Successful Non-operative Management of Intra-abdominal Hemorrhage in Two Patients with Hemophilia A

Mi Jin Kim, M.D., Eun Hye Lee, M.D., and Hoi Soo Yoon, M.D.
Department of Pediatrics, College of Medicine, Kyung Hee University, Seoul, Korea

Spontaneous intra-abdominal hemorrhages are uncommon in hemophilic patients. They can cause complications in patients with severe hemophilia, and are associated with a high mortality rate. To date, there is no guideline for the management of intra-abdominal hemorrhage in patients with hemophilia. Management of intra-abdominal hemorrhage ranges from conservative treatment to emergent embolization or surgery. We describe two children with hemophilia A, who were successfully treated non-operatively by administering coagulation factor concentrates and embolization, and were later discharged from the hospital. We emphasize the role of an active approach in the evaluation and management of intra-abdominal hemorrhage without any surgical intervention.

Key Words: Intra-abdominal hemorrhage, Non-operative management, Hemophilia

Introduction

Hemophilia is a severe bleeding disorder that can result in significant morbidity and mortality [1]. Although a spontaneous intra-abdominal hematoma in patients with hemophilia is a rare condition, it can be fatal in patients with hemophilia [2,3].

The etiology of a spontaneous intra-abdominal hemorrhage is unclear [4]. Spontaneous intra-abdominal hematoma may be due to injury of the intra-abdominal muscles by physical efforts such as stretching, which is usually postulated as the cause in cases of severe hemophilia [5]. It is possible for physicians to doubt the presence of other abdominal and pelvic disorders because of the symptoms that patients complain of; thus, a high level of clinical suspicion is required to diagnosis a spontaneous intra-abdominal hematoma. In these cases, a radiograph is helpful in making the diagnosis. Ultrasonography serves as an effective and inexpensive modality to diagnose these bleeds and hematomas, especially in regions not easily accessible clinically. Computed tomography (CT) and magnetic reso-
nance imaging enable physicians to make a more definitive diagnosis and follow-up [6].

There is no clear guideline for managing intra-abdominal hemorrhage in patients with hemophilia. Various methods have been introduced to treat huge intra-abdominal hemorrhage including surgical therapy. However, the invasive procedure is risky in patients with hemophilia, so it should be carefully considered [7]. Many coagulation factor concentrates have been developed, and these factors are often used to control the bleeding episodes in patients with hemophilia. Herein, we describe two patients with intra-abdominal hemorrhage in whom bleeding was successfully controlled with non-operative management.

**Case Report**

1) Case 1

A 15-year-old boy, on first admission, presented with gradually increasing lower abdominal pain for about 2 days (Table 1). There was no history of trauma. He was diagnosed as having severe hemophilia A at 7 months after birth, and he had been treated with on-demand replacement therapy with recombinant activated factor VII (rFVIIa, NovoSeven, Novo Nordisk, Kalundborg, Denmark) because of the presence of an inhibitor. On admission, his vital signs were stable. On physical examination, a firm, palpable mass measuring $4 \times 5$ cm was located in the left lower quadrant of the abdomen. The prothrombin time (PT) was less than 10 seconds (reference range: 11-15 seconds), and the partial thromboplastin time (PTT) was prolonged by 71.9 seconds (reference range: 25-35 seconds). His hemoglobin level was 10.9 g/dL, hematocrit level was 32.9%, and platelet count was $317 \times 10^3/\mu$L. The initial abdominal computed tomography CT scan confirmed the presence of the hematoma in the left paracolic gutter ($11.3 \times 4.07$ cm) and no active bleeding (Fig. 1A). The patient was treated with 90 $\mu$g/kg of rFVIIa every 2 hours for 4 days after hospital admission. Then from hospital days 4-6, rFVIIa was administered every 3 hours. Since his vital signs were stable without any change in the hemoglobin level, we administered rFVIIa at 6-hour intervals until discharge. He was discharged on day 9 with no abdominal pain. We gradually reduced the dose by tracking his condition on an outpatient basis, and two months later, the abdominal CT scan showed resolution of the left lower quadrant mass (Fig. 1B). We then irregularly injected rFVIIa, and he has since been without any problems. However, he was hospitalized again with aggravated abdominal pain at 3 months after discharge. On his second admission, the abdominal CT scan showed a new, large hematoma at the left iliopsoas muscle with active bleeding. We closely monitored his vital signs and performed serial

