoracic spine, and lumbosacral spine followed by noncontrast magnetic resonance (MR) imaging of the cervical and thoracic spine. Computed tomography images demonstrated evidence suspicious for subarachnoid hematoma surrounding the cervical and upper thoracic spine measuring up to 4 millimeters (Fig. 1). Examination of the bony structures and soft tissues was otherwise unremarkable including no evidence of vertebral fracture or subluxation and no evidence of superficial soft tissue bruising. MR imaging of the cervical and thoracic spine revealed isointense T1 and decreased T2 signal along the cervicothoracic spine, measuring up to 10 millimeters in width. In addition, focal areas of isointense T1 and decreased T2 signal were identified with associated posterolateral cord flattening and anterior displacement. The epidural fat was preserved and otherwise unremarkable. The findings were consistent with acute diffuse subarachnoid hematoma involving the thecal sac of the cervicothoracic spine with a focus of acute subdural hematoma causing anterolateral cord displacement.

The patient was admitted to the medical intensive care unit with neurology and neurosurgery consultation. Dabigatran was held, and intravenous solumedrol therapy was initiated. Idarucizumab, the recently approved reversal agent for dabigatran, was not immediately available and the patient refused hemodialysis. A Foley was placed to manage the patient's urinary retention. Pain control was effectively managed with intravenous hydromorphone. Patient's clinical status improved to baseline over the course of several days, with the patient's symptoms fully resolved in 2 days' time. Interval MR studies obtained 1 week after the onset of symptoms demonstrated resolution of patient's subdural hematoma and a small amount of residual subarachnoid blood. Dabigatran therapy was resumed 2 weeks after the onset of symptoms on an outpatient basis.

Discussion

Dabigatran etexilate offers a convenient option for anticoagulation in the management of patients at risk for complications of AF, prevention of recurrent PE and DVT, and even treatment of existing PE and DVT [11]. While there have been a number of reported cases of intracranial hemorrhage in the setting of dabigatran use [15,16], to our knowledge, there have not been any reported cases of spinal cord hemorrhage or a Brown-Séquard-like myelopathy. In addition, nearly all previously reported cases involved significant trauma, such as a fall or accident [15], as opposed to the minor shoving incident in our case. We do not believe the minor trauma caused the bleeding; direct cause and effect are difficult to prove in these cases. Spinal bleeding from other causes such as vascular malformations, lumbar puncture, bleeding diatheses, spinal surgery, or spinal tumors were ruled out based on our clinical investigation.

Admittedly, BSS is rare and oftentimes difficult to diagnose because the clinical picture shows a variety of neurologic signs whose severity ranges from mild to severe. The appearance of a pure form of BSS, characterized by a total hemisection of the cord, is rarely encountered. The less pure forms with a clinical presentation characterized by some signs and symptoms of BSS, plus additional ones which are not specific of this injury are more commonly seen, which fits the description of our case.

One potentially confounding factor in our case is the concurrent use of tacrolimus, a known prostaglandin-p inhibitor, which thus may affect dabigatran bioavailability and potentially cause an increased risk for bleeding. That said, however, the patient's coagulation profile only demonstrated a minimally elevated PT and a normal PTT, 13.7 seconds and 31.5 seconds, respectively. A recent in vitro study suggested an increase of up to 111% and 231% in PT and PTT, respectively, in the concomitant use of dabigatran and tacrolimus [14]. In addition, a recently reported case regarding bleeding in the setting of dabigatran and tacrolimus also demonstrated significantly elevated PT and PTT of 46.1 seconds and 75.1 seconds, respectively [17].

Despite concomitant use of tacrolimus, thrombin time or the diluted thrombin time was not investigated. However, there was no evidence or laboratory findings of supratherapeutic anticoagulation, including gingival bleeding, melena, anemia, microscopic hematuria, or other clinical stigmata of coagulopathy at the time of presentation.

Our case illustrates the need for vigilance when working up patients with focal neurologic deficits who are receiving dabigatran anticoagulation therapy. Any new neurologic deficits in patients on dabigatran etexilate therapy should be particularly investigated for spinal syndromes (such as Brown-Sequard syndrome among others), in order to diagnose spinal hematoma or exclude this serious bleeding complication.

