Successful resection of giant abdominal hemophilic pseudotumor
Surgical treatment and follow-up outcomes in one single center

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Abstract
Giant abdominal hemophilic pseudotumor is exceedingly rare, thus may bring great challenges to the timely and proper diagnosis and treatment of clinicians. The only definitive management is complete removal of the abdominal hemophilic pseudotumor. The objective of this article is to report surgical treatment and follow-up outcomes of three unusual cases with giant abdominal hemophilic pseudotumor. We describe 3 patients with giant hemophilic pseudotumor involving the abdomen who were successfully treated with tumor resection. On presentation to our institution, the patients all had signs of giant cystic lesions in abdomen, and the patients’ most outstanding complaints were aggravated abdominal pain. All of three patients underwent complete excision of abdominal hemophilic pseudotumor. The patients showed adequate pain relief compared with the previous status. Surgical resection is the most effective treatment option for patients with giant abdominal hemophilic pseudotumor who can undergo appropriate surgical treatment. This represents a safe and reasonable approach to sustainably relieve pain and other symptoms with giant hemophilic pseudotumor in the abdomen. Perioperative coagulation factor replacement therapy is also of great significance in reducing the risks and complications.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, VAS = visual analogue scale.

Keywords: abdomen, complication, definite diagnosis, hemophilia, hemophilic pseudotumor, perioperative management, surgical treatment.

1. Introduction
Hemophilic pseudotumors are rare entities, which are only found in severe cases of hemophilia (1%–2%) and mainly located in the limbs.1–3 Pseudotumors consist of encapsulated, chronic, slowly expanding hematomas. Abdominal pseudotumors are exceedingly rare and their management is still controversial. Replacement therapy is often the first therapeutic approach, however, surgery is the most effective and the only definitive treatment even though it may be associated with higher rates of complications.4,5 Therapeutic options include radiotherapy, percutaneous drainage, embolization, and surgical excision.1–3 Herein, we describe our experience in the surgical management of giant intra-abdominal hemophilic pseudotumors in three patients with hemophilia A. The management of these unique cases has yet to be well-documented. Therefore, the majority of clinicians are less aware of this rare disorder and clinical experience in diagnosis and treatment of abdominal hemophilic pseudotumor is still lacking. Our focus is to emphasize the importance of considering hemophilic pseudotumor as a diagnosis and guiding the proper perioperative management strategy upon surgical treatment. We present an illustrative case describing the presentation, treatment, and postoperative course of three patients with giant abdominal hemophilic pseudotumor whose symptoms resolved significantly postoperatively (Table 1), followed by a review of the pertinent literature concerning the diagnosis and management for such lesions.

2. Case reports
2.1. Case 1
2.1.1. Presentations and examinations. A 30-year-old man with a 10-year history of severe pain in his right waist, was
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Table 1
Clinical characteristics of 3 patients with giant abdominal hemophilic pseudotumors in our single center.

| Patients | Age (yr), sex | Symptoms and signs | Location and size | Preoperative laboratory tests | Treatment | Postoperative outcome and follow-up visit |
|----------|--------------|--------------------|-------------------|-------------------------------|-----------|-------------------------------------------|
| 1        | 36,M        | Insidious swelling in the right wrist | 20 cm mass | activated partial thromboplastin time 31.8 seconds, factor VIII activity 51.6% (after factor VIII replacement) | Recombinant factor VIII concentrating 1000 to 2000 IU almost once a week for the past 10 years and painkillers | Complete resection of the right iliac wing was almost empty. The mass was about 25 cm × 20 cm × 15 cm in size, with clear boundaries, fixed basement, poor mobility and high texture and tension. After decompression, the tumors were divided into several cysts, and a large number of dark brown or chocolate-like viscous liquids were absorbed (Fig. 1D). The mass was totally excised and specimens were sent for pathological examination. No residual mass was found in the further follow-up visit. | 25 days |
| 2        | 15,F        | Aggravated right waist pain with inability to walk | Retroperitoneal mass | activated partial thromboplastin time 14.1 seconds, factor VIII activity 32,800/μL | Recombinant factor VIII concentrating 1000 to 2000 IU almost once a week for the past 6 years and painkillers | Complete resection | 30 days |
| 3        | 37,M        | Aggravated abdominal pain | Retroperitoneal mass | activated partial thromboplastin time 11.1 seconds, factor VIII activity 800 IU | Recombinant factor VIII concentrating 1000 to 2000 IU almost once a week for the past 6 years and painkillers | Complete resection | 40 days |

