

Could anticoagulation with Rivaroxaban have precipitated a spinal epidural hematoma: From independent mobility to paraplegia

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Abstract

A 81 year-old male, with atrial fibrillation and a bovine prosthetic valve on aspirin and rivaroxaban, presented with acute back pain, limb weakness and paraplegia within six hours. Urgent spine magnetic resonance imaging showed a massive epidural bleed from T1 to T12. A spontaneous spinal epidural hematoma (SSEH) was diagnosed. The exact etiology remains unclear, however, it was believed to have been secondary to the patient's underlying hypertension and modest hypocoagulation. Urgent decompression offers the best probability of neurologic recovery, however, the patient was not a surgical candidate as the cord had infarcted and the risk of a fatal intra-operative bleed was high. He was ultimately transferred for rehabilitation on aspirin. His spinal cord injury was graded as T10 American Spinal Injury Association (ASIA) Grade B. Anticoagulation was never restarted and the patient received an atrial appendage closure to reduce the risk of clot formation. To our knowledge, this is the first report of a long segment SSEH and adverse reaction to rivaroxaban with unusually rapid and permanent neurologic sequelae.

Background

Spontaneous spinal epidural hematomas (SSEH) were first described by Jackson in 1869.¹ It is rare and estimated in incidence at 0.1 per 100,000 people, but carries devastating neurological morbidity.²⁻⁴ A spontaneous bleed is defined as one not associated with lumbar puncture, spinal anaesthesia, blunt force trauma, blood dyscrasias, vascular malformations, or tumours.^{2,5-8} SSEH should be suspected in any anticoagulated patient who presents with new onset back pain associated with paraparesis, altered sensation, or bowel and bladder dysfunction.^{2,9,10}

Urgent spinal MRI remains the gold standard in localizing and examining the craniocaudal extension of the hematoma as well as demonstrating the compressive effects on the cord.¹¹⁻¹³ Early decompressive laminectomy and hematoma evacuation remain most effective at preventing permanent neurological sequelae if performed within twelve hours from the onset of symptoms related to cord compression.¹⁴⁻¹⁷

We present our case for several reasons. Despite a typical presentation and rapid neurosurgical workup under eight hours, the patient suffered an extensive bleed and concomitant cord infarct, making him a poor candidate for successful surgery. Therefore, SSEH has the potential for rapid and permanent neurologic compromise despite attempts at prompt decompression. Such a case has not been reported with rivaroxaban. To our knowledge, only a single case of SSEH with ibuprofen and rivaroxaban has been presented where conversely, the patient made a complete and spontaneous recovery.¹⁸ Second, our case poses a dilemma on whether to resume antithrombotic therapy. Discontinuing therapy increases the risk of a cardioembolic stroke, whereas restarting it raises the possibility of a recurrent bleed.

Case presentation

An 81 year-old male with a history of paroxysmal atrial fibrillation

(AF) (CHADS2 score 4) and a bovine aortic valve on rivaroxaban (Xarelto) 20mg daily and low-dose aspirin, presented with sudden onset, sharp mid-thoracic back pain that started while at rest. There was no history of recent surgery, spinal anaesthesia, or trauma. He was previously mobilizing and functionally independent. His past medical history included hypertension, hyperlipidemia, and a history of multiple transient ischemic attacks. He was initially treated with low-dose aspirin and warfarin from 2002 until August 2014, when he was changed to rivaroxaban because of labile International Normalized Ratio (INR) values.

On presentation to the Emergency Room, he complained of excruciating back pain and bilateral lower extremity paraparesis, but was able to demonstrate a non-antalgic gait. Six hours later, while awaiting investigations, the patient lost all motor function in his lower extremities and noted no sensation to light touch or painful stimuli below his waist.

On examination, the patient was alert and oriented with a blood pressure of 155/65 and a pulse of 90 bpm and regular. There was no blood pressure asymmetry between the upper limbs. He had a normal head, neck, cardiovascular, and abdominal physical exam. A neurological exam revealed complete loss of sensation and flaccid paralysis below T10 bilaterally. There was no spasticity, clonus, or Babinski reflex at the toes. Rectal tone and a bulbocavernosus reflex were absent.

Investigations

The INR was elevated at 1.7, but the platelet count and activated partial thromboplastin time (aPTT) were normal. Renal function was also preserved. Thrombin time was not measured.

Spinal MRI and a computed tomography (CT) scan revealed an extensive long segment hyperacute dorsal epidural hematoma that extended from T1 to T12 (Figure 1). Cord compression was diffuse but worst at the T9 T10 level. The hematoma measured 10x15 mm at its maximum extent in cross section. There was no dural arteriovenous (AV) fistula or vascular malformation noted.

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Figure 1 | Sagittal T2 weighted MRI image demonstrating an extensive epidural hematoma extending from T1 to T12 spinal level.

Differential diagnosis

The differential diagnosis included a spinal abscess, tumour, transverse myelitis, and an acute disc herniation. However, the above findings and radiological evidence were consistent with an atraumatic SSEH on dual antithrombotic therapy, which as previously reported, is rare.

Treatment

SSEH is a neurosurgical emergency, and early decompressive laminectomy and hematoma evacuation remain the treatment of choice.^{14,15} Non-surgical treatment is only valid if the neurologic deficits resolve spontaneously soon after onset or in cases without neurological deficits or cases with advanced and irreversible spinal cord injury.¹⁹

Given our patient's neurologic deficits and above findings, it was felt the spinal cord had already infarcted, making him a poor candidate for successful surgery. Due to the lack of an antidote to rivaroxaban, the patient remained anticoagulated, which increased his risk of a fatal intra-operative bleed. Accordingly, non-surgical management was recommended and further anticoagulation was held, including deep vein thrombosis prophylaxis.

Outcome and follow-up

Thoracic spinal CT scans performed two and four weeks after the patient's initial presentation showed no further bleeding and no new abnormalities to suggest a previously missed vascular malformation or AV fistula. Low-dose aspirin was restarted two weeks after without recurrence of symptoms. A month later, he regained scant sensation in the sacral region but had not gained any sensory or motor function in his lower extremities. Accordingly, his injury was graded a T10 American Spinal Injury Association (ASIA) grade B injury, and the patient transferred for inpatient rehabilitation. He also remained incontinent of both bowel and bladder function, and as such, he continues to receive intermittent urinary catheterization and bowel care to manage these routines.

Given his neurologic deficits, he was engaged in physiotherapy aimed at improving his functional independence with transfers and wheel chair mobility.

Restarting anticoagulation, however, posed a dilemma. Off anticoagulation, he faced a 5% per year risk of a cardioembolic stroke, whereas restarting anticoagulation increased the possibility of a recurrent bleed.²⁰ Ultimately, the patient received a percutaneous left atrial appendage closure device to reduce the risk of clot formation.

Discussion

In the background of anticoagulation, though rare, a SSEH should be considered in cases of sudden onset back pain with symptoms of spinal cord compression. It represents 40% of all spinal epidural bleeds, whereas anticoagulation therapy accounts for 17% of such cases.^{21,22} The exact cause remains unknown.⁶ The literature cites an association with the use of anticoagulants, antiplatelet therapy, thrombolysis, hypertension, or a coagulopathy such as haemophilia or leukemia.^{19,23-28} In our patient, the combined antiplatelet effect of aspirin and Factor Xa inhibition by rivaroxaban likely contributed to modest hypocoagulation. With a concomitant history of hypertension, the cause was likely multifactorial.

Non-steroidal anti-inflammatory drugs such as aspirin often cause a transient but modest increase in bleeding time.²⁹ Typically, this does not exceed the reference limits unless combined with an anticoagulant. It does not, however, explain the INR at 1.7. This was likely secondary to rivaroxaban, as the patient denied using warfarin for over three months. Rivaroxaban has been shown to be effective in non-valvular AF, as evaluated in the ROCKET trial (Rivaroxaban—once daily, Oral, direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation).³⁰ The incidence of major bleeding was found to be comparable between rivaroxaban and warfarin at 3.6% and 3.4% respectively.³⁰ Major bleeding included intracranial and spinal bleeds, amongst others. With the addition of aspirin, we expect the risk of major bleeding to be increased. Smith *et al.* have reported that routine coagulation assays like the INR and aPTT are ineffective at determining the presence and concentration of novel anticoagulants, including rivaroxaban.³¹ They often test normal, and elevated levels may be consistent with supratherapeutic concentrations. As such, it would have been difficult to acutely determine the patient's anticoagulation status. He was likely excessively anticoagulated, given the elevated INR and concurrent aspirin use. However, our patient had valvular AF, and we were unable to find literature supporting the use of rivaroxaban. He had been started on this agent in the community due to labile INR values, albeit warfarin remains the

agent of choice in patients with valvular AF.

The most common site of an epidural spinal hemorrhage is the thoracic spine, which was evident in our patient.³¹ The bleeding is believed to originate from the epidural venous plexus.^{6,22} This explains why the majority of all epidural hematomas are located posterior to the cord, which is in the vicinity of the venous plexus, as seen in our case.²⁰ This network of weakened veins or “locus minoris resistentiae” can rupture on sudden increases in thoracic or abdominal pressure.^{6,22} Our patient was at rest during the onset of symptoms and as such, we do not believe this was a contributory factor.

