EPIDURAL HEMATOMA FOLLOWING LOW-MOLECULAR-WEIGHT-HEPARIN PROPHYLAXIS AND SPINAL ANESTHESIA FOR CESAREAN DELIVERY

A case-report

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Abstract: Epidural hematoma is a very uncommon complication of spinal anesthesia. Its incidence has been reported to be between 1:200,000 and 1:250,000 in the obstetric population following neuraxial anesthesia (1). In recent years, it has become evident that cesarean delivery increases the risk of maternal venous thromboembolism significantly, and recommendations to decrease its incidence and morbidity have been developed (2,3,4). Accepted strategies to decrease venous thromboembolism include pharmacologic prophylaxis with unfractionated and low-molecular-weight heparin. We report a case of spinal epidural hematoma occurring in a parturient who received spinal anesthesia for a planned, repeat cesarean delivery after low-molecular-weight heparin thromboprophylaxis.

Keywords: Subdural hematoma; spinal anesthesia; thromboembolism; low molecular weight heparin; deep venous thrombosis prophylaxis; complications of regional anesthesia

Case report: The patient was a 31-year-old G2P1, parturient at 39+0 weeks EGA, who had undergone a previous cesarean delivery (CD) under general anesthesia approximately one year prior. The current pregnancy had been unremarkable. The parturient was admitted to the hospital one day before scheduled CD and evaluated in a pre-anesthesia clinic. On physical examination, she was 162 cm tall and weighed 110 kg (BMI of 41.9 kg/m^2) and a Mallampati score of 2**.** The remainder of the physical examination was unremarkable. Routine laboratory examination tests were all within normal limits: complete blood count (hemoglobin 11.6 g/dl and hematocrit 33%), platelet count ($306x10^9/dl$), coagulation tests (activated partial thromboplastin time - PTT and prothrombin time - PT were normal, fibrinogen 4.8mmol/l). Blood pressure was 120/70 mmHg, pulse rate 85/min with normal electrocardiogram.

The evening prior to her delivery she received one single prophylactic dose of low molecular weight heparin (LMWH) 14h before the scheduled delivery (0.3ml nadroparine-Fraxiparine®). The 0.3 ml dose of nadroparine is 2850 anti-factor Xa IU.

The following day, immediately prior to the delivery, an experienced anesthesiologist performed spinal anesthesia with the patient in the sitting position. A 26-g Quincke needle was used and clear cerebrospinal fluid flow was obtained on the first pass of the needle at the L3-4 spinal level. Anesthesia was induced with 11 mg hyperbaric bupivacaine 0.5%, and 25 mcg of fentanyl. The needle was withdrawn, the patient positioned supine with left-uterine-displacement, and a healthy male infant (3570g) was delivered with Apgar scores of 10 and 10, at 1 and 5 minutes**.** The surgery was completed uneventfully. Following surgery, because the obstetrician believed she was at elevated risk for deep venous thrombosis (DVT) due to her BMI, she received nadroparine 0.3ml twice daily until discharge, beginning at 8 pm in the evening, 9 hours after conclusion of her surgery.

Recovery was unremarkable until post-operative day 3 when the patient complained of back pain, with bilateral lower extremity pain in both thighs. Physical examination at this time was unremarkable, without sensory or motor deficits elicited. A mild fever of 38 Celsius degrees was noted, which was believed to be due to small hematoma discovered in abdominal wall (34x32mm). Her symptoms were treated with oral acetaminophen 500mg two times per day and she received no antibiotics. The fever and back pain abated over the next 3 days and she was discharged home on postoperative day 7.

On postoperative day 10 she presented to the hospital complaining of severe back pain, which made walking and sitting very painful. Upon admission at this time, she had a low-grade fever (37.7 °C), and intermittent headache. Bladder and bowel function were normal, and neurologic examination did not reveal any focal findings. Laboratory tests for coagulation were normal (PT, APTT, international normalized ratio - INR, and platelet count), as was screening for von Willebrand disease. C-reactive protein (CRP) was elevated at 200 mg/l (normal value is $\leq$5). A swab of the cervix revealed Staphylooccocus aureus, and antibiotic therapy was begun: ciprofloxacin 200mg x 2 IV, metronidazole 500mg x 3 IV, followed by a course of ceftazidime 2g twice-daily for three days, then1g twice-daily for five days. Diclofenac

(75mg intramuscular for 2 doses), dexamethasone (4mg intravenously for 2 doses), and pantoprazol 20mg orally daily were also begun. Consultation with a neurologist was obtained, who recommended magnetic resonance imaging (MRI scan) of the thoraco-lumbar spine. The MRI scan of the lumbar spine showed an epidural haemathoma measuring 10x14x30mm in the spinal canal at L4 vertebral body level (Figure 1). The hematoma was located dorsolateral to the right side of the dura, with moderate compression of dura. Additionally, partial herniation of the L3-4 intervertebral disc was noted. A neurosurgeon was consulted; in light of the moderate impingement by the hematoma on the dural sac, and the patient's only subjective complaint being pain in the lumbar spine without neurologic deficit, he felt there was no indication for surgical decompression. Given the patient's subjective improvement following diclofenac and acetaminophen, he recommended continued conservative treatment.