On physical examination, an intra-abdominal 20 × 20 cm mass was found, with hard texture and fluctuation feeling (Fig. 1A). Laboratory tests were performed for further detection including electrolytes, liver and kidney function tests, complete blood count, tumor markers, and serum infectious index. Results of laboratory tests confirmed that hemoglobin 9.7 g/dL, platelets 32,800/μL, prothrombin time 15.7 seconds (normal 10.4–12.6 seconds), activated partial thromboplastin time 36.2 seconds (normal 22.7–31.8 seconds), factor VIII activity 51.6% (after factor VIII replacement). Plain radiograph at his pelvic disclosed a regular shadow of a soft tissue mass (Fig. 1B). Computed tomography (CT) revealed a giant and well-defined mass involving the right pelvis and ilium in the retroperitoneum (Fig. 1C). Magnetic resonance imaging (MRI) of the abdomen and pelvis revealed widespread abnormal signal of the mass in keeping with components of hemophilic pseudotumor.

2.1.2. Surgical treatment. In consultation with the department of Hematology, we decided to perform surgical resection of the giant hemophilic pseudotumor. During the operation, the mass involving the right pelvis and ilium was successfully excised, and the reconstruction of the right pelvic ring was performed after D-J tube of the right ureter was placed preoperatively. The right ilium was invaded by the mass, and the middle part of the right iliac wing was almost empty. The mass was about 25 cm × 20 cm × 15 cm in size, with clear boundaries, fixed basement, poor mobility and high texture and tension. After decompression, the tumors were divided into several cysts, and a large number of dark brown or chocolate-like viscous liquids were absorbed (Fig. 1D). The mass was totally excised and specimens were sent for pathological examination. No residual mass was found in the further examination, and the bleeding was completely stanched. Visual inspection using the intraoperative fluoroscopy showed optimal position of all pedicle screws. Intraoperative blood loss was approximately 1600 mL, thus we used erythrocyte 4 U and plasma 400 mL. Postoperatively, the patient was referred to the ICU and transferred to general ward the next day. An x-ray after the surgery confirmed the correct positioning of the implants and no signs of displacement of the screws and rod (Fig. 1E and F). In the immediate postoperative period, the patient was given an infusion of factor VIII in order to maintain factor VIII activity between 40% and 50%. Postoperatively, therapeutic factor VIII levels were maintained till wound healing on the tenth postoperative day. The postoperative pathology report was consistent with a hemophilic pseudotumor (Fig. 1G). Chronic inflammation was observed in the fibrous cyst wall, multilocular hemorrhage was seen in the cyst wall, and polykaryocyte reaction was also observed.

2.1.3. Follow-up. One week after the operation, the patient’s right waist pain was significantly relieved. Moreover, VAS score
of his waist pain improved to 0–1 points compared to the preoperative status, 7 points. Following wound healing, the patient underwent rehabilitation therapy and was monitored as an outpatient. The postoperative 2-year follow-up visit showed no tumor recurrence and no new symptoms.

2.2. Case 2
2.2.1. Presentations and examinations. A 51-year-old man with 50 years history of hemophilia A presented to our institution with aggravated abdominal and left hip pain. The pain in his abdomen could reach 6 points using visual analogue scale and could not be alleviated with rest. Physical examination revealed the giant mass around his left hip with tenderness. Ultrasonography demonstrated a giant retroperitoneal mass sized 10 cm × 6 cm, and part of the tumor herniated from the left abdominal wall and located under the subcutaneous adipose layer. His medical treatment includes recombinant factor VIII concentrate 800 IU almost once a week for the past 6 years and painkillers. A computed tomographic scan and magnetic resonance imaging demonstrated the giant retroperitoneal hemophilic pseudotumor (Fig. 2A–E). Abdomino-pelvic imaging showed further irregularities including compression of adjacent organs and significant bone destruction of left ilium. No relevant special circumstances regarding his family history or personal history were identified. The neurological examination result was essentially normal. Based on these findings, the giant retroperitoneal hemophilic pseudotumor was considered.

2.2.2. Surgical treatment. After detailed analysis, the patient underwent surgical excision of the giant hemophilic pseudotumor and the patient was given an infusion of factor VIII in order to maintain factor VIII activity between 40% and 50% in the immediate postoperative period. Histopathologic examination including immunohistochemical staining was performed, and the diagnosis of hemophilic pseudotumor was made according to the criteria. The postoperative pathology together with symptoms and examinations was reported to be consistent with the giant retroperitoneal hemophilic pseudotumor.

