Case report

Spontaneous spinal epidural hematoma in a patient with acquired Factor X deficiency secondary to systemic amyloid light-chain amyloidosis

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Background: Spontaneous spinal epidural hematoma (SSEH) is relatively rare. SSEH with anticoagulants including warfarin and rivaroxaban (Factor Xa inhibitor) have been reported; however, SSEH with Factor X deficiency has not been described yet.

Methods: Case report.

Findings: An 82-year-old woman with acquired Factor X deficiency complained of sudden onset of severe posterior neck pain. Magnetic resonance imaging demonstrated an epidural hematoma from C3 to T3 levels. Because she showed tetraparesis on the third hospital day, we performed surgery. Just before surgery, her prothrombin time-international normalized ratio was 2.49, which was immediately reversed by infusion of prothrombin complex concentrate. The patient safely underwent an emergency laminectomy from C3 to T2, in which the epidural hematoma was evacuated. Post-operatively, the patient recovered completely without rebleeding. Hematologists found acquired deficiency of Factor X in this patient with systemic amyloid light-chain amyloidosis.

Conclusion: To our knowledge, this is the first report of a case of SSEH with Factor X deficiency. A blood coagulation disorder should be considered in patients with SSEH.

Keywords: Amyloidosis, Factor X deficiency, Prothrombin complex concentrate, Spinal cord, Spontaneous spinal epidural hematoma

Introduction

Spontaneous spinal epidural hematoma (SSEH) is relatively rare with an incidence of 0.1 patients per 100 000 individuals.¹ The etiology remains unknown; however, it has been increasingly reported in patients with blood dyscrasias,² platelet dysfunction,³ anticoagulation therapy, or thrombolysis.⁴

Congenital Factor X deficiency is an extremely rare severe homeostatic disorder with an incidence of 1 in 10⁶ in the general population, and may present with nosebleeds and hemarthrosis,⁵ while acquired Factor X deficiency occurs occasionally in a number of disease states,⁶ mainly amyloidosis, where Factor X

may be adsorbed onto amyloid fibrils.⁷ We report the first case of SSEH causing tetraparesis in an elderly woman with acquired Factor X deficiency due to amyloidosis. We successfully operated using prothrombin complex concentrate (PCC).

Case report

History and examinations

An 82-year-old woman visited the emergency department of another hospital with severe posterior neck pain which had occurred suddenly. She had a bleeding tendency with repeated subcutaneous bleeding. Detailed hematological examination revealed that she had Factor X deficiency persisting for 2 months, with a prothrombin time (PT) of 23.8 seconds, an activated partial thromboplastin time (APTT) of 38.5 seconds,

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Table 1 Progress of coagulation times, Factor X activation, and anticoagulants in this case

	Previous hospital	First day	Second day	Third day	Third day just before Op	Fourth day	Fifth day	Sixth day	Seventh day	15th day
PT (seconds)	23.8	31	27.4	28.9	19.2	23.5	21.5	22.5	22	22.5
PT-INR	2.49	2.72	2.36	2.49	1.67	2.02	1.84	1.96	1.92	2.23
APTT (seconds)	38.5	45	50.2	43.1	37.3	37.6	35.4	33.8	36.3	39.8
Factor X activation (%)	9.6		7							
FFP (ml)		720	720		720					
PCC (U)				1500		500	500			

APTT, activated partial thromboplastin time; FFP, fresh frozen plasma; PCC, prothrombin complex concentrate; Op, operation; PT, prothrombin time; PT-INR, Prothrombin time-international normalized ratio; U, unit.
Hemostatic agents (FFP and PCC) were administered after confirmation of coagulation times.

PT-international normalized ratio (PT-INR) of 2.49 (Table 1), and very low Factor X activation of 9.6%. She was transferred to our hospital.

Neurological examinations in our hospital showed no neurological deficits, only severe neck pain. Her height was 150 cm and her weight was 38 kg. Magnetic resonance (MR) imaging demonstrated an epidural mass from C3 to T3 levels, which was isointense on T1-weighted imaging and heterogeneous on T2-weighted imaging (Fig. 1A and B). These findings revealed an epidural hematoma. Coagulation examination showed prolongation of clotting time as PT of 31.0 seconds, APTT of 45.0 seconds, and PT-INR of 2.72 (Table 1). We performed conservative therapy with infusion of fresh frozen plasma (FFP) 720 ml on the first and second hospital days; however, coagulation times could not be

reversed. PT-INR was between 2.36 and 2.49. Preparing for emergent surgery, we ordered PCC (PPSB-HR®), which our hospital did not keep.

Pre-operative course and operation

On the third day of her hospital stay, the patient suddenly showed tetraparesis (manual muscle testing 3). We immediately decided to perform surgery. Because we had to make the coagulation times as short as possible before surgery, we intravenously administered PCC. Finally, her PT-INR improved from 2.49 to 1.67 with 1500 U PCC. We were able to start surgery within 6 hours of the onset of symptoms. Laminectomy from C3 to T2 exposed the epidural hematoma, which was totally removed. Intraoperatively, we found no specific

Figure 1 (A) Pre-operative sagittal T1-weighted MR image showing an isointense space occupying lesion (arrows) of the spinal canal from C3 to T3 levels. (B) Pre-operative axial T1-weighted MR image at the C7 level also showing an isointense space occupying lesion (arrows) of the spinal canal.

