

Received: 2014.12.16
Accepted: 2015.02.26
Published: 2015.06.19

ISSN 1941-5923
© Am J Case Rep, 2015; 16: 377-381
DOI: 10.12659/AJCR.893320

Non-Traumatic Spontaneous Spinal Subdural Hematoma in a Patient with Non-Valvular Atrial Fibrillation During Treatment with Rivaroxaban

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 69
Final Diagnosis: Spontaneous spinal subdural hematoma
Symptoms: Paraplegia
Medication: Rivaroxaban
Clinical Procedure: —
Specialty: General Internal Medicine • Hospital Medicine • Cardiology • Hematology • Neurology

Objective: Diagnostic/therapeutic accidents





Background: Spontaneous spinal subdural hematoma (SSDH) is a rare but disabling condition, accounting for only 4.1% of all intraspinal hematomas. Risk factors include arteriovenous malformations, coagulopathy, therapeutic anticoagulation, underlying neoplasms, or following spinal puncture. Vitamin K antagonists, antiplatelet agents, and heparinoids have been associated with SSDHs in prior reports. To the best of our knowledge, no cases have reported this association with the factor Xa inhibitor, rivaroxaban, and SSDHs.

Case Report: We report the case of a 69-year-old Honduran man with a 5-year history of symptomatic palpitations due to non-valvular atrial fibrillation. He was initially refractory to pharmacologic therapy. He underwent cardioversion in February 2014. After cardioversion, he remained asymptomatic on flecainide. He was anticoagulated on rivaroxaban 20 mg daily without incident since early 2013 until presentation in August 2014. He presented with sudden onset of excruciating upper and lower back pain after minimal movement. This was immediately followed by bilateral lower extremity paresis rapidly progressing to paraplegia with bowel and bladder dysfunction over 15 minutes. Magnetic resonance imaging demonstrated an acute spinal subdural hematoma extending from T3 inferiorly to the conus medullaris. Six months after undergoing cervical and lumbar drainage procedures, he has not recovered bowel, bladder, or lower extremity neurologic function.

Conclusions: Non-traumatic spontaneous spinal subdural hematoma is a rare neurological emergency that may occur during the use of rivaroxaban in patients with non-valvular atrial fibrillation. Physicians should suspect SSDH in patients on rivaroxaban with acute onset of severe back pain and neurologic symptoms to improve the odds of a favorable outcome.

MeSH Keywords: Anticoagulants • Atrial Fibrillation • Hematoma, Subdural, Spinal

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/893320>

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Background

Spontaneous spinal subdural hematoma (SSDH) is a rare but disabling condition, accounting for only 4.1% of all intraspinal hematomas [1]. Although the exact etiology is uncertain, risk factors include arteriovenous malformations, coagulopathy, therapeutic anticoagulation, underlying neoplasms, or following a spinal puncture (iatrogenic) [1,2]. Out of 106 cases of non-traumatic acute SSDHs, 37 cases (35%) were associated with acute or chronic anticoagulation [2].

Vitamin K antagonists, antiplatelet agents, and heparinoids have all been associated with SSDHs in prior reports [2–6]. Currently, there are 4 FDA-approved novel oral anticoagulants (NOACs) available for use for therapeutic anticoagulation in atrial fibrillation. However, to the best of our knowledge, no studies have documented a non-traumatic spontaneous SSDH during treatment with the factor Xa inhibitor, rivaroxaban, or other NOACs. We present a case of a 69-year-old man with atrial fibrillation on rivaroxaban who presented with lower extremity paraplegia and was found on magnetic resonance imaging (MRI) to have a spontaneous SSDH.

Case Report

A 69-year-old Honduran man was transferred to our hospital with lower extremity paraplegia. He had a 5-year history of atrial fibrillation with a CHA₂DS₂-VASc score of 2 (age 65–74 years and hypertension). He was initially refractory to pharmacologic therapy. He underwent unsuccessful pulmonary vein isolation ablation in September 2013, then cardioversion in February 2014. After the cardioversion, the patient remained asymptomatic on flecainide 100 mg twice daily. He was anticoagulated on rivaroxaban 20 mg daily without incident since early 2013 until his presentation to our hospital in August 2014. His only other medical history included hypertension, which was well-controlled on irbesartan 300 mg daily.

The patient was in his usual state of health when he presented to his cardiologist in Honduras for a routine follow-up on July 31, 2014. After a routine electrocardiogram, the patient was sitting up and felt a sudden onset of excruciating pain in his upper and lower back. This pain was followed immediately by bilateral lower extremity paresis that progressed to complete paraplegia with bowel and bladder dysfunction over 15 minutes. The patient was taken to a local hospital where an MRI was performed that demonstrated a spinal subdural and subarachnoid hematoma extending from T5 to the cauda equina (widest portion at T7-8) with some intramedullary enhancement noted. A diagnosis of transverse myelitis was made and he received treatment with steroids and pain medications without clinical improvement during his 3 days of

hospitalization. He was continued on his home medications excluding rivaroxaban, which was stopped on admission. Of note, his anticoagulation was not reversed with vitamin K or plasma in Honduras. Due to lack of clinical improvement, the family brought him to Miami for further evaluation. He was initially admitted to a community hospital, and then transferred to our facility for further comprehensive evaluation on August 8, 2014.

On admission, the patient reported stable paraplegia but with increasing loss of sensory level from T10 up to approximately T8 level. He denied upper extremity complaints. His bowel and bladder dysfunction persisted, requiring a urinary catheter. The patient denied history of spinal anesthetic procedures, tuberculosis, trauma, injuries, recent traveling, weight loss, or parasitic infections. He denied usage of herbal supplements, selective serotonin reuptake inhibitors (SSRIs), antifungal medications, or other medications that could have potentially interacted with rivaroxaban.

On physical exam, the patient was found to have 5/5 strength in upper extremities bilaterally, 0/5 strength in lower extremities with areflexia, no clonus, negative Babinski, and no sensation to light touch, pinprick, or proprioception up to level of approximately T8. Although laboratory results done in Honduras were unavailable, the family reported all were within the normal values, including a normal PSA. Initial laboratories at our hospital were also within normal limits except for a slightly elevated prothrombin time of 13.0 seconds (normal value 10.1–12.6 seconds), mild thrombocytopenia with platelets of 106 K/ μ L (normal range 140–400 K/ μ L), and hyponatremia with a sodium of 130 mmol/L (normal range 137–145 mmol/L). The elevated prothrombin time and thrombocytopenia normalized when repeated during the hospitalization without intervention. An MRI on admission demonstrated evolving subdural hematoma extending from T3 level inferiorly to the conus medullaris, which terminated at the L1 level (Figure 1). Abnormal low signal was identified within the central cord, suggestive of hematomyelia. Moderate compression of the thoracic cord and conus medullaris were noted.

The patient was initially considered for complete thoracic laminectomy and intradural washout of blood product by neurosurgery. However, due to the extensive blood that was now visualized filling the lumbar thecal sac, neurosurgery determined placement of lumbar and cervical drains was the best option for potential neurological recovery. Two days after admission, the patient underwent attempted drainage insertion at both cervical and lumbar region. The lumbar drain was placed but immediately clogged due to liquefied blood that, despite multiple attempts to flush the drain, would not drain appropriately. Drain insertion at C1-C2 site was performed without complications. Bloody cerebrospinal fluid (CSF) was immediately obtained and

