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Spinal epidural hematoma following epidural catheter removal during antiplatelet therapy with cilostazol

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Abstract
A 90-year-old man underwent emergency thrombectomy for acute occlusion of the right femoral and popliteal arteries. After an epidural catheter (used for intraoperative/postoperative management) was removed, a spinal epidural hematoma involving the Th12 to L3 areas developed. Emergency removal of the hematoma and decompression of the spinal cord were performed. Possibly, the hematoma had developed due to therapy with an antiplatelet agent, cilostazol, which had been started on the first postoperative day, and due to the removal of the catheter, on the third postoperative day, in addition to the patient's advanced age. This case may be the first report of spinal epidural hematoma associated with both cilostazol and epidural anesthesia. From the time course in this patient, important knowledge of drug actions and follow-up may be gained for determining the timing of catheter removal in a patient receiving antiplatelet therapy with cilostazol.

Key words Spinal epidural hematoma · Cilostazol · Epidural anesthesia · Epidural catheter removal

Introduction

Spinal epidural hematomas (SEHs) related to epidural anesthesia are rare, but they are recognized as a serious complication. The administration of antiplatelet agents and anticoagulants is involved in the pathogenesis of SEH. In addition, puncture of the epidural space in elderly patients is also considered to be a risk factor [1]. In this case report, we describe a 90-year-old man in whom an SEH developed, possibly because an epidural catheter was removed 2 days after therapy with an antiplatelet aggregation inhibitor, cilostazol, which was begun on the first postoperative day (POD).

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Case report

The patient was a 90-year-old man. Height and body weight were 150 cm and 38 kg. He had a medical history of pulmonary emphysema and chronic gastritis. No medicinal agent had been prescribed. As an emergency, the patient consulted our hospital for acute left lower-limb pain. He was diagnosed as having acute arterial occlusion involving the left femoral and popliteal arteries. Emergency thrombectomy with a Fogarty catheter was scheduled. In the preoperative laboratory data, the platelet count was $90\,000 \cdot \mu l^{-1}$. However, other tests results, including coagulation system, liver/kidney function, and electrolytes, were within the normal ranges. Chest X-ray showed a drop-shaped heart (cardiothoracic ratio [CTR], 45%) and emphysematous changes. Electrocardiography revealed grade I atrioventricular block and incomplete right bundle branch block.

Spinal anesthesia combined with epidural anesthesia was scheduled, considering his advanced age, the emergency surgery, history of pulmonary emphysema, and the schedule of thrombectomy (short surgery). The epidural space was punctured at the intervertebral space between L1 and L2 using the loss-of-resistance method, and a catheter was inserted 10 cm cephalad from the skin puncture site. As puncture was rather difficult, it was performed several times over a few intervertebral spaces, using the paramedian approach. But there were no abnormal findings such as blood regurgitation. After this, spinal anesthesia was performed at L2-L3 with 0.5% isobaric bupivacaine 2.5 ml. After confirming the anesthesia level at Th12, using cold sensation, surgery was begun. Heparin at 3000 units was administered intraoperatively. The activated clotting time (ACT) was 292 s. Protamine was not administered after the surgery. The intraoperative transfusion volume was 600 ml (extracellular fluid), blood loss was 11 g, and urine volume was 400 ml. The durations of surgery and anesthesia were 45 and 75 min, respectively. For post-

operative analgesia, we used continuous epidural administration of 0.2% ropivacaine at 4 $ml \cdot hr^{-1}$.

