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Conservative therapy for spinal epidural hematoma in a child with hemophilia A with high-titer VIII inhibitors

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Abstract

The occurrence of a spinal epidural hematoma in patients with hemophilia A with high-titer VIII inhibitors is extremely rare and intractable. A 15-year-old male patient presented to our institution with acute back pain and progressive sensorimotor disorder of the bilateral lower extremities. He had hemophilia A with high-titer VIII inhibitors and had experienced recurrent hemorrhagic episodes for many years. Prompt magnetic resonance imaging revealed a spinal epidural hematoma. We administered bypassing agent therapy with prothrombin complex concentrates and performed intensive neurological monitoring. The neurological dysfunction improved with days, and the patient recovered completely within 3 weeks. Magnetic resonance imaging 1 year later showed that the hematoma had been completely absorbed. Spinal epidural hematomas in patients with hemophilia A with high-titer inhibitors can be successfully treated using prothrombin complex concentrates. Multidisciplinary discussions based on intensive neurological monitoring should be performed as early in the clinical course as possible.

Keywords

Spinal epidural hematoma, hemophilia A, inhibitors, conservative therapy, prothrombin complex concentrates, magnetic resonance imaging

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Introduction

Hemophilia is the most common hereditary bleeding disorder, with an incidence of 0.7 to 0.8/10,000. Hemophilia A is characterized by an inherited deficiency of factor VIII. Central nervous system hemorrhage

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is an uncommon but severe complication in patients with hemophilia, occurring in only 2% to 8% of children with hemophilia. Less than 10% of these hemorrhages are intraspinal.[1] The occurrence of a spinal epidural hematoma (SEH) in patients with hemophilia A with high-titer factor VIII inhibitors is even more rare. In this report, we describe a hemophilic child with an SEH treated with bypassing agent therapy using prothrombin complex concentrates (PCCs).

Case report

A 15-year-old male patient presented to our institution with acute back pain and progressive sensorimotor disorder of the bilateral lower extremities. He had known hemophilia A with inhibitors. One week previously, he had developed a hemorrhagic episode of the left knee joint and was treated with PCCs at 20 U/kg per day for 2 days; however, the hemorrhage persisted, and he therefore received preliminary treatment with a 400-mL plasma transfusion. Despite this treatment, his symptoms deteriorated with increased weakness, numbness, and hypoesthesia of the bilateral lower extremities and urinary incontinence. He presented again to our institution 22 hours after the onset of back pain.

The patient had a 14-year history of severe hemophilia A (FVIII $<1\%$) with a 4-year history of high-titer (>5 BU) factor VIII inhibitors of 8.8 BU and recurrent episodes of subcutaneous ecchymosis, hematuria, and swelling of large joints. The hemorrhage had occurred at a frequency of about one to two times per year. However, hemorrhagic episodes had occurred three times during the past 4 months. His medical treatment included repeated infusion of factor VIII before the appearance of inhibitors 4 years previously, and PCCs and plasma transfusion treatment had been administered thereafter. The symptoms were rapidly alleviated each time. The quadriceps exhibited decreasing compliance because of the repeated hemorrhage of the left knee.

Physical examination showed that the patient's sensory functions had decreased below the bilateral inguinal level, along with decreased muscle strength of the bilateral lower extremities (including the iliopsoas, quadriceps, ankle dorsiflexion, and plantar flexion), a negative testosterone reflex, a hyperactive knee jump reflex and ankle reflex, positive patellar clonus and malleolus clonus, a questionably positive Babinski sign, and normal perianal sensory function (American Spinal Injury Association (ASIA) grade B). The sensory function over the inguinal level and the strength of the bilateral upper extremities were normal. Immediate T2-weighted sagittal magnetic resonance imaging showed a biconcave, hypointense mass lesion in the spinal epidural space with cord compression from T10 to L1 (Figure 1).

The diagnosis was as follows: spontaneous spinal epidural hematoma, incomplete bilateral lower extremity paraplegia, cauda equina syndrome, and hemophilia A with inhibitors.