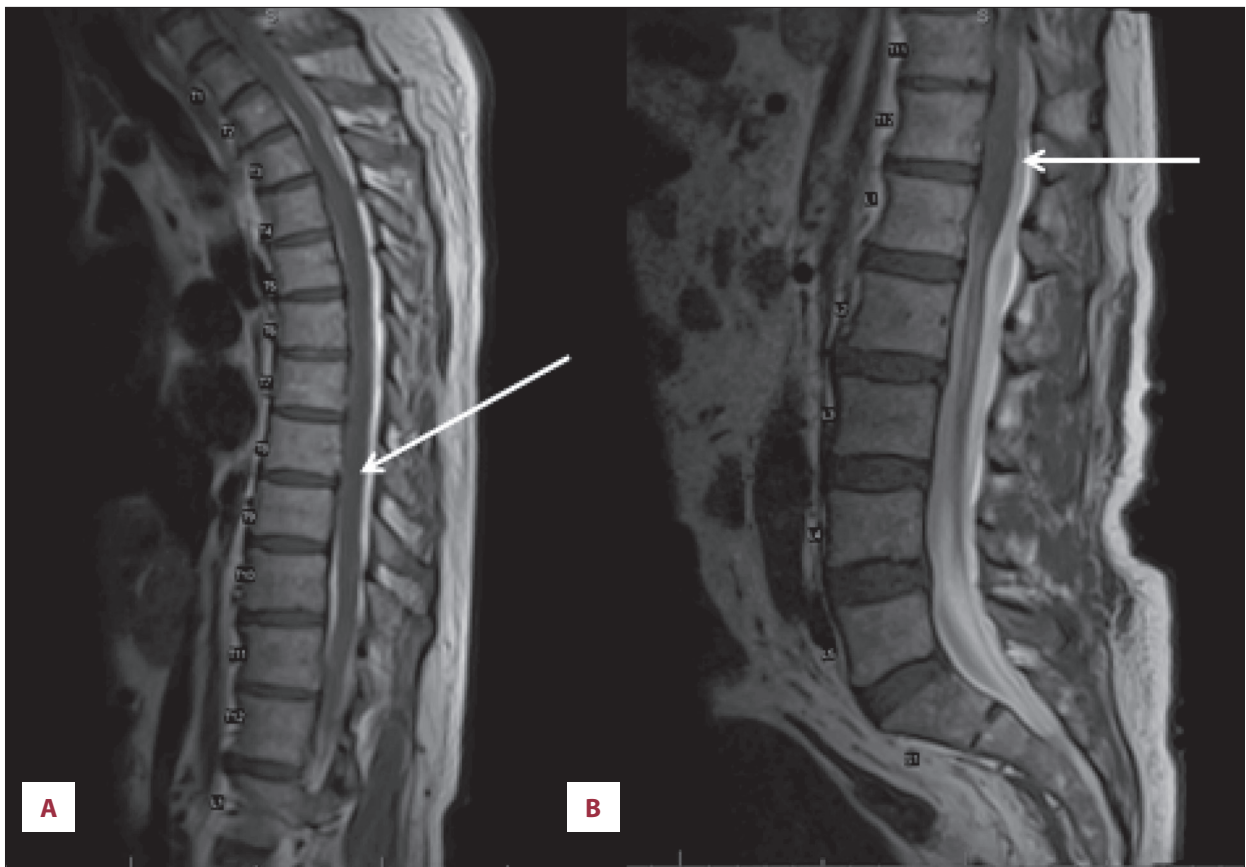


Figure 1. Magnetic resonance imaging images: (A) The T1-weighted sagittal image of the thoracic spine illustrates the extensive heterogeneous signal predominately in the subdural space extending from the T3 level inferiorly with cord expansion (arrow). (B) The T1-weighted sagittal image of the lumbar spine demonstrates the evolving blood products (arrow) predominately in the subdural space throughout the lumbar spine inferiorly to the conus.

continued to drain slowly at approximately 10 milliliters (mL) per hour. CSF drains were removed 14 days after placement after CSF remained consistently clear for several days. CSF cultures were negative. The hospital course was complicated by a urinary tract infection treated appropriately. The urinary catheter was removed and bladder dysfunction was managed with periodic straight catheterization. The hyponatremia persisted throughout hospitalization, so further laboratory investigations were done. The patient was found to have a low serum osmolality of 263 mOsm/kg (normal range 275–295 mOsm/kg), high urine osmolality (790 mOsm/kg), and high urine sodium excretion (96 mmol/L). The results were consistent with a SIADH presentation, presumed secondary to central nervous system disturbance. Once fluid was restricted, his sodium remained slightly low (134 mmol/L) but improved at the time of discharge without sodium supplementation. Clinically, the neurological exam results remained unchanged with no functional ability below approximately the T8 level throughout the hospitalization.

The patient was discharged to a rehabilitation center on hospital day 29 for further treatment. While in the rehabilitation

center, a repeat MRI 6 weeks after initial presentation in Miami illustrated interval decrease in the subdural and subarachnoid spinal canal hemorrhages, but no significant change in the signal abnormality and expansion representing edema extending from C4 level inferiorly to the conus medullaris (Figure 2). The patient was finally discharged home to Honduras to continue physical rehabilitation 8 weeks after presentation. The paraplegia persisted at the time of discharge home in October 2014. On follow-up contact with the patient and family, the patient continued to do home physical therapy. However, 6 months after undergoing cervical and lumbar drainage procedures here, he has not recovered bowel, bladder, or lower extremity neurologic function.