REFERENCES

[1] Yabe H, Ishii A, Niikawa N, Matsubayashi H, Kakei M, Kawakami M, et al. An elderly patient who developed spontaneous spinal epidural hematoma during warfarin therapy. Intern Med 2012;51(11):1429–32.
[2] Sandvig A, Jonsson H. Spontaneous chronic epidural hematoma in the lumbar spine associated with Warfarin

intake: a case report. Springerplus 2016;5(1):1832. eCollection 2016.
[3] Kobayashi Y, Nakada J, Kuroda H, Sakakura N, Usami N, Sakao Y. Spinal epidural hematoma during anticoagulant therapy for pulmonary embolism: postoperative complications in a patient with lung cancer. Ann Thorac Cardiovasc Surg 2014;20 Suppl:493–6.
[4] Maingi M, Glynn MF, Scully HE, Graham AF, Floras JS. Spontaneous spinal epidural hematoma in a patient with a mechanical aortic valve taking warfarin. Can J Cardiol 1995;11(5):429–32.
[5] Heppner PA, Monteith SJ, Law AJ. Spontaneous spinal hematomas and low-molecular-weight heparin. Report of four cases and review of the literature. J Neurosurg Spine 2004;1(2):232–6.
[6] Jaeger M, Jeanneret B, Schaeren S. Spontaneous spinal epidural haematoma during factor Xa inhibitor treatment (Rivaroxaban). Eur Spine J 2012;21(supplement 4):S433–5.
[7] Radcliff KE, Ong A, Parvizi J, Post Z, Orozco F. Rivaroxaban-induced epidural hematoma and cauda equina syndrome after total knee arthroplasty: a case report. Orthopaedic Surg 2014;6(1):69–71.
[8] Zaarour M, Hassan S, Thumallapally N, Dai Q. Rivaroxaban-Induced nontraumatic spinal subdural hematoma: an uncommon yet life-threatening complication. Case Rep Hematol 2015;2015:275380.
[9] Castillo JM, Afanador HF, Manjarrez E, Morales XA. Non-traumatic spontaneous spinal subdural hematoma in a patient with non-valvular atrial fibrillation during treatment with rivaroxaban. Am J Case Rep 2015;16:377–81.
[10] Dargazanli C, Lonjon N, Gras-Combe G. Nontraumatic spinal subdural hematoma complicating direct factor Xa inhibitor treatment (rivaroxaban): a challenging management. Eur Spine J 2016;25 Suppl 1:100–3.
[11] Pradaxa US Prescribing Information. Ridgefield: Boehringer Ingelheim Pharmaceuticals, Inc; 2015. Available at: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf. Accessed 25 Nov 2015.
[12] Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139–51.
[13] Hart R, Benavente O, McBride R, Pearce LA. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. Ann Intern Med 1999;131(7):492–501.
[14] Sayani S, Iqbal O, Hoppensteadt D, Fareed J. Drug interactions of newer oral anticoagulants dabigatran, rivaroxaban, and apixaban with routinely used nonanticoagulant/antiplatelet drugs. Paper presented at the 56th American Society of Hematology Annual Meeting and Exposition, San Francisco, USA. Received online. Available at: https://ash.confex.com/ash/2014/webprogram/Paper73247.html.
[15] Garber S, Sivakumar W, Schmidt R. Neurosurgical complications of direct thrombin inhibitors—catastrophic hemorrhage after mild traumatic brain injury in a patient receiving dabigatran. J Neurosurg 2012;116:1093–6.
[16] Komori M, Yasaka M, Kokuba K, Matsuoka H, Fujimoto S, Yoshida M, et al. Intracranial hemorrhage during dabigatran treatment: case series of eight patients. J Japan Circ Society 2014;78:1335–41.
[17] Lehman N, Bryant G, Bender J, Koenigsfield C, Logemann C, Sayler M. Left subconjunctival hemorrhage • renal dysfunction • international normalized ratio of 4.5 • Dx? J Fam Pract 2015;64(10):E3–4.