On the first POD, therapy with 200 $mg \cdot day^{-1}$ of cilostazol was started. On the third POD (platelet count, $85\,000 \cdot \mu l^{-1}$), the epidural catheter was removed in the morning. Immediately after the removal, lumbar pain was noted, but there were no abnormal findings such as paralysis. In the evening of the same day, the patient fell down when standing up for urination. Simultaneously, numbness of the right lower limb was observed. Under a tentative diagnosis of reperfusion disturbance, the patient was observed without treatment. The attending physician did not inform the anesthesiologist of this episode. On the fourth POD, the lumbar pain had become exacerbated and lumbar X-ray examination was performed. There were no abnormal findings, such as a fracture. The score for the manual muscle test (MMT) of the right lower limb was 3. Magnetic resonance imaging (MRI) examination was scheduled for the next day. On the fifth POD, the MMT score for the bilateral lower limbs had further decreased to 1. Emergency MRI examination revealed an SEH involving the Th12 to L2 areas. The MRI findings are shown in Fig. 1. After this examination, emergency removal of the hematoma and posterior decompression of spinal cord were performed with the patient under general anesthesia with oxygen, nitrous oxide, and sevoflurane. The intraoperative findings, showing the hematoma compressing the spinal cord, and the removed hematoma, are shown in Fig. 2. On an MMT given 2 days after removal of the hematoma, the respective scores for the left/right quadriceps muscles of the thigh were 2/3, those for the left/right biceps muscles of the thigh were 2/3, and those for the left/right anterior tibial muscles were 1/1. On discharge (28 days after surgery), an MMT showed scores of 3/3, 3/3, and 2/2, respectively. On the thirty-first POD, the patient, who was then in a wheelchair, was referred to another hospital for rehabilitation.

Discussion

SEHs related to epidural anesthesia are rare, but they are recognized as a serious complication. The incidence is reported to be 1:190 000 punctures [2]. With respect to hematoma formation during epidural/spinal anesthesia, Vandermeulen et al. [3] retrospectively reviewed 61 patients who had developed SEHs between 1906 and 1994. In 41 patients (67%), disorders of the coagulation system were etiologically involved in the hematoma formation. Horlocker et al. [1] have reported that significant risk factors for microhemorrhage on puncture for epidural/spinal anesthesia included: age over 65 years,