Discussion

To the best of our knowledge, this is the first reported case of a non-traumatic SSDH associated with a NOAC, in this case, rivaroxaban. This case is important because front-line practitioners may not have an index of suspicion for this diagnosis

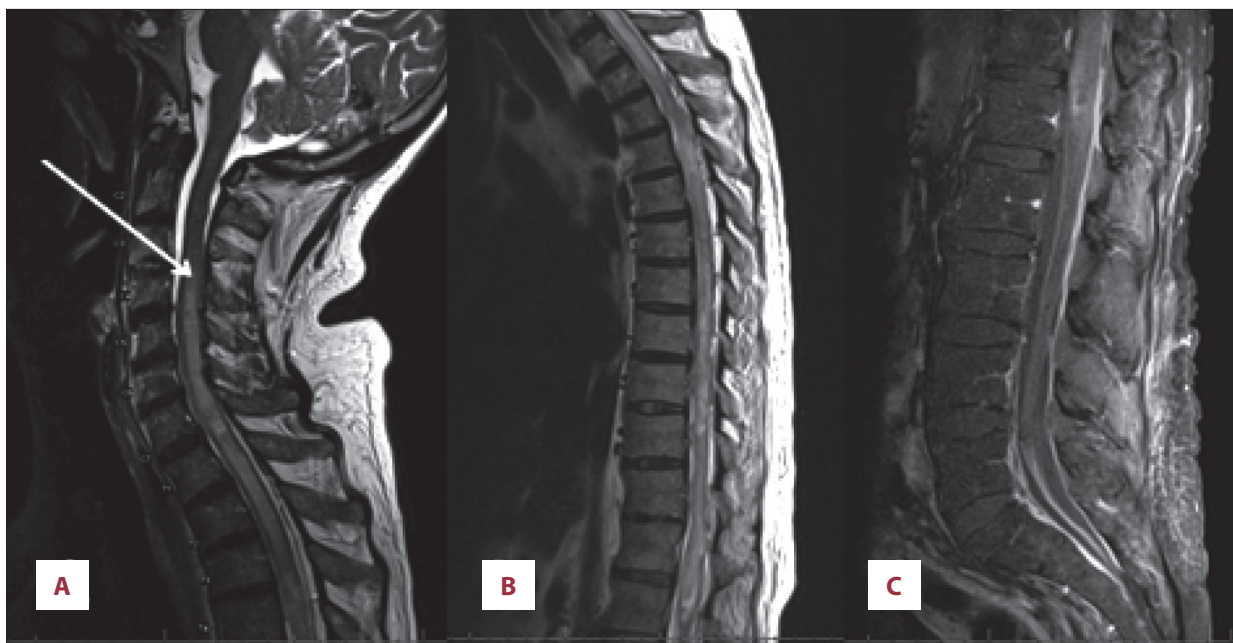


Figure 2. Magnetic resonance imaging images: (A) The T2-weighted sagittal image of the cervical spine shows the extension of signal abnormality from the C4 level (arrow) inferiorly through the visualized upper thoracic cord. (B) The T2-weighted sagittal image of the thoracic spine demonstrates the diffuse signal abnormality within the cord, representing cord edema. (C) The T1-weighted sagittal image of the lumbar spine illustrates the degeneration of blood products.

given the safety profile of the NOACs as they have been marketed to practitioners.

Regarding diagnosis, the most common presenting symptom of spontaneous SSDH is progressive motor weakness. Almost half of all patients will experience some type of spinal or radicular pain, described as an intense, knife-like pain at the location of the hematoma [2]. Our patient followed the very classical presentation of this condition. Unfortunately, given that this diagnosis is very rare, the diagnosis was missed due to lack of clinical suspicion.

Treatment most frequently consists of a laminectomy and surgical evacuation of the hemorrhage. Conservative management may also be considered for those with minimal neurological deficits or those considered medically high risk for surgery [2,3]. For those with rapid deterioration of neurological status, early surgical management is essential.