A multidisciplinary consultation, which included professionals from the departments of medicine, anesthesiology, orthopedics, neurosurgery, and radiology, was immediately conducted, and an agreement regarding treatment was reached. Because of the risk of thrombosis, we treated the patient with bypassing agent therapy using regular PCCs at a volume of 20 U/kg. Intravenous pulse methylprednisolone therapy was administered for 1 day to prevent obstructive complications in the spinal column. The patient's symptoms were intensively monitored and neurological examinations were strictly implemented. The multidisciplinary team decided that urgent surgical intervention for the SEH would be the alternative treatment if no

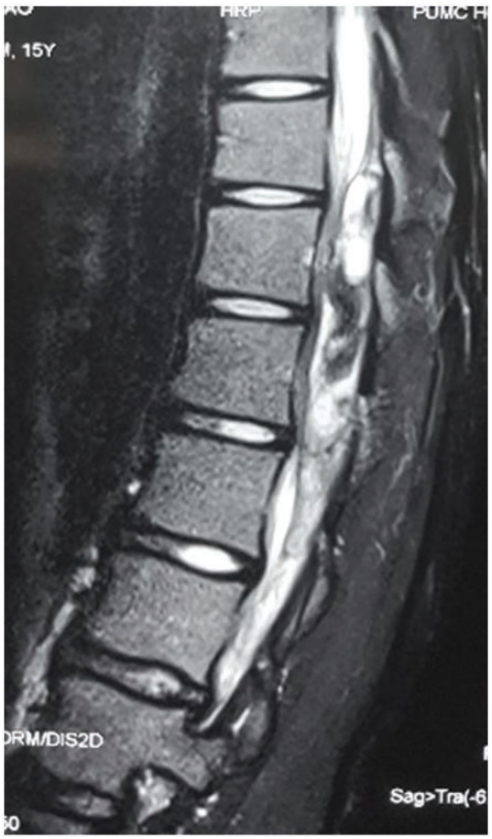

Figure 1. T2-weighted magnetic resonance imaging showing a spinal epidural hematoma from T10 to L1.

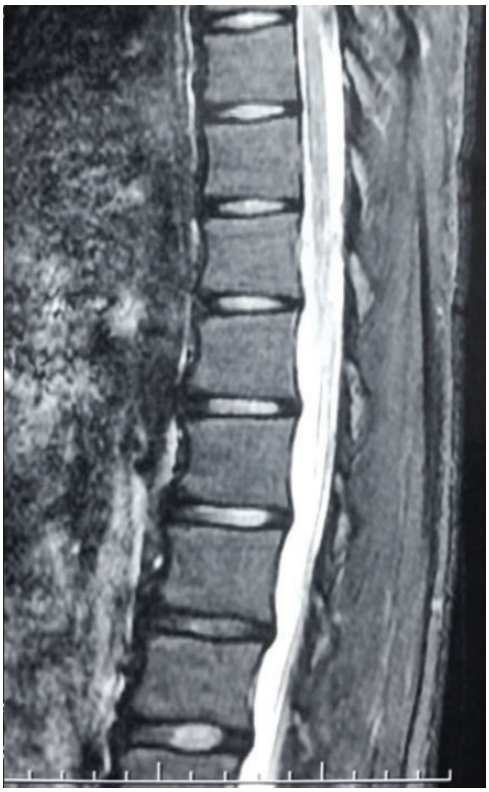

Figure 2. T2-weighted magnetic resonance imaging showing complete absorption of the hematoma 1 year later.

improvement in the neurological deficits was observed.

Ten hours after PCC infusion, autonomic urination and improvement of weakness and sensory loss were observed (ASIA grade B→C). Bypassing agent therapy with PCCs at 20 U/kg was subsequently administered continuously twice a day for the next 6 days until the patient was discharged. During this period, the numbness, muscle strength, and sensory abilities of the bilateral lower extremities recovered rapidly. After 5 days of conservative therapy, the patient was discharged with normal sensory function and almost complete muscle strength recovery of the lower extremities, mild numbness of the left dorsalis pedis and plantar regions (ASIA grade D), and a hypoactive bilateral knee jump reflex.

Three weeks later, the patient had completely recovered (ASIA grade E). Magnetic resonance imaging conducted 1 year later showed that the hematoma had been completely absorbed (Figure 2).

Discussion

The development of an SEH in hemophiliacs is a rare condition characterized by acute back or neck pain followed by rapidly progressive sensorimotor disorder of the extremities and cauda equina syndrome. Surgery, conservative therapy, or both are

selective approaches for SEHs. Although there is no consensus on the treatment of SEHs in hemophiliac patients with inhibitors, conservative therapy with intensive monitoring of symptoms and neurological examination is preferred, and surgical interventions are needed if the neurological deficits do not improve.[2] Only a few reports have described SEHs in hemophiliac children with inhibitors. Leach et al.[3] successfully treated a 21-year-old man with severe hemophilia A and inhibitors who presented with an extensive SEH using recombinant activated factor VIIa. Oymak et al.[4] also successfully treated an infant with severe hemophilia A and inhibitors who presented with an SEH using recombinant activated factor VIIa. Erkutlu et al.[5] reported the successful treatment of a 5-year-old child with an SEH using activated PCCs (aPCCs).

For SEHs in hemophiliac patients with high-titer inhibitors, infusion of corresponding coagulation factor VIII is not recommended. PCCs and aPCCs are effective bypassing agents. In 1980, Lusher et al.[6] first confirmed the efficacy of PCCs on hemarthrosis in 51 hemophiliac patients with inhibitors of factor VIII. Later, in a double-blind clinical trial,[7] 117 joint bleeding events and 29 muscle bleeding events occurred in patients with hematomas with high-titer inhibitors (>5 BU) to factor VIII, and PCC therapy was effective for 52% of the episodes. In 1983, Lusher et al.[8] compared the effectiveness of aPCCs and PCCs. When used for 82 hemarthrosis episodes in 26 patients with inhibitors (>2 BU) to factor VIII, aPCCs showed no additional benefits at a dose of either 50 or 75 FECU/kg compared with the use of PCCs of factor IX at a dose of 75 U/kg.[8]

Surgery, mainly laminectomy, remains an option for SEHs in hemophiliacs with inhibitors because it can immediately decompress the spinal cord. However, a coagulation disorder places the patient at higher risk of infection, excessive bleeding, and a recurrent hematoma, which can result in recurrence of spinal cord compression.[9] A 74-year-old man with an unacknowledged diagnosis of mild hemophilia A underwent surgery for an SEH. However, complete paraplegia developed because of redevelopment of large epidural hematomas that completely blocked the epidural canal. An emergency intervention was performed, and the diagnosis of mild hemophilia A was confirmed.[10]

At our institution, we have chosen to use PCCs as the bypassing agent. Intensive monitoring of symptoms and neurological examinations are crucial in such cases. If neurological deficits have not improved or have deteriorated in a patient with an SEH, urgent surgical interventions should be immediately performed because delayed decompression of the spinal canal can lead to severe morbidity.[11] Inspiringly, remarkable neurological improvement was observed in our patient.

In summary, the occurrence of an SEH in patients with hemophilia A with inhibitors is extremely rare. These hemorrhage episodes are characterized by acute back pain, progressive sensorimotor disorders of the extremities, and cauda equina syndrome and can be accurately diagnosed using magnetic resonance imaging. Without immediate medical intervention, the hematoma develops rapidly, increasing the risk of irreversible paralysis. Multidisciplinary discussions should be performed as early as possible, and intensive monitoring of symptoms accompanied by regular neurological examinations are essential. The hemorrhagic episodes can be cured through early administration of PCCs.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics

This case report was performed under a waiver of authorization approved by the Institutional

Review Board of Peking Union Medical College Hospital, Beijing, China. Both the patient himself and his parents provided written informed consent.

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