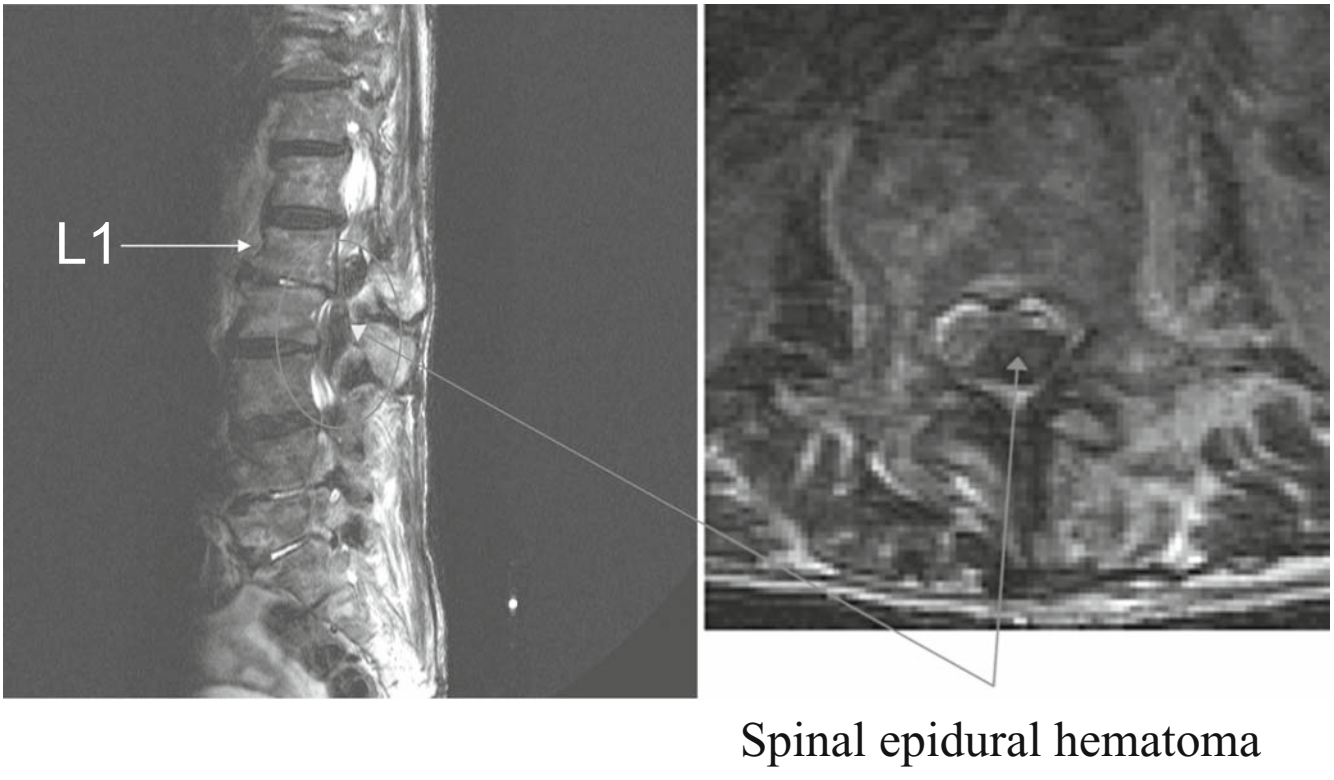

Fig. 1. Magnetic resonance imaging (MRI) findings (sagittal and horizontal images)

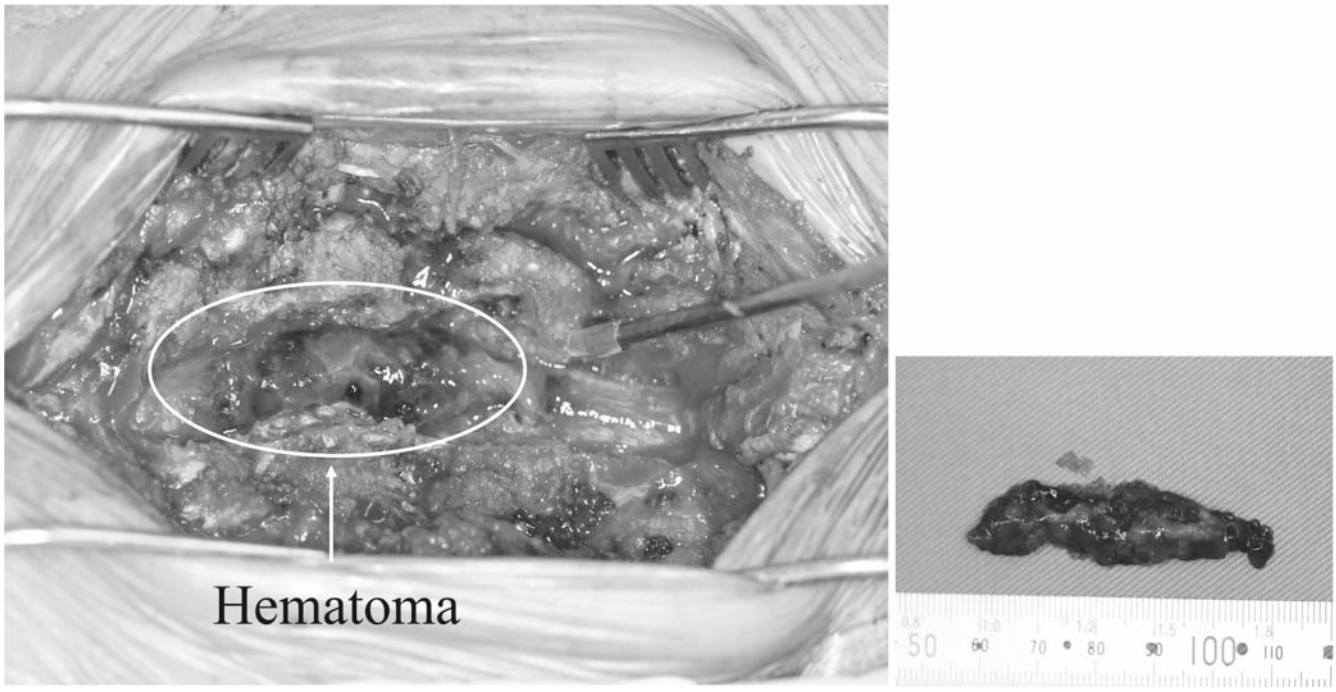

Fig. 2. Intraoperative views. Hematoma compresses the spinal cord. There is no macroscopic abnormality of the blood vessel system

female sex, a history of excessive trauma and hemorrhage, hip surgery, thick puncture needles, repeated punctures, and the insertion of a catheter for continuous infusion. However, they indicated that preoperative antiplatelet therapy did not increase the incidence of microhemorrhage on epidural puncture [1].

To avoid the onset of hematomas during epidural/spinal anesthesia, Haljamae [4] proposed reference ranges for the prothrombin time (PT; 50% or more), activated partial thromboplastin time (APTT; upper limit of the normal range), platelet count ($80\,000 \cdot \mu l^{-1}$ or more), and bleeding time (8 min or less) as parameters of the coagulation system. In addition, they presented parameters that must be evaluated in individual patients, and examined them as reference values. At our hospital, epidural puncture is indicated according to our criteria (platelet count, $100\,000 \cdot \mu l^{-1}$ or more; APTT, 50 s or less; PT, 50% or more; and INR < 1.5).

In preoperative anticoagulant therapy, it is important to investigate the risks-benefits in individual patients and to make a final decision in accordance with these findings. However, administration of anticoagulant agents is discontinued in many pateints. In many patients treated orally with antiplatelet agents before surgery, the agents are temporarily discontinued. The discontinuation period for each antiplatelet agent is described in the American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines [5]. According to these guidelines, the period has been established based on the action mechanism of each agent, and differs among agents.

Concerning the action mechanism of the antiplatelet agent, cilostazol, which was orally administered to our patient starting from the day after surgery, this agent is a selective and potent inhibitor of phosphodiesterase (PDE) 3A, the isoform of PDE3 in the cardiovascular system, and it increases the cAMP level via the inhibition of synthesis of AMP from cyclic adenosine monophosphate (cAMP). As a result, platelet activation is suppressed. Cilostazol has also been reported to inhibit the platelet aggregation that is related to various aggregation-inducing substances [6,7]. The discontinuation period for this agent is not described in the ASRA guidelines. However, in other guidelines for anticoagulant/antiplatelet therapy in patients with cardiovascular diseases, it is described that the agent should be discontinued for 3 days prior to major surgery [8]. This was based on the following findings: the plasma concentration of this agent reached a peak 3 h after the start of oral administration; platelet aggregation was inhibited at a maximum of 6 h after administration; and the plasma concentration of the agent decreased to approximately 1/20 48 h following discontinuation, with improvement in platelet aggregation [9].

The pathogenesis of the SEH in our patient may have involved the low platelet count ($85\,000 \cdot \mu l^{-1}$) on the removal of the epidural catheter, the cilostazol therapy, the difficulty in puncture of the epidural space, the

patient's advanced age (90 years), and continuous epidural administration via the epidural catheter (for postoperative analgesia and blood flow maintenance). As the most likely reason to think about, SEH developed possibly because the epidural catheter was removed during therapy with the antiplatelet agent, cilostazol, with the patient showing risk factors for microhemorrhage on puncture of the epidural space. In addition, it might be thought that the dose of cilostazol was too high for this old patient. Concerning the timing of the onset of SEH, lumbar pain occurred on the removal of the catheter, and then the nervous symptoms gradually became exacerbated; therefore, hemorrhage may have occurred via the catheter removal, resulting in hematoma formation. The pathogenesis of hematomas has been clarified in many patients, as demonstrated in our patient, but not in some others [10,11]. In our patient, cilostazol may have been involved in the pathogenesis. However, no study has reported the onset of SEH associated with cilostazol therapy and epidural anesthesia; the present case may be the first such report.

About the prognosis of SEH, a study reported that emergency surgery was performed for a diagnosis of hematoma in approximately 62% of patients with this diagnosis, and that various treatments achieved good neurological recovery in approximately 20% of the patients [3]. In some case reports, conservative therapy resulted in the spontaneous disappearance of the hematoma [12,13]. In our patient, the emergency surgery was selected according to the judgment of orthopedic surgeons, because of the MRI findings and the progress of clinical symptoms.

Concerning the onset time of SEH, there are many case reports noting that it occurred after the removal of an epidural catheter [14]. So sufficient education/knowledge of epidural catheter removal is important. Miyazaki et al. [15] reported that the initial symptoms of SEH were recognized within 24 h after the removal of an epidural catheter in 50% of 40 patients with SEH. If a patient presents with symptoms suggesting spinal cord compression after epidural catheter removal, SEH formation should be suspected. Moreover, when antiplatelet therapy has been started for a patient who has had an epidural catheter inserted, special care should be taken with the removal of the catheter. In conclusion, it is important to consider the risk of SEH formation when an epidural catheter is removed from a patient who is receiving antiplatelet therapy using cilostazol.

References

1. Horlocker TT, Wedel DJ, Schroeder DR, Rose SH, Elliot BA, McGregor DG, Wong GY. Preoperative antiplatelet therapy does not increase the risk of spinal hematoma associated with regional anesthesia. Anesth Analg. 1995;80:303–9.
2. Wulf H. Epidural anaesthesia and spinal haematoma. Can J Anaesth. 1996;43:1260–71.
3. Vandermeulen EP, Aken HV, Vermylen J. Anticoagulants and spinal-epidural anesthesia. Anesth Analg. 1994;79:1165–77.
4. Haljamae H. Thromboprophylaxis, coagulation disorders, and regional anaesthesia. Acta Anaesthesiol Scand. 1996;40:1024–40.
5. Horlocker TT, Wedel DJ, Benzon H, Brown DL, Enneking FK, Heit JA, Mulroy MF, Rosenquist RW, Rowlingson J, Tryba M, Yuan CS. Regional anesthesia in the anticoagulated patient: defining the risks (The second ASRA consensus conference on neuraxial anesthesia and anticoagulation). Reg Anesth Pain Med. 2003;28:172–97.
6. Ozeki Y. Efficacy and pharmacology of cilostazol. Bio Clinica. 2005;20:909–14.
7. Schror K. The pharmacology of cilostazol. Diabetes Obes Metab. 2002;4 (Suppl 2):S14–9.
8. Yasunaga K, Mase K. Antiaggregatory effect of oral cilostazol and recovery of platelet aggregability in patient with cerebrovascular disease. Arzneimittelforschung. 1985;35:1189–92.
9. Kasanuki H. Guidelines for management of anticoagulant and antiplatelet therapy in cardiovascular disease (JCS2004). Circ J. 2004;68 (Suppl IV):1221–30.
10. Culln DJ, Bogdanov E, Htut N. Spinal epidural hematoma occurrence in the absence of known risk factors: a case series. J Clin Anesth. 2004;16:376–81.
11. Kaneda T, Suzuki T, Takeda T. A case of acute spinal epidural hematoma after abdominal aortic aneurysm operation. Tokai J Exp Clin Med. 2006;31:45–8.
12. Yoshida T, Mori E, Yamadori A. Acute spinal epidural hematoma in MRI-CT, following continuous epidural anesthesia with spontaneous recovery. Rinsho Shinkeigaku (Clin Neurol). 1989; 29:226–9.
13. SreeHarsha CK, Rajasekaran S, Dhanasekararaja P. Spontaneous complete recovery of paraplegia caused by epidural hematoma complicating epidural anesthesia: a case report and review of literature. Spinal Cord. 2006;44:514–7.
14. Varitimidis SE, Paterakis K, Dailiana ZH, Hantes M, Georgopoulou S. Epidural hematoma secondary to remove of an epidural catheter after total knee replacement. J Bone Joint Surg Am. 2007;89:2048–50.
15. Miyazaki M, Takasita M, Matsumoto H, Sonoda H, TsumuraH, Torisu T. Spinal epidural hematoma after removal of an epidural catheter: case report and review of the literature. J Spinal Disord Tech. 2005;18:547–51.