Outcomes were found to be poor (paraplegia and/or subarachnoid hemorrhage) in 58% of patients who had a late surgical intervention such as in this patient [2]. Due to a misdiagnosis at presentation and necessity for transfer to a higher level of care, this patient had a delay in initiation of treatment.

The exact mechanism of subdural bleeding remains unknown but is thought to be related to the sudden increase of pressure in the thoracic or abdominal cavities. This increased pressure is hypothesized to also raise the pressure of the vessels

traversing the subdural and subarachnoid space, and if the CSF is unable to regulate the fluid, the vessels may rupture, leading to a SSDH [7]. Our patient had minimal movement rising from a supine position, which could have contributed to increased abdominal or thoracic pressure.

Collectively speaking, SSDHs are the rarest of all spinal hematomas, but often lead to devastating effects [1]. The first case of an SSDH was described by Schiller et al. in 1948 [8]. A literature review of 106 cases of non-traumatic SSDHs found that 35% were on treatment with short- or long-term anticoagulant therapy [2]. Vitamin K antagonists, antiplatelet agents, and heparinoids have been associated with SSDHs in prior reports [2–6]. One case reported a patient taking warfarin, who presented to the emergency room with sudden excruciating lower back pain and flaccid paralysis and was found to have an acute SSDH [4]. Four cases of spinal hematomas (1 subdural and 3 epidural) were described in patients on treatment doses of low-molecular-weight heparin [5]. Another report found an SSDH in a patient on aspirin following a spinal anesthesia procedure [6]. At present, there have been only 2 case reports of any type of spinal hematoma with a patient taking an NOAC [9,10]. However, both cases reported the more common epidural spinal hematoma rather than a subdural hematoma, as in our patient. Jaeger et al. described the case of a patient on rivaroxaban for prevention of venous thromboembolic events following an orthopedic surgery of the lower extremity that developed an epidural spinal hematoma [9]. The other case

reported a patient treated with dabigatran who developed an epidural spinal hematoma following an epidural steroid injection [10]. To the best of our knowledge, this is the first report of a non-traumatic SSDH in a patient receiving treatment with a NOAC, in this case, rivaroxaban.

For more than 50 years, warfarin was the only oral anticoagulant effective in preventing cardio-embolic stroke in patients with atrial fibrillation, reducing the risk of stroke by approximately two-thirds [11]. Unfortunately, warfarin has many disadvantages, including need for frequent laboratory monitoring, variability of dose response, and drug and food interactions [11]. NOACs were developed to address these disadvantages of warfarin. There are 4 FDA-approved NOACs for use in patients with non-valvular atrial fibrillation for stroke prevention. These medications include factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban) and a direct thrombin inhibitor (dabigatran). All have been compared in large randomized, double-blind trials with warfarin and reported risks of major bleeding and intracranial hemorrhages [12–15]. In comparison to warfarin, rivaroxaban and dabigatran were found to have comparable risks of major hemorrhage [12,13]. Apixaban and edoxaban were found to have significantly lower risk of major hemorrhage compared to warfarin [14,15]. All 4 NOACs were found to have a significantly lower incidence of intracranial hemorrhage compared to warfarin [12–15]. Although spinal hemorrhage was not reported in the large studies, one may consider a relationship between intracranial and spinal hemorrhages.

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Both intracranial and spinal hemorrhages involve the central nervous system (CNS) and may lead to devastating neurological outcomes, as seen in our patient. This is important because clinicians must consider CNS hemorrhage in a presentation of acute neurologic symptoms in patients taking NOACs.

Our patient was indicated for anticoagulation for atrial fibrillation with a CHA₂DS₂-VASc (congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, female) score of 2, estimating a moderate-high risk of 3.7% stroke risk per year [16]. His bleeding risk while on anticoagulation as calculated by the HAS-BLED score was at 3.4% risk per year [17], a relatively low risk of bleed.

Conclusions

Non-traumatic spontaneous SSDH is a rare neurological emergency that may occur during the use of rivaroxaban in patients with non-valvular atrial fibrillation. Physicians should suspect SSDH in patients on rivaroxaban with acute onset of severe back pain and neurologic symptoms to improve the odds of a favorable outcome.

Conflict of interest

The authors declare they have no conflicts of interest.