SSEH has been shown in nearly all age groups but is predominantly seen in patients between 55 and 70 years of age.²¹ This is likely because such patients are often on an anticoagulant medication or suffer from hypertension, all of which are recognized as precipitants of SSEH. The gender ratio (male:female) is 1.4:1.¹⁰ The best choice for imaging is an urgent spine MRI, because it is non-invasive and able to localize and measure the longitudinal extension of the hematoma as well as demonstrate cord compression and signal changes characteristic of cord infarction.¹¹⁻¹³ The age of the hematoma can also be determined because the signal intensity changes over time.³³ Early MRI images appear isointense or hypointense on T1-weighted images and hyperintense on T2-weighted images.³³ Most importantly, an MRI can distinguish SSEH from a differential that includes a spinal neoplasm, abscess, acute disc herniation, and transverse myelitis, while identifying underlying vascular anomalies like AV malformations, vertebral hemangiomas, or hemorrhagic tumours that may cause an epidural bleed.³² MRI imaging performed on our patient demonstrated a hyperacute spinal epidural hematoma, thus confirming the diagnosis. It helped with treatment planning because the patient was found to be a poor operative candidate given evidence of global cord infarction secondary to compression from the hematoma. It also ruled out an underlying vascular anomaly that may have triggered the SSEH. Repeat CT scans confirmed no new vascular abnormalities that may have been overlooked on the original MRI.

The most common clinical symptom of an epidural spinal hematoma is a sharp, knife-like pain at the level of the bleed, followed by altered sensation and paralysis below the affected level due to compression of the spinal roots and cord.^{34,35} Complete sensorimotor loss including a flaccid muscle tone, saddle anaesthesia, and loss of rectal tone suggest cord infarction, all of which signify irreversible cord injury. These findings were evident in our patient, making him a poor candidate for surgery. Consequently, he was treated conservatively. Apart from this indication, non-surgical management can only be considered if the neurologic deficits resolve spontaneously soon after onset or in cases without neurological deficits.

The treatment for SSEH is reversal of anticoagulation and an urgent decompressive laminectomy and hematoma evacuation. The neurologic recovery varies with the severity of the preoperative deficit and the operative interval.³⁴⁻³⁶ In a study by Foo *et al.*, 45% of patients with complete neurological deficit returned to baseline function after surgery versus 95% who had incomplete deficits.³⁵ Preoperative cord infarction was not present in either of these patients. A review by Liu *et al.* reported that a long segment hematoma predicted a poorer prognosis as well.³⁸ Finally, the possibility of

complete neurologic recovery was greatest if surgery was performed within 12 hours from presentation.^{15,16} Therefore, despite a rapid surgical workup under eight hours, the severity of cord compression from the extensive hematoma and resultant cord infarct rendered an extremely poor prognosis for successful decompression. Consequently, the patient was managed non-surgically.

In rivaroxaban trials, spinal hematomas were not encountered.³⁹ Prior to our case, Jaeger *et al.* reported a patient who developed a SSEH while on ibuprofen and rivaroxaban.¹⁸ Once again, there was no clear etiology, but it was attributed to a combination of factors, including dual antithrombotic therapy and a sudden increase in abdominal pressure secondary to straining. The patient, however, recovered spontaneously while enroute for surgery. Spontaneous resolution was believed to have been caused by leakage through the intervertebral foramina or cranio-caudal extension of the hematoma within the spinal canal, thus alleviating cord compression.¹⁸

Unfortunately, there are no recommendations in the literature for the prevention of SSEH because many of the reported cases were anticoagulated in the therapeutic range. With the increasing prevalence of polypharmacy, the risk of combined antiplatelet and anticoagulation therapy warrants a raised awareness. Further studies are needed to explore their effects on precipitating SSEH. More importantly, physicians should be aware of the possibility of a SSEH when sudden, unexplained back pain occurs in anticoagulated patients.

Patient's perspective

I used to go on walks daily with my wife and 5-6 other seniors to the mall. That was my routine. Now I guess that will never happen again. My legs do not work, and I cannot feel anything below my waist. The worst part of this entire experience is that, despite having seen so many doctors and surgeons, no one can tell me exactly what caused this and what I did to bring this on. I am scared to think what will happen the next time I feel back pain, that is, if I'll have any sensation to begin with.

My memory is bad enough, and now I have to remember my ‘routines’ because I cannot use the bathroom like I used to. I literally have appointments with my nurse to help me with my stool and urinary catheters, because apparently there have been times I have been sitting in my own pee.

I celebrated my first birthday with this condition on Feb 20th while in bed surrounded by my family and grandchildren. The children kept poking at all the plastic tubes and blue pads and sheets I had around me. It was a bad day for me, as my knees kept jumping up every time they poked at my legs. But they are just children.

I cannot remember what I wanted on my last birthday. It was probably unimportant. On Feb 20th, I just wished I did not have an accident in front of my family.

I don't know if this paper will ever help me recover, but I just want my message to any doctor reading this be heard; please tell your patient of ALL side effects, no matter their age, and do not simply hand us a pamphlet on it.

Learning Points

- SSEH is rare, idiopathic, and requires an urgent spinal MRI followed by decompressive surgery to facilitate neurological recovery.
- Decompression performed within twelve hours gives SSEH patients the best probability of neurologic recovery.

- Factors predicting recovery after SSEH include the preoperative neurological status and the operative interval.
- Conservative management is only recommended if the neurologic deficits resolve spontaneously after onset, in cases without neurological deficits, or in cases with advanced and irreversible spinal cord injury.
- SSEH should be suspected in patients on anticoagulants who present with new onset back pain and symptoms of cord compression, especially those on dual antithrombotic agents.

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