Spinal epidural hematoma (SEH) is a rare neurosurgical emergency in which pressure on the spinal cord leads to acute neurological deficits, and is a rare complication in children with hemophilia. We report three cases of SEH in severe hemophilia A. An 8-month-old boy who presented with non-traumatic acute-onset irritability was found to have SEH and was later diagnosed with hemophilia. The two other patients presented with neck pain and magnetic resonance imaging confirmed the diagnosis of SEH. Two patients who received conservative management fully recovered, however the patient who presented with progressive neurological abnormalities at the time of diagnosis, received surgery but later developed breathing difficulties and quadriplegia. Early diagnosis and immediate, aggressive, clotting factor replacement therapy are crucial when managing SEH in children with hemophilia, Immediate and aggressive factor replacement, accompanied by both neurological monitoring and early imaging, are essential for hemophiliacs with suspected SEH.

Key Words: Hemophilia, Spinal, Epidural, Hematoma, Management

Introduction

Hemophilia is the most common serious congenital coagulation factor deficiency. Central nervous system bleeding is one of the most common causes of mortality in hemophiliacs [1]. Even though a Spinal epidural hematoma (SEH) is a very rare hemophilia, it can lead devastating result such as neurologic deficits and even death [2]. Hemophilia is also the leading underlying disorder in cases with known diseases [3]. The treatment for blood-induced spinal compression is surgical decompression and hematoma evacuation. Especially in patients with hemophilia, immediate infusion of clotting factor concentrate after the first symptom develops may avert the need for surgery [4].

In this article, we report on three cases of SEH in children with hemophilia who underwent different treatments and had varying prognoses.
Case Report

1) Case 1

An 8-month-old boy who had been previously healthy presented to a local emergency department with torticollis and irritability 1 day in duration. There was no underlying illness and no history of any significant trauma. Abdominal ultrasound and cranial computerized tomography were normal. Initial laboratory studies revealed a prolonged acti-
vated partial thromboplastin time (aPTT: 136.8 s), but a normal international normalized ratio (INR: 0.96). Both the abnormal coagulation results and the constant irritability suggested a spinal lesion, and spinal magnetic resonance imaging (MRI) revealed a posterior epidural hematoma extending from C2 to S1 (Fig. 1A). Fresh frozen plasma was immediately transfused and intravenous dexamethasone administered. He was then transferred to our hospital for correction of the coagulopathy and surgical management. He was evaluated in the neurosurgery department and observed without surgery, as the neurological signs were normal. He was finally diagnosed with severe hemophilia A and factor VIII (FVIII) replacement started to reach 100% of factor FVIII activity. This was successful; he recovered from the SEH without any neurological sequelae. His total in-patient treatment time was 19 days; 1 month later, repeat MRI showed improvement of the posterior epidural hematoma (Fig. 1B). However, he developed transient antibody to FVIII after treatment.

2) Case 2

A 14-year-old patient with severe hemophilia A complained of the inability to move an arm and a leg commencing 12 hours prior, and of a severe headache and neck pain commencing 18 hours prior. He had been diagnosed severe hemophilia A at the age of 8 years old in a local clinic and taking on-demand factor replacement therapy. There was no history of trauma or any exercise that might have damaged the neck. He visited a local emergency medical center and cervical spine MRI revealed a cervical SEH (Fig. 1C). He was given intravenous dexamethasone and factor replacement to reach 100% of FVIII activity 27 hours after symptoms developed, and was then transferred to our hospital for further work-up and treatment. On physical examination, his vital signs were stable and he was alert, but exhibited flaccid lower-extremity paralysis with decreased power (right I, left I). Both upper extremities exhibited rather favorable neurological signs and antigravity power (right III, left IV). After careful examination, he was evaluated in the neurosurgery department and underwent laminectomy from C3 to C6, to decompress the spinal cord and remove the hematoma, with continuous factor replacement. We continued factor replacement therapy post-operatively. However, on the morning of post-operative day 9, he complained of difficulty in breathing, and of further loss of strength and sensation in the right arm. A repeat MRI was performed; the spinal cord compression had slightly improved but diffuse spinal cord swelling and spinal cord infarction were observed (Fig. 1D). He underwent conservative inpatient treatment for 4 weeks, accompanied by factor replacement, but developed quadriplegia and a need for permanent ventilator care because of an inability to breathe spontaneously.

3) Case 3

An 18-year-old severe hemophilia A patient with antibody to factor VIII presented to the emergency room with posterior neck pain and limitation of neck motion. He was diagnosed with SEH by cervical-spine MRI in a primary medical center and then transferred to our hospital. He had been on immune tolerance induction (ITI) for the previous 8 months and was also taking an activated prothrombin complex concentrate (aPCC) for bleeding episode.

Neurological examination revealed normal sensation and antigravity responses in both the upper and lower extremities. A coagulation study revealed a high titer of antibody to FVIII (45.0 Bethesda Units). Initial cervical spine MRI revealed a subacute SEH (Fig. 1E). Initially, we prescribed a bypassing agent (aPCC, 200 IU/kg/day) commencing 36 h after the initial symptoms developed. He was consulted and observed by the neurosurgery department without surgery. The neck pain and movement improved 1 day after admission. However, he complained of further weakness in both legs and developed persistent urinary incontinence on day 5 of admission. Spinal MRI performed on that day revealed that the SEH along the cervicothoracic spine had improved (Fig. 1F). Factor replacement continued, but was tapered by 3 weeks. The patient recovered fully from his neck pain and urinary symptoms, and was discharged.

Discussion

Central nervous system bleeding is one of the most com-
mon causes of mortality in hemophiliacs [2,5]. Even though an SEH is a very rare complication in hemophilia, it can lead devastating result such as neurologic deficits and even death [2]. Hemophilia is also the leading underlying disorder in cases with known diseases [3]. In all of our three patients are diagnosed with severe hemophilia, the FVIII activity was $<1\%$, and no trauma history was reported.

The pathogenesis of SEH remains unclear; the general consensus is that the hemorrhage is venous in origin. Bleeding is presumed to be attributable to rupture of epidural veins after a sudden increase in intra-abdominal or intrathoracic pressure [5]. The most probable cause of bleeding is minor trauma experienced during play or physical activity; toddlers are at higher risk because their mobility is associated with frequent falls [6,7].

A spinal hematoma usually presents with sudden pain reflecting a lesion of the innervated cord. Neurological deficits can present hours or even days after the initial pain [5]. Infants exhibit less specific clinical features of irritated spinal cords, such as poor feeding, irritability, and crying, because of the immaturity of their motor system and difficulty in eliciting sensory deficits [7,8]. Our infant patient exhibited irritability and torticollis as the chief complaints; the two older patients presented with initial neck pain.

MRI is the optimal imaging modality for a suspected spinal epidural hematoma even when some time has elapsed between symptom development and diagnostic work-up [9]. If the hematoma is small on MRI, and the symptoms mild, MRI monitoring should be considered to avoid surgery if possible.

Surgical decompression and hematoma evacuation have been suggested as the conventional management in patient with symptomatic SEH [5,10,11]. However, surgical intervention in a hemophiliac with SEH is problematic because of the compromised coagulation status. The clinical course, coagulation status, and size, location, and extent of the hematoma should be considered when choosing an optimal management strategy [12]. Although no definitive consensus on SEH treatment has yet emerged, recent studies have suggested that factor replacement should be initiated promptly based on careful examination; a multi-disciplinary approach toward treatment is needed [13]. Complete neurological recovery with conservative therapy is possible if a diagnosis is made early and factor replacement therapy is intense [13]. However when neurological impairment is progressive, surgical interventions should be contemplated. A recent meta-analysis emphasized that the duration of preoperative paralysis was the only independent predictor of poor outcomes [14].

In another cohort study about association between prophylaxis and intracranial hemorrhage, performed in United States, prophylaxis was effective in lowering the risk of in-

### Table 1. Characteristics of hemophilia patients with spontaneous spinal epidural hematoma and their treatment strategies

| Characteristics of patients | Case 1 | Case 2 | Case 3 |
|-----------------------------|--------|--------|--------|
| Age                         | 8 months | 14 years | 18 years |
| Hemophilia Type             | A      | A      | A      |
| Hemophilia Severity         | Severe ($<1\%$) | Severe ($<1\%$) | Severe ($<1\%$) |
| Inhibitor                   | No     | No     | Yes    |
| Medical history             | Previously healthy | On-demand factor replacement | Immune tolerance therapy |
| Initial symptoms            | Torticollis, Irritability | Neck pain, Headache | Neck pain, Shoulder pain |
| Interval from symptom onset to treatment | 17 hours | 27 hours | 36 hours |
| Affected spinal cord levels | C2-S1  | C2-C6  | C2-thoracic spine |
| Treatment                   | Fresh frozen plasma, Factor VIII replacement | Laminectomy, Factor VIII replacement | Activated prothrombin complex concentrate replacement |
| Total factor replacement period | 19 days | 28 days | 21 days |
| Outcomes                    | Full neurological recovery, Transient anti-FVIII antibody | Quadriplegia, | Full neurological recovery |

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tracranial hemorrhage in severe hemophilia or those with inhibitors [15]. In our case report, case 2 patient had the on-demand therapy while case 3 patient was under the ITI with a prophylactic usage of bypassing agent. We speculate that prophylaxis might affect the favorable prognosis of the case 3 patient and further investigations are need to evaluate the effect of prophylaxis for development of SEH.

Our cases highlight the various management options for spinal hematoma in hemophilic patients. The characteristics of patient and their treatment strategies were summarized on Table 1. Two patients received aggressive replacement therapy when the SEH was diagnosed and the other underwent emergency decompressive laminectomy because of progressive neurological deficits. For two of our patients, conservative management was a reasonable option because they presented with only minimal neural deficits, and their symptoms improved as clotting factors were replaced. In addition, MRI reflected marked absorption of both SEHs. However, although the third patient who presented with progressive neurologic abnormalities underwent emergent neurosurgery, significant neurological sequelae developed post operatively.

We have reviewed the different clinical courses and outcomes of severe hemophilia patients with SEH and outline a best-practice therapeutic approach. In brief, we suggest that immediate and aggressive factor replacement accompanied by both neurological monitoring and early imaging, are essential for hemophilic with a suspected SEH and may obviate need for surgery. When patient presented with rapid progression of neurologic abnormalities or aggravated neurological sign with conservative therapy, albeit cautiously, neurosurgery should be considered.

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