2.2.3. Follow-up. One week after the operation, the visual analogue scale score of his abdominal pain improved to 0–1 points compared to the preoperative status, 6 points. The coagulation factor index remained within the ideal range. Subsequently, we administered combination medical treatment, the symptoms were successfully relieved gradually. At the 5-year follow-up visit, he had nearly full complete remission and reported palliative pain. There was no complication during the postoperative period.

2.3. Case 3
2.3.1. Presentations and examinations. In August of 2016, a 37-year-old man with 30 years history of hemophilia A presented to our institution with aggravated abdominal pain. In the medical journal of his current illness, the patient stated he had been experiencing a worsening abdominal pain for approximately 2 years. Ultrasonography demonstrated severe hydronephrosis of the right kidney and a giant retroperitoneal mass sized 20 × 15 cm. His medical treatment includes recombinant factor VIII concentrate 800 IU almost once a week for the past years and painkillers. A computed tomographic scan of abdomen also
demonstrated severe hydronephrosis of the right kidney and multiple giant retroperitoneal hemophilic pseudotumors (Fig. 3A–D). Abdominal enhanced magnetic resonance imaging showed further irregularities including significant compression of adjacent right ureter (Fig. 3E). In the medical journal of his current illness, the patient stated he had a family history of hemophilia A. No other relevant special circumstances regarding his family history or personal history were identified.

2.3.2. Surgical treatment. After detailed analysis, the patient underwent surgical excision of the giant hemophilic pseudotumor on the basis of perioperative coagulation factor replacement therapy. The tumor was excised completely and sent for pathological examination. Pathological examination confirmed the diagnosis of hemophilic pseudotumor. Postoperatively, her factor VIII activity returned to normal range. Moreover, the patient experienced pain relief and was then discharged and monitored on an outpatient basis.
2.3.3. Follow-up. One week after the operation, the patient’s VAS score of his abdominal pain improved to 0–1 points compared to the preoperative status, 7 points. Postoperatively, the patient underwent rehabilitation therapy and was regularly monitored for coagulation factor index level. To date, the patient has no recurrent symptoms in the three-year follow-up visit. There were no complications associated with the operation during the follow-up period.

3. Discussion

Hemophilia A is a congenital disease transmitted by the X chromosome with a recessive trait, characterized by a deficiency in the production of factor VIII. Hemophilia A is 10 to 20 cases per 100,000 people. Clinical manifestations vary a lot depending on the severity of the disease. Hemophilia A is classified as mild (>5%), moderate (1%–5%) or severe (<1%). Most common complications are spontaneous bleeding into joints and muscles. A rare complication is the hemophilic pseudotumor occurring in approximately 1% to 2% of patients suffering from severe hemophilia, which may present with painless or palpable masses, or with painful crises due to episodic acute bleeding into the tumor. The pseudotumor is caused by recurrent bleeding episodes into bone or soft tissue leading to the formation of an encapsulated mass of blood and necrotic tissue. Hemophilia pseudotumors are rare entities which are caused by bleeding from the fracture site or soft tissue with recurrent hemorrhage. The hematopoietic components and necrotic tissues that the body cannot absorb completely may constitute the tumor, brocysts which are formed by hemosiderin-containing macrophages. Abdominal hemophilia pseudotumors grow over time, leading to compression of adjacent tissues and organs, bone destruction, muscle and skin necrosis, and even organ failure. Spontaneous rupture of the tumor sometimes occur causing fatal consequences. Trauma, use of anticoagulant drugs and surgery are reported to be the main predisposing factors in literature.

In children, pseudotumors are most likely to involve the limbs or jaw bones, while in adults they predominantly arise in large muscles of the abdomen, pelvis or thigh. In literature, case reports or studies of patients with intra-abdominal hemophilic pseudotumors are extremely scarce. The majority of symptoms from hemophilic pseudotumors is due to their compressive effect on the adjacent tissues and organs causing bone destruction, muscle and skin necrosis, and visceral or vascular compression. Erosion into a blood vessel or spontaneous rupture of the tumor can lead to massive bleeding with fatal consequence. Few reports of successful resection of intra-abdominal hemophilic pseudotumor with bone involvement are seen in literature, which makes our reported case noteworthy.