Over the next several days, the patient's pain continued to improve on conservative therapy and she was able to ambulate without difficulty.

Electromyography was performed on postoperative day 17, which showed radicular lesions in L3 and L4 dermatomes, and L5-S1 level. The abnormalities noted were felt to be chronic, secondary to the patient's disc disease at the L3-4 level, and not related to the hematoma found on MRI scan previously.

At the neurologist's recommendation, the patient remained hospitalized until a follow-up MRI scan could be performed, which was performed on postoperative day 30 and showed minimal right-sided dorsolateral compression of the dural sac (Figure 2).

Patient was discharged on postoperative day 34 in good condition**.** Her back pain had resolved, and she was ambulating and able to sit without any problems. Her only complaint was a mild headache from time to time.

Discussion:

Spinal epidural hematoma (SEH) has been described following neuraxial anesthesia. It is reported to be more common after epidural than spinal anesthesia and is usually seen in conjunction with coagulation abnormalities or administration of anticoagulants (5). Several anesthesia societies (American Society for Regional Anesthesia and Pain Management – ASRA; the Society for Obstetric Anesthesia and Perinatology – SOAP; the Royal College of Obstetricians and Gynaecologists - RCOG) have published guidelines for the administration of anticoagulants in conjunction with regional anesthetic techniques to minimize any iatrogenic contribution to the problem (2,4,6)**.** Given the wide utilization of regional anesthesia in the obstetric patient, these recommendations are particularly relevant.

Deep venous thrombosis (DVT) has been recently highlighted as a significant cause of morbidity and mortality in the obstetric population, leading to recommendations that all parturients receive preventative prophylaxis (2-4). Recommended strategies include stratification of risk factors, and mechanical (sequential compression stockings, SCDs) and pharmacologic prophylaxis. For elective cesarean delivery, a

prophylactic treatment regimen is dependent on the number and severity of risk factors applicable to any given patient.

In the case reported above, body weight (110 kg and BMI 41.9 kg/m^2) and elective cesarean delivery would constitute 2 additional risk factors under the RCOG Guidelines (2), which advocate both mechanical and pharmacologic prophylaxis. Likewise, the American College of Chest Physicians Guidelines would classify this patient at increased risk, and also recommend mechanical and pharmacologic prophylaxis (6). The ACOG Guidelines are less precise but state all parturients undergoing cesarean delivery should receive mechanical prophylaxis, early ambulation and hydration; additional risk factors may warrant the use of pharmacologic prophylaxis (3). None of the guidelines state precise timing of institution of pharmacologic prophylaxis for parturients at elevated risk for elective cesarean delivery, though mechanical prophylaxis would clearly be instituted pre-incision at cesarean delivery.

Though mechanical prophylaxis is generally considered the most convenient means of prophylaxis in developed countries, in many middle-income countries SCDs are cost-prohibitive and not readily available. This case is from a middle-income country (Serbia), and an institution where SCDs were not available. As a result, the protocol adopted called for pharmacologic prophylaxis with LMWH for all elective cesarean deliveries, administered at least 12 hours before surgery, and was followed in this case. This protocol conformed to both the ASRA guidelines (7) for neuraxial anesthesia after pharmacologic prophylaxis for DVT, and the recently published guidelines from the SOAP (4). While there is little or no literature regarding how widespread the use of similar protocols is, one report from the Netherlands (8) included 1500 women who received LMWH prophylaxis (dalteparin or one of 2 regimens of nadroparine) for cesarean delivery, including pre-operative dosing with nadroparine.

An exhaustive literature review performed by Leffert et.al., (9) in 2017 did not identify any reports of SEH in an obstetric patient receiving neuraxial anesthesia for cesarean delivery following prophylactic therapy with either LMWH or unfractionated heparin, when the recommendations of either the ASRA or the SOAP were followed.

Several aspects of this case are notable. The preoperative dose of nadroparine administered was actually slightly lower than recommended in the manufacturer's prescribing instructions for the patient based on weight and BMI (10). However, the dose administered following delivery, while appropriate with regard to timing (recommended delay following neuraxial anesthesia), was slightly higher than the recommended prophylactic dose. After delivery, the patient received 0.3 ml twice daily for the first 3 days postoperatively, when the prescribing instructions recommend 0.4 ml once daily for the first 3 days followed by 0.6 ml daily from the 4^{th} postoperative day forward (the patient received this dose on postoperative days 4 through 7). The clinical presentation was also somewhat unusual from most previously published reports of SEH in the literature: the patient did not present with symptoms until the 10^{th} postoperative day, after nadroparine therapy had been discontinued for 3 days, and at time of presentation the chief complaint was back pain, rather than sensory or motor deficit. Finally, despite MRI documented presence

of SHE and some mass effect within the spinal canal, the neurosurgical recommendation was to manage the patient conservatively due to the lack of focal neurologic deficit. Immediate surgery and decompression are generally recommended when neurologic deficits are present (11).

The lack of other reported cases of this complication does not allow any estimate of its overall incidence. Spontaneous occurrence of spinal epidural hematoma has been reported in a number of cases during pregnancy (12, 13), and it is possible that this patient suffered a spontaneous lumbar epidural hematoma. There are no reported cases of spontaneous epidural hematoma occurring after cesarean delivery however. Further, if this epidural hematoma was casually related to the nadroparine administered for prophylaxis, it raises questions about the safety of pre-operative administration for these patients; thromboembolism prophylaxis may be just as well served by keeping parturients as ambulatory out-patients until the morning of surgery.

In summary, a case of SEH after prophylactic therapy for DVT prevention at cesarean delivery is presented. All applicable guidelines for management of anticoagulation were followed. In a patient presenting with back pain after cesarean delivery in this setting, the diagnosis of SEH should be considered, even with delayed presentation. In the absence of neurologic deficit, conservative management may be possible, though careful continued observation and neurosurgical consultation are essential.

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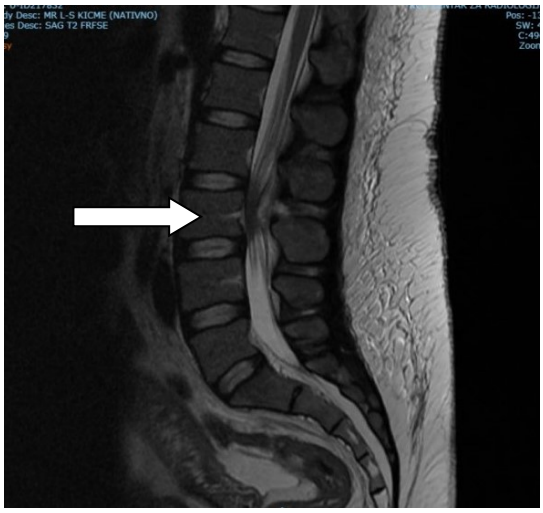
Legends

Figure 1: Initial MRI of the lumbar spine, 12 days after spinal anesthetic. A: sagittal section, B: axial section. Arrows indicate location of epidural hematoma.

Figure 2: Repeat/follow-up MRI scan 30 days after spinal anesthetic. The epidural has decreased in size and density, with decreased mass effect. A: sagittal section, B: axial section. Arrows indicate location of epidural hematoma.

Figure 1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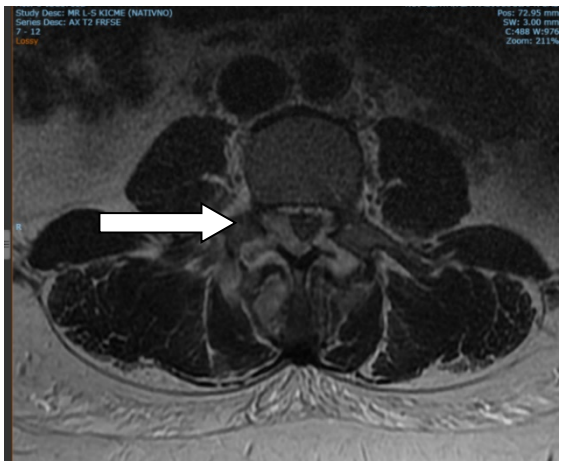
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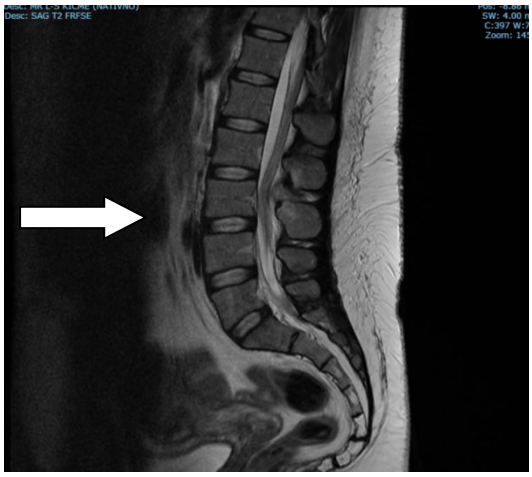
Figure 2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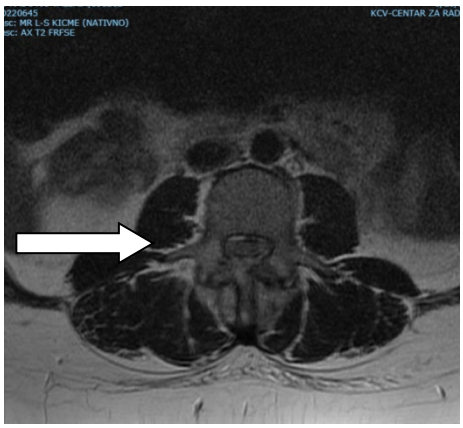
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