Figure 2 (A) Post-operative sagittal T1-weighted MR image showing removal of epidural hematoma of the spinal canal from C3 to T3 levels. (B) Post-operative axial T1-weighted MR image at the C7 level also showing removal of the epidural hematoma.

findings of an abnormal vascular lesion; therefore, we thought that this case was an SSEH. We were able to control bleeding from the epidural venous plexus using absorbable hemostats. Although blood loss during surgery was 100 ml, the anesthesiologists added FFP 720 ml for hemostasis.

Post-operative course

After the operation the patient recovered without neurological deficit, and her severe neck pain disappeared. For 2 days after the operation, 500 U/day PCC was administered and then stopped (Table 1). After surgery, PT-INR was between 1.82 and 2.33 (Table 1); however, no bleeding occurred during 1-month follow-up. From biochemical examination of her blood, a hematologist found acquired deficiency of Factor X in this patient with systemic amyloid light-chain amyloidosis. Post-operative MR imaging showed removal of the spinal epidural hematoma (Fig. 2), and she was transferred to another hospital. To our knowledge, neither neurological deficits nor hemorrhagic complications have been reported 8 months following surgery, although the Factor X activation still has been very low.

Discussion

SSEH is relatively rare in comparison with traumatic spinal epidural hematoma.¹ Although the etiology of SSEH remains unknown, anticoagulants including warfarin have been reported as one of the important risk factors.⁴ In recent years, new oral anticoagulants, oral Factor Xa inhibitors and oral direct thrombin inhibitors, have been used for patients with atrial fibrillation, and a case of SSEH associated with rivaroxaban has been reported.⁸ We think that a bleeding tendency due to Factor X deficiency might have caused SSEH in this case. To the best of our knowledge, there has been no report of SSEH with Factor X deficiency.

Factor X deficiency is a rare coagulopathy due to congenital and acquired deficiency.⁵ Congenital Factor X deficiency is an autosomal recessive condition with an incidence of 1 in 10⁶ in the general population.⁵ Acquired Factor X deficiency is also rare; however, when it occurs, it is usually in association with amyloidosis, with light-chain amyloidosis being the most common form.⁷ It presumably occurs due to absorption of Factor X into amyloid fibrils.⁷ Our patient was also diagnosed as acquired Factor X deficiency with light-chain amyloidosis. Acquired Factor X deficiency may also be caused by other conditions such as a lack of vitamin K, severe liver disease, and use of drugs that prevent clotting.⁶ If surgeons encounter SSEH patients

with prolonged clotting time without anticoagulants, they should consider rare blood coagulation disorders. Fortunately, we knew that the patient had been recently diagnosed with Factor X deficiency, and our patient successfully underwent laminectomy with Factor X replacement using PCC.

When patients with coagulation disorders undergo emergency surgery, FFP and/or PCC are usually used for emergency vitamin K antagonist reversal.⁹ Although FFP contains all soluble coagulation factors, including the vitamin K-dependent Factor II, VII, IX, and X, the amount of each factor is not very high in FFP.⁹ Therefore, the total dose of FFP needed to reverse vitamin K antagonist anticoagulation will be quite large. Volume overload should be considered, which might lead to incomplete reversal.^{9,10} In this case, we administered FFP 720 ml on the first and second days in our hospital; however, coagulation times hardly changed (Table 1). We were afraid of volume overload because the patient was elderly with a small body. Insufficiency of the absolute amount of Factor X from FFP might cause no change in coagulation times. There was another possibility that Factor X slowly supplied by intravenous drip injection of FFP might be adsorbed onto amyloid fibrils, and consequently, administration of FFP would not improve coagulation times.

PCC typically contains a combination of either three or four vitamin K-dependent clotting factors.¹⁰ PCC is used for the rapid replacement of vitamin K-dependent clotting factors in patients with clinically significant bleeding events, especially for the treatment of bleeding due to rivaroxaban, an oral Factor Xa inhibitor, or dabigatran, an oral direct thrombin inhibitor.¹¹ Some authors have reported their experiences of Factor X deficiency treated with PCC and showed its safety and effectiveness.¹² PPSB-HT[®] containing four Factors (II, VII, IX, and X) is used as PCC only in Japan.¹³ PPSB-HT[®] 500 U contains about 500 U of each Factor, and is usually used with a small amount of solute (25 ml). In our case, we immediately treated the patient surgically because her symptoms deteriorated significantly. PPC can be quickly administered in large doses with a small amount of solute; therefore, it was useful in our case. PPC should be used with caution as infusion may be associated with an increased risk of thrombosis.¹⁴

To the best of our knowledge, there has been no report of SSEH with Factor X deficiency; therefore, we can recommend no additional remedy for this condition. In our experience, PCC might have prevented bleeding during surgery in this case.

Conclusion

We report the first case of successful surgery for SSEH with acquired Factor X deficiency using PCC. If SSEH patients show a prolonged clotting time without anticoagulant agents, physicians should consider coagulation factor deficiency.

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Disclaimer statements

Contributors Author contribution to the study and manuscript preparation include the following. Conception and design: HA. Analysis and interpretation of data: all authors.

Conflicts of interest None.

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