The hemophilic pseudotumor of the abdomen is a rare entity but it may lead to disabling conditions, potentially fatal in patients with severe hemophilia. For diagnosing a hemophilic pseudotumor, invasive techniques including aspiration and biopsy are not advisable due to the increased risks of hemorrhage, infection, or other severe complications. Ultrasonic examination shows a central anechoic region with increased echoes behind the lesion due to enclosed fluid in the pseudotumor. CT and MRI are the most useful means to diagnose this disorder, allowing recognition of blood products in various stages of disease course. CT is particularly helpful in the evaluation of bone involvement and boundary of pseudotumor, whereas MRI is superior to CT for presentation of soft tissue lesions.

There is no consensus for the proper treatment of intra-abdominal hemophilic pseudotumors due to their rarity. Minimizing complications and preserving the function of the affected tissue or organ is the primary aim of clinicians. The greatest challenge to treat surgically is the high risk of bleeding in the perioperative periods. The conservative approach includes factor replacement, percutaneous drainage, and vascular embolization. Indeed, the contents of pseudotumors are too thick to permit complete drainage and its aspiration increases the risk of hemorrhage, infection, relapse, or chronic fistula.

Surgical treatment has been recommended in the management of hemophilic pseudotumors with progressive enlargement of the hematomas, hemodynamic deterioration or occurrence of other complications. When surgery is considered, surgeons should aim at complete resection but actually it is quite difficult in some cases. In general, both major neurovascular involvement and anatomy distortion caused by the hemophilic pseudotumors often prevent safe and complete resection. For intra-abdominal hemophilic pseudotumors, indications for surgery include evidence of enlargement of the pseudotumor, hemodynamic deterioration, or compressive complications. The risk of surgical bleeding can be minimized by rational administration of factor VIII at induction, during and after operation under the close supervision of hematology specialists. Frequent monitoring to maintain adequate levels of factor VIII makes surgical procedure safe. As is stated in our cases, continuous factor VIII replacement therapy was proven effective in preventing bleeding complications during the operation and the prolonged hospitalization. There are several studies in literature in favor of surgery in patients with hemophilia A combined with continuous or interrupted infusion of factor VIII to decrease risk of hemorrhage.

In such situations, radiotherapy and arterial embolization should be considered either alone or in combination with surgery. The decision to operate on this patient was made based on the gradually increasing size and long-term symptoms displayed by the patient. Surgical resection after major arterial embolization to reduce the vascularization of the pseudotumor is a good alternative, thereby reducing the size of the pseudotumor and the risk of bleeding during the operation. The best time interval between 2 procedures is to allow the mass to shrink but it is insufficient for vessel restoration. Radiotherapy is an alternative option where surgery is not feasible and conservative management is not effective, but further research is urgently needed to clarify the mechanisms and clinical effects of radiotherapy.

Nevertheless, there are several considerations to be kept in mind when deliberating on surgical intervention to intra-abdominal hemophilic pseudotumors, including perioperative hemodynamic instability and coagulation function control, possible incomplete tumor resection, intraoperative blood loss and hemodynamic instability, as well as postoperative adjuvant therapy. As the tumor is highly vascular, there may be significant intraoperative blood loss which may influence the hemodynamic instability and necessitate blood transfusion. In terms of our single-center experience, on the day of operation and the first day after operation, the dose of factor VIII should be 50 IU/kg, three times a day; during the 2nd and 3rd days after operation, the dose of factor VIII should be 30 to 40 IU/kg, twice daily; during the 4th
and 7th days after operation, the dose of factor VIII should be 20 to 30 IU/kg, twice daily; during the 8th and 14th days after operation, the dose of factor VIII should be 15 to 20 IU/kg, twice daily, according to the patient’s actual situation after operation. After discharging from hospital, abdominal ultrasound should be performed regularly, coagulation factor VIII should be infused properly to prevent recurrence of symptoms, and continue to treat primary hemophilia.[1–3,24]

In conclusion, this is a report of three exceedingly rare cases of large intra-abdominal hemophilic pseudotumor which was managed by surgical excision. Although uncommon, intra-abdominal hemophilic pseudotumor should be part of the differential when the patient has a history of abdominal pain and symptoms of other organs. We recommend completely surgical treatment of the intra-abdominal hemophilic pseudotumor, and it is the most effective treatment option for patients with symptomatic intra-abdominal hemophilic pseudotumor to sustainably relieve pain and destroy the tumor. If hemophilic pseudotumor is suspected, surgical treatment and perioperative coagulation factor replacement therapy should be performed and the patient should be followed up closely.

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