

Outcome of surgical management of hemophilic pseudotumor: Review of 9 Cases from single-center

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Abstract

Background: Pseudotumours are a rare and serious complication of haemophilia, A slowly growing pseudotumour frequently destroys structures of bone and soft tissues. Surgical resection is the primary method for treatment of proximal pseudotumours. The purpose of this retrospective study was to evaluate the operative methods and clinical results of surgical treatment for those rare cases.

Methods: We reviewed nine patients with hemophilic pseudotumours, who received surgical resection treatment in our hospital. The age range was 20-51 years. All operations were performed by one group surgeons. The method of operation depends on the origin and the extent of pseudotumor involvement. With the supplementary of recombinant coagulation factor VIII, six cases received complete resection; one received cytoreduction surgery as the pseudotumor closing to iliac vessel and nerve; two cases received complete resection and construction as bone destruction. Factor substitution was maintained for 14 days.

Results: In our series, the average intraoperative blood loss volume was 710 ± 35 ml (range, 240-2100ml). Six patients received blood transfusion during perioperative period. All wounds healed smoothly, no infection or chronic sinus formation. There is no iatrogenic vascular nerve injury in our series. Complete follow-up was performed in all patients. Mean follow-up duration was 14.5 months (range, 6–26 months). One patient with pseudotumor in the thigh had a recurrence of one year after operation, then secondary operation was performed,

Conclusions: Surgical resection for haemophilic pseudotumours is an effective and safe method. The choice of surgical procedure must be individualized according to the localization and the progress of pseudotumor. However, as relatively few cases and shorter follow-up time in our series. The long-term effects of these patients need further follow-up.

Background

Haemophilia is an inherited, sex-linked and recessive disorder of blood coagulation, which can be classified into types A (factor VIII deficiency) and B (factor IX deficiency). Its clinical symptoms are often related to the availability of standardized preventive treatment. Due to the differences in economic development, approximately 80% of patients with severe haemophilia live in developing countries, where they encounter economic constraints that prevent adequate prophylaxis [1, 2]. Repeated and unresolved haematomas may lead to the development of a pseudotumour, a serious and rare complication of haemophilia,

Pseudotumours occur in 1–2% of patients with severe haemophilia, and their development is associated with encapsulated blood after soft tissue or subperiosteal bleeding [3, 4]. Three types of pseudotumours have been identified [5], Type I is a simple cyst that develops within the muscle; Type II is a cyst that develops in a muscle and has an extensive blood supply in the region of its attachment to bone, type III is considered to be a true pseudotumour and originates from the bone itself. Some authors also classify pseudotumours as proximal or distal according to their anatomical location [6]. There were various protocols to treat hemophilic pseudotumours in the literatures, including immobilization measures, replacement therapy, radiotherapy, aspiration, embolization, and surgery. Surgical treatment was the most common method, especially the proximal pseudotumor [3]. However, due to the characteristics of this disease and the fewer clinical cases, treatment of complex haemophilic pseudotumour still be a challenge for orthopaedics.

We herein reviewed nine patients with hemophilic pseudotumours, who received surgical resection treatment in our hospital. The purpose of this retrospective study was to evaluate the operative methods and clinical results of surgical treatment for those rare cases.

Patients And Methods

Patient's characteristics

Between January 2017 and July 2019, there were nine patients diagnosed as hemophilic pseudotumour and underwent surgical resection in our hospital. The age range was 20–51 years (average: 32.8 years). Local pain, swelling, deformity and joint

disfunction were the most common reasons for a visit to hospital. All patients were defined as hemophilia A, family history of hemophilia in 7 patients. Three patients had history of resection treatment before admission (recurrent pseudotumour). Three patients had two or more pseudotumours on admission. All those are proximal pseudotumor, five in thigh, three in lower leg, one in iliac fossa. Two patients suffered from fistula formation.. No neurological impairment was found in all cases. Four patients had explicit trauma history. All characteristics of patients were recorded in Table 1, including age, typing, localization, clinical symptoms, duration of disease and others.

Table 1
The patient's characteristics, management methods and outcomes

Patient	Age (y)	Typing	Localization	symptoms	Duration (y)	Primary/recurrent	Management	outcome
1	39	⊖	thigh	Pain ,swelling	10	Recurrent	Resection	resolved
2	33	⊖	thigh	Pain ,swelling	4	Primary	Resection	Recurence and resection
3	25	⊖	Lower leg	Pain ,swelling	5	Primary	Resection	resolved
4	20	⊖	Lower leg	Swelling	3	Primary	Resection	resolved
5	51	⊖	thigh	Ulceration, fistules	6	Primary	Resection+ skin grafting	resolved
6	43	⊖	Pelvis	Pain,swelling	8	Recurrent	Resection	resolved
7	32	⊖	Lower leg	Pain ,swelling	5	Primary	Resection+ construction	resolved
8	23	⊖	Distal femur	Pain,fistules, disfunction	3	Recurrent	Resection + Arthroplasty	resolved
9	20	⊖	Distial femur	Pain,swelling disfunction	4	Primary	Resection + excluson	Waiting for reconstruction

Typing: According to Fernandez de Valderrama JA[5]

Preoperative examination and preparation

For the intra-muscular pseudotumor, which can be quickly and easily assessed with ultrasound, MRI can present more definite results, including size, boundary and the involvement of blood vessels and nerves around pseudotumor. If it appears in the ilium fossa, MRI can be used to determine whether the surrounding organs are involved. Duo to the different signal characteristics of haemoglobin breakdown products, MRI appearances of pseudotumor vary depending on the timing of the bleed[7, 8]. For bone pseudotumors, X-ray exam can find bone destruction and soft tissue rspnse generally. Three dimensional computed tomography (CT) can define the outlines and extent of bone destruction. In our series, four cases showed bone destruction.

The inhibitor and concentration of coagulation factor were examined after admission. None of the patients tested positive for inhibitor against factor VIII. According to the concentration of o factor VIII, seven cases were classified as severe hemophilia (< 1% factor VIII:). Two were moderate hemophilