Neurocrit Care (2019) 31:583–586
https://doi.org/10.1007/s12028-019-00832-2

NEUROCRITICAL CARE SOCIETY

A DAY IN THE LIFE OF A NEUROCRITICAL CARE TRAINEE

Hemorrhagic Shock After Lumbar Puncture

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Introduction

Lumbar puncture is a routine procedure frequently done in the intensive care unit, operating room, and medical wards for therapeutic and diagnostic purposes such as cancer, infections, and autoimmune diseases workups. It usually carries a low risk of complications. There have been tremendous efforts to prevent thromboembolic events in high-risk patients using different classes of antithrombotic drugs. Multiple societies including the American Society of Regional and Pain Medicine have developed consensus guidelines regarding safe time intervals to perform different procedures on patients that are anticoagulated [1]. We encountered a case of active bleeding from left L2 and L4 lumbar arteries after a lumbar puncture that leads to hemorrhagic shock.

Description of the Case

A 59-year-old female patient with a past medical history significant for Sjogren syndrome, hypothyroidism, diabetes mellitus type 2, atrial fibrillation status post-cardioversion and ablation (on apixaban 5 mg twice daily), and hypertension presented as an outside hospital transfer to University of Virginia Medical Center. The patient acutely developed progressive bilateral lower extremities motor and sensory deficits. Neurology accepted the patient and was concerned for possible transverse myelitis. MRI showed multifocal CNS lesions in the brain and spine with leptomeningeal enhancement (Fig. 1). Admission CBC, BMP, PT, PTT, and INR were normal. A lumbar puncture (LP) was planned to be done as part of the diagnostic workup to rule out infectious and cancerous causes. Apixaban was held on the hospital day 2. The neurology team made the decision to bridge the patient with heparin. The patient was transitioned to a heparin drip 4 h after the apixaban was held per hospital protocol. PTT was checked 6 h later which was 27.1. Anti-Xa levels were not checked prior to the start heparin infusion. The heparin drip was stopped 8 h before the procedure. Prior to the LP, the anti-Xa level was 0.73 which was concerning for residual apixaban effect (Fig. 2). The neurology team attempted the LP at L4–L5 in the lateral position but was unsuccessful. Because of the patients high BMI and the difficulty of the initial bedside LP, the neurology team was not comfortable with re-attempting the LP. Interventional radiology was consulted on the same day and performed a successful lumbar puncture in the lateral position at L2–L3 interspace. CSF results showed pleocytosis with lymphocytic predominance, elevated protein, and elevated lactic acid. Anti-NMO A and anti-MOGFS Ab were both negative. Infectious workup was negative for serum HIV-1/2, HbSAg/Ab, HCV Ab Lyme Ab, TB (QuantiFERON Gold), and CSF HSV1/2. CSF flow cytometry showed no abnormalities. CT chest, abdomen, and pelvis lacked any abnormal findings. CSF ACE level elevated at 2.9. The heparin drip was restarted 4 h after the LP was completed. She maintained good kidney function throughout the admission and was transitioned to enoxaparin therapeutic dosage (120 mg bid SQ) on the second day post-procedure. The follow-up anti-Xa was reported > 2.0. This continued to be concerning for residual apixaban. A corrected heparin (CH) laboratory was ordered to confirm the residual apixaban. This laboratory uses quantified values from a chromogenic anti-Xa assay with heparin calibrators prior to and following heparinase treatment to detect any residual oral anticoagulant (OAC) still present within the patient sample. The CH laboratory was 1.98 (reference range 0.30–0.70 IU/ml) confirming residual OAC. On hospital day 5(post-procedure day 3), the patient became hypotensive, tachycardia, less responsive so she was transferred to neuro-ICU for further investigation of her hemodynamic instability. A stat EKG showed sinus tachycardia with no ST segment changes. Bedside TTE showed left ventricular ejection fraction of 65% with a severely under

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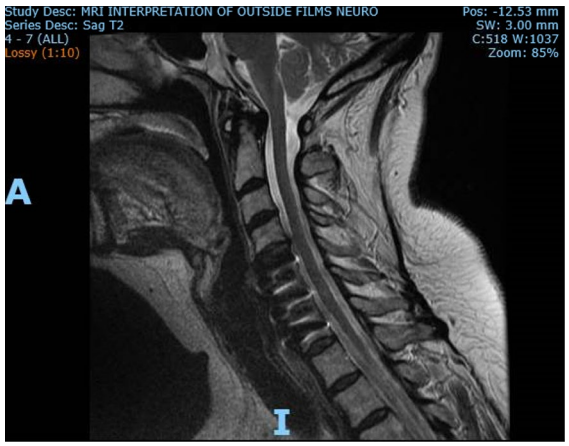

Fig. 1 MRI C-spine showing leptomeningeal enhancement

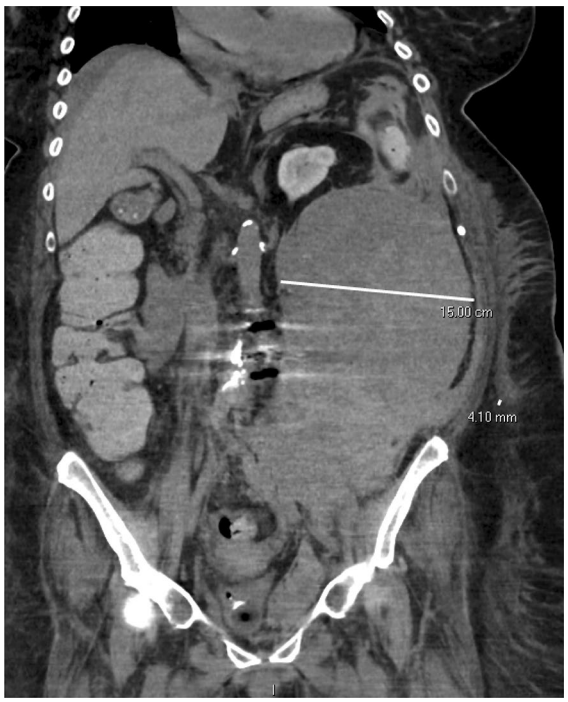

Fig. 3 Coronal: CTA abdomen showing large hematoma

filled left ventricle. CBC showed hemoglobin of 4.5 and a hematocrit of 13. The patient was immediately resuscitated with 2 packed red blood cells and 2 L of crystalloid. Two units of fresh frozen plasma were given to reverse the effects on apixaban. A ROTEM was sent after initial blood products were administered. The clot formation time in the EXTEM was prolonged, and the FIBTEM A10 was low. Another unit of FFP and a unit of cryoprecipitate were given. The clot time on the INTEM was normal; therefore, protamine was not administered. Fibrinolysis was not seen on the FIBTEM; therefore, TXA was not started. Norepinephrine and vasopressin infusions were started. Norepinephrine infusion peaked at 25 mcg/min

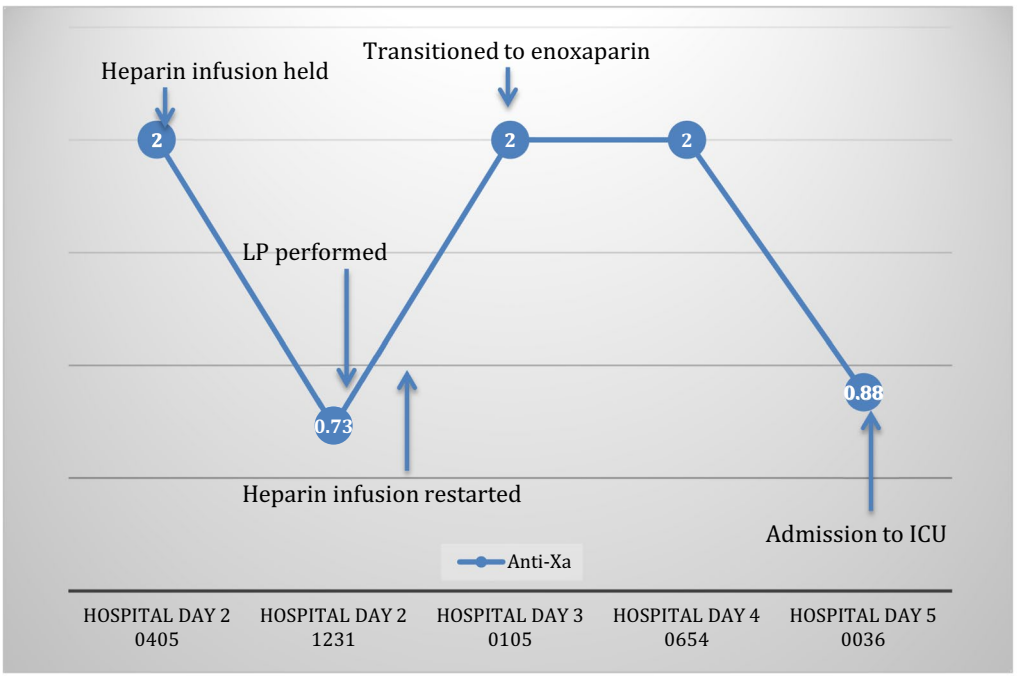

Fig. 2 Clinical timeline in relation to anti-Xa levels

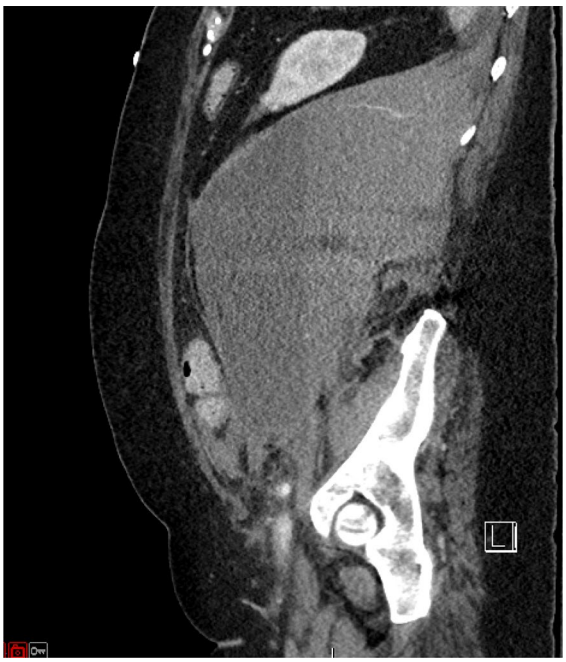

Fig. 4 Sagittal: CTA abdomen pelvis showing large retroperitoneal hematoma

and vasopressin infusion at 0.04 units/min. Two grams of calcium chloride were given during resuscitation. CTA abdomen and pelvis showed the presence of a huge retroperitoneal bleed with mass effect on the left kidney and active bleeding from left intercostal and left lumbar L2 artery (Figs. 3, 4, 5).

Management

After initial resuscitation with crystalloids and massive transfusion protocol and reversal of residual apixaban, the patient was emergently sent to the interventional radiology suite for embolization of the left lumbar L2 artery. The patient remained hemodynamically unstable, and her hemoglobin levels kept trending down which warranted further investigation in the interventional radiology suite. Additional bleeding was noted at the left T12 subcostal artery as well as left L4 lumbar artery. Both arteries were embolized with coils and gel foam. The patient stabilized after the second intervention. The patient required one more unit of packed red blood cells and a liter of crystalloid after the second intervention. Vasopressors were slowly weaned off over the next 24 h. The neurological workup was completed, and she was discharged with a potential diagnosis of neurosarcoidosis.

Discussion

Lumbar puncture is a routine procedure that carries an overall low complication risk of 0.1–0.5% [1]. Headaches, subdural hematoma, spinal epidural hematoma, and cerebral herniation have been reported although rare. Apixaban (Eliquis) is an oral highly selective reversible factor Xa inhibitor. The drug has an oral bioavailability of 51–85%, and the maximum plasma concentration is reached within 2–4 h after oral intake [2]. According to the recent regional anesthesia guidelines, apixaban should be discontinued 40–75 h before proceeding with regional anesthesia [1]. Of note, there are very few prospective data concerning the use of

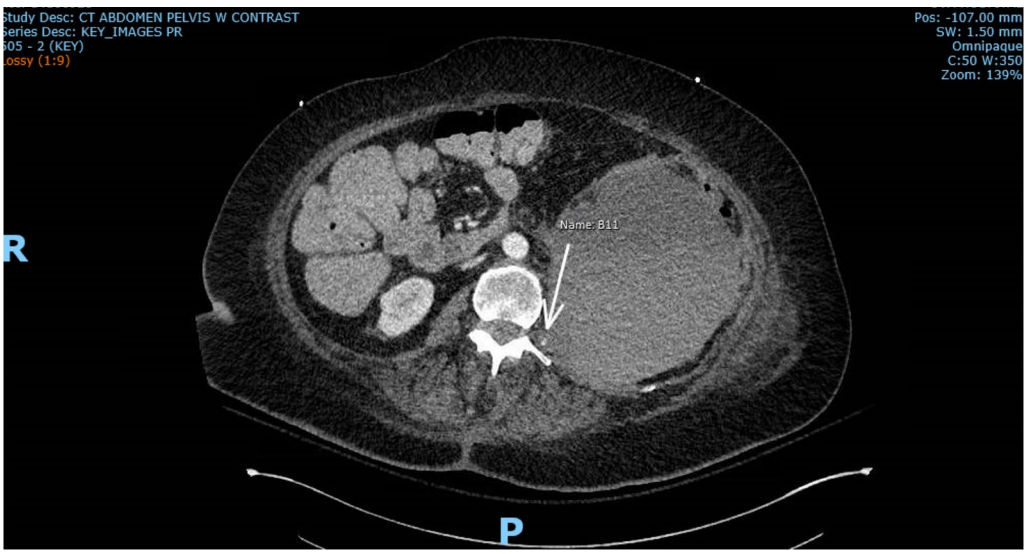

Fig. 5 CTA abdomen pelvis showing active bleeding from lumbar artery

neuraxial blocks in apixaban-treated patients. Our literature search up to November 2017 found no reports of epidural/spinal bleeding associated with a neuraxial anesthesia, although a single spontaneous hematoma has been reported [2]. Intravenous unfractionated heparin bridge is not uncommon in patients with nonvalvular atrial fibrillation as these patients have a twofold–sevenfold increase in stroke risk [3]. Unfortunately, there are no sufficient data to guide clinicians for the appropriate dosing regimen for heparin infusions in atrial fibrillation. The dosing regimen normally is a bolus followed by an infusion which tends to increase the risk of bleeding [3]. Our patient was bridged with a heparin infusion after the apixaban was discontinued, and her heparin infusion had to be adjusted multiple times for supratherapeutic values. This was most likely related to the presence of residual anticoagulation from apixaban in her system even after 72 h of stopping the medication, putting the patients at a higher risk for post-procedural hemorrhage. In conclusion, there is little evidence to guide clinicians performing neuraxial procedures on apixaban-treated patients. Even though the recommended time intervals for stopping apixaban and heparin infusion were respected, the unexpected residual effects of apixaban placed our patient at a high bleeding risk. This raises the question of safety with apixaban in neuraxial procedures, and at the appropriate time, the medication should be held prior to procedures.

Author contributions
MB contributed to the body of the case report. Collected data and reviewed the final versions. DT contributed to the intro and discussion of the case report. Designed the figures and edited the case report.

Source of Support
There was no funding or support.

Conflict of interest
The authors declare that they have no conflict of interest.

Ethical Approval/Informed Consent
The patient was consented and signed the University consent form allowing the clinicians to obtain and publish the medical case.

Publisher's Note

Published online: 22 August 2019

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