Table 1. Clinical and laboratory features of two patients with hemophilia A with intra-abdominal hemorrhage

| Clinical and laboratory features                     | Patient 1                          | Patient 2                          |
|------------------------------------------------------|------------------------------------|------------------------------------|
| Age at presentation (years)                          | 15                                 | 6                                  |
| Clinical symptoms                                    | Abdominal pain with nausea, vomiting | Periumbilical pain with febrile sensation |
| Factor VIII level at diagnosis (%)                   | <1                                 | 9                                  |
| Presence of the inhibitor of the factor              | (+)                                | (−)                                |
| Initial laboratory findings                          |                                    |                                    |
| Hb (g/dL)/Hct (%)                                    | 10.9/32.9                          | 9.8/28.2                           |
| Platelet count ($10^3/\mu$L)                         | 317                                | 295                                |
| PT/aPTT (sec)                                        | <10/71.9                           | 14/65.9                            |
| Size of the hematoma on the CT scan (cm)             | $11.3 \times 4.07$                | $7.8 \times 5.0 \times 5.9$         |
| Factor replacement therapy                           | rFVIIa (NovoSeven)                 | Advate                             |
| Duration of hospitalization (days)                   | 5                                  | 100 IU/kg every 8 to 12 h for 8 days|
| Size of the hematoma on the follow-up CT scan (cm)   | $9.3 \times 3.2$                   | 4.1 $\times 3.2$                   |

PT, prothrombin time; aPTT, activated partial thromboplastin time; CT, computerized tomography; NovoSeven, recombinant coagulation factor VII (Novo Nordisk, Kalundborg, Denmark); Advate, recombinant factor VIII (Baxter, Neuchatel, Switzerland).
follow-up of his hemoglobin level while administering rFVIIa. On admission, his hemoglobin level was 11.9 g/dL, and despite continued rFVIIa replacement therapy, the follow-up hemoglobin level decreased to 6.6 g/dL within only 2 days. Moreover, his blood pressure was 80/50 mmHg on the third day of hospitalization. He underwent successful embolization using microcoils at the left lumbar artery after rFVIIa was administered. After the procedure, as before, he was treated with 90 μg/kg of rFVIIa every 2 hours for 2 days, and then his vital signs stabilized. He was discharged after medical management with the rFVIIa (Fig. 1C).

2) Case 2

A 6-year-old boy with moderate hemophilia A complained of periumbilical pain and a febrile sensation for 3 days (Table 1). On admission, the patient had an acutely ill appearance, his temperature was 38.2°C, heart rate was 142 beats/min, and blood pressure was 106/64 mmHg. His
Non-operative Management in Hemophilia

Fig. 2. Computed tomography (CT) scan of the abdomen and pelvis showing an intra-abdominal hematoma in a 6-year-old boy. (A) The initial CT scan (A-1) showing a huge hematoma, about 7.8×5.0×5.9 cm, on the right side along the gastrocolic ligament. (A-2) Coronal CT scan of the same patient. (B) Follow-up abdominal CT scans 1 month later. (B-1 and B-2) A smaller hematoma, about 4.1×3.2 cm, with liquefaction is observed in the right upper quadrant of the abdomen, and less hemoperitoneum is observed in both the paracolic gutter and pelvis.

physical examination showed severe abdominal tenderness that was more prominent in the periumbilical area with rigidity and muscle guarding.

Initial laboratory investigations showed a prolonged activated PTT of 65.9 seconds, factor VIII activity of 9%, hemoglobin level of 9.8 g/dL, hematocrit level of 28.2%, and platelet count of 295×10³/µL. An abdominal CT scan showed a hematoma in the right upper quadrant of the abdomen along the gastrocolic ligament measuring 7.8×5.0×5.9 cm, active bleeding from the branch of the right gastroepiploic artery, and diffuse hemoperitoneum in the right paracolic gutter and pelvic cavity (Fig. 2A).

The patient was treated with 50 IU/kg of the clotting factor concentrates (Advate, Baxter, Neuchatel, Switzerland) every 12 hours, and serial follow-up hemoglobin levels were monitored. On hospital day 3, his abdominal pain improved. Treatment continued for 8 days in the hospital, and then he was discharged home. After discharge, his condition was assessed on an outpatient basis, as with case 1, and we gradually decreased the dose of the coagulation factor concentrates.

One month later, the abdominal CT scan showed improvement of the intra-abdominal hematoma. The size of the hematoma on the CT scan decreased from 7.8×5.0 cm to 4.1×3.2 cm (Fig. 2B).

Discussion

Abdominal pain is usually the initial manifestation in patients with hemophilia with intra-abdominal hemorrhage; additionally, it may be related to discomfort due to hemoperitoneum, and it is non-specific [8]. Accordingly, it is difficult for physicians to easily suspect intra-abdominal hemorrhage. Ultrasound guidance plays an important role in the early detection of these bleeds and hematomas, and it can prevent significant morbidity. In addition, CT scans are more definitive for diagnosis and follow-up.

If no active bleeding is noted on a CT scan, as in the case of our first patient, coagulation factors can be administered alone with satisfactory results. Even if bleeding
from an artery appears to be minimal on a CT scan, as in the case of our second patient, physicians can expect a mass effect, i.e., parts of the hematoma pressing on the artery. If the hematoma is large enough, it may exert a mass effect on adjacent tissue; the hematoma can become biconvex and press against the vessel, avoiding further bleeding [9]. Thus, by carefully observing changes over time in the blood pressure and hemoglobin level, it is possible for physicians to achieve successful results by administering coagulation factor concentrates instead of performing a surgery. Despite using high-dose clotting factor replacement, as in the case of the second admission for our first patient, other treatments should be considered if there is a persistent decrease in the hemoglobin level and symptoms worsen due to active bleeding, such as increasing the dose or frequency of administering coagulation factor concentrates or performing embolization in patients with an inhibitor [10]. Surgical management remains the mainstay of therapy for patients with abdominal hemorrhage with active bleeding; however, it is associated with significant morbidity and mortality [11].

Intra-abdominal hemorrhage in patients with hemophilia is rarely reported worldwide, and its management is extremely difficult. However, we were able to successfully treat both of our patients. Our patients responded well to the medical treatment, and they were discharged safely from the hospital.

In conclusion, we described two patients with hemophilia A with intra-abdominal hemorrhage who were successfully treated with the proper factor replacement and embolization.

References

1. Mannucci PM, Tuddenham EG. The hemophilias-from royal genes to gene therapy. N Engl J Med 2001;344:1773-9.
2. Santagostino E, Morfini M, Rocino A, Baudo F, Scaraggi FA, Gringeri A. Relationship between factor VII activity and clinical efficacy of recombinant factor VIIa given by continuous infusion to patients with factor VIII inhibitors. Thromb Haemost 2001;86:954-8.
3. Yoshimi A, Takahashi T, Motokura T, Yatomi Y, Chiba S, Kurokawa M. Hemoperitoneum due to spontaneous rupture of the left gastroepiploic artery in a patient with hemophilia A. Ann Hematol 2009;88:811-2.
4. Farrelly C, Fidelman N, Durack JC, Hagiwara E, Kerlan RK Jr. Transcatheter arterial embolization of spontaneous life-threatening extraperitoneal hemorrhage. J Vasc Interv Radiol 2011;22:1396-402.
5. Yilmaz S, Oren H, Irken G, et al. Life-threatening mediastinal-retroperitoneal hemorrhage in a child with moderate hemophilia A and high inhibitor titer: successful management with recombinant activated factor VII. J Pediatr Hematol Oncol 2005;27:400-2.
6. Takahashi Y, Watanabe T, Uchiyama T, Gobda F, Sato M. Case report: Acquired hemophilia A with a severe hematoma in the iliopsoas muscle: a case report. Nihon Naika Gakkai Zasshi 2011;100:3052-4.
7. Sucandy I, Akmal YM, Gabrielsen JD. Spontaneous massive hemoperitoneum: A potentially life threatening presentation of the wandering spleen. N Am J Med Sci 2011;399-102.
8. Morichika K, Tomoyose T, Nishi Y, Nakachi S, Fukushima T, Masuzuki H. The intractable intra-abdominal hemorrhage with unknown etiology in a patient with severe hemophilia A. Am J Emerg Med 2015;33:129.e1-3.
9. Law EK, Lee RK, Hung EH, Ng AW. Radiological diagnosis and management of idiopathic spontaneous intra-abdominal haemorrhage (abdominal apoplexy): a case series. Abdom Imaging 2015;40:343-51.
10. Monahan PE, Aledort LM; Hemophilia Inhibitor Study Group. Factors affecting choice of hemostatic agent for the hemophilia patient with an inhibitor antibody. Am J Hematol 2004;77:346-50.
11. Samanci C, Ayvaci A, Korkmaz O, Bas A. Pelvic haemophilic pseudotumour in a patient with haemophilia. BMJ Case Rep 2013;2013.