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Peer Review File

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Reviewer A

The authors presented a case report titled "Postoperative Spinal Epidural Hematoma Following Therapeutic Anticoagulation: Case Report and Review of Literature." in this report, they presented a 56-year-old male who underwent spinal decompression and fixation for metastatic disease. He underwent a preoperative IVC filter due to renal vein thrombosis. He received a therapeutic Clexane SQ injection on day #7 after surgery. But he presented one day later with a spinal epidural hematoma that required urgent evacuation.

There are a few points that need to be clarified in the case presentation section:
• The authors need to provide the detailed coagulation profile of the patient with probable hypercoagulable status.
Reply: Details on initial blood investigation results, including a normal coagulation profile, has been added into the case description (line 83-87).

• There are no preoperative images for significant findings: CT scan of the renal mass and renal vein thrombosis and MRI spine showing the conus compression.
Reply: We have accordingly added in Figure 1 MRI images showing the conus compression and Figure 2 CT images showing the renal mass and renal vein thrombosis.

• The IVC filter was inserted for prophylactic extension of thrombus and risk of PE. What is the indication for therapeutic heparin? Obviously, not the renal thrombosis of the renal mass! There is no indication.
Reply: Therapeutic clexane was initiated based on the recommendation from a hematology specialist for the following indications: "(1) Prothrombotic state from metastatic disease, (2) prevention of thrombus propagation, and (3) prevention of IVC filter blockage." (line 100-102)

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• What was the exact surgical procedure done? Laminectomy/corpectomy!
Reply: The patient underwent complete L1 laminectomy, partial T12 laminectomy, T11-L3 stabilization, posterior lateral and inter-facet fusion. The surgery was uneventful with 500ml of blood loss, and there were no complications or dural tear intraoperatively. This has been added into the case description (line 91-94).

• Please provide T1 images of postoperative MRI. Were the clot signals of acute that was related to the heparin or just a progression of the postoperative fluid collection that was only slowly progressed? There is marked compression from the compression fracture of L1, which was not treated and added to the recurrence of symptoms! Any reasons why it was not treated from the beginning?
Reply: His surgical wound was dry, and the surgical drain was removed without issues on POD 4 with minimal output. It is unlikely that there was progression of any significant postoperative fluid collection. Therapeutic clexane was initiated on the night of POD 6 which was the more likely cause of the subdural hematoma seen on MRI on POD 8 when he was readmitted for neurological symptoms.

• The exact heparin dose is unknown and should be mentioned, not per Kg, as the patient weight was not known!
Reply: The exact dose was 80mg. This has been added into the case description (line 99).

• How can the authors explain such rapid deterioration after two doses of heparin? Do you have a PTT result before the second surgery?
Reply: We thank the reviewer for this question. The rapid deterioration was unfortunate and was likely due to the rapid onset and high (therapeutic) dose of clexane used, accounting for his coagulopathy. This resulted in the significant hematoma formation and generalised bleeding during the second procedure (1.5L blood loss). (line 112)

• There is no good follow-up, and the word “hemiplegia” should be changed to hemiparesis unless they had other complications like a stroke!
Reply: We have changed hemiplegia to “hemiparesis” accordingly (line 116).
• What was the management plan for the renal mass?

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Reply: The patient was managed palliatively, as for metastatic renal cell carcinoma.

The title implies that postoperative SEH was developed due to therapeutic anticoagulation from postoperative thromboembolism related to spine surgery! But this is not factual because the indication to heparinize case in addition to IVC filter is not indicated without documented progression of the renal vein thrombus.

The aim to report this case is not informative; this complication rare after spine surgery, but there is nothing special about it to be a case report.
Many cohort studies have presented a medium-size series describing the incidence and risk factors for postoperative SEH in the literature, and some are recently reported. [1,2,3] One study addressed the postoperative SHE in patients following spine surgery for tumors. [4,5]

The authors did a good discussion on the topic but had to improve the citation of relevant literature. One crucial issue that is not correct is the initiation of heparin in patients with the metastatic spine. recent paper support early than late heparin administration after spine surgery to decrease the risk of venous thrombosis and pulmonary embolism. [6]

1. Selected references:
2. Park JH, Park S, Choi SA. Incidence and risk factors of spinal epidural hemorrhage after spine surgery: a cross-sectional retrospective analysis of a national database. BMC Musculoskelet Disord. 2020;21(1):324. Published 2020 May 25. doi:10.1186/s12891-020-03337-8
3. Masuda S, Fujibayashi S, Takemoto M, et al. Incidence and Clinical Features of Postoperative Symptomatic Hematoma after Spine Surgery: A Multicenter Study of 45 Patients. Spine Surg Relat Res. 2019;4(2):130-134. Published 2019 Nov 1. doi:10.22603/ssrr.2019-0080
4. Hohenberger C, Zeman F, Höhne J, Ullrich OW, Brawanski A, Schebesch KM. Symptomatic Postoperative Spinal Epidural Hematoma after Spinal Decompression Surgery: Prevalence, Risk Factors, and Functional Outcome. J Neurol Surg A Cent Eur Neurosurg. 2020;81(4):290-296. doi:10.1055/s-0039-1697024
5. Gao X, Li L, Cao J, et al. Symptomatic postoperative spinal epidural hematoma after

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spine tumor surgery: Incidence, clinical features, and risk factors. Spinal Cord. 2019;57(8):708-713. doi:10.1038/s41393-019-0281-5
6. De la Garza Ramos R, Longo M, Gelfand Y, Echt M, Kinon MD, Yassari R. Timing of Prophylactic Anticoagulation and Its Effect on Thromboembolic Events After Surgery for Metastatic Tumors of the Spine. Spine (Phila Pa 1976). 2019;44(11):E650-E655. doi:10.1097/BRS.0000000000002944
Reply: We thank the reviewer for this insightful comment and suggestion. We have accordingly updated our discussion and citation of recent literature with the aforementioned references (line 54-55, 132 and 180-184).

Reviewer B

1. The authors did not demonstrate the operation in detail, such as dural tear, bleeding, drain, and postoperative treatment. Please describe the treatment during operation.
Reply: The patient underwent complete L1 laminectomy, partial T12 laminectomy, T11-L3 stabilization, posterior lateral and inter-facet fusion. The surgery was uneventful with 500ml of blood loss, and there were no complications or dural tear intraoperatively. This has been added into the case description (line 91-94).

2. This patient had renal cell carcinoma and metastasis, so he might have liver dysfunction, abnormal coagulation, or renal dysfunction. But the authors did not show the results of the laboratory test. Please describe the laboratory test.
Reply: We have added in further details on the laboratory test results in the case description (line 83-87).

3. The authors did not demonstrate MRI image before surgery. The lamina of L1 might be metastasis. Please show MRI image before surgery.
Reply: Figure 1 has been added to demonstrate MRI image of before surgery showing significant conus compression.

4. IVC filter insertion have a risk of complications. Did this patient need IVC filter? Was the timing of IVC filter appropriate?
Reply: As mentioned in the case description, the CT scan showed a left renal carcinoma

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(9.4 x 8.1 cm) with filling defect in left renal vein and IVC thrombus. In the discussion, we have also explained the role of IVC filters "as a management alternative in the treatment of patients who are at a high risk of PE after surgery" and "that prophylactic IVC filter placement in high-risk spine surgery patients significantly reduced the odds of developing a PE as compared to control populations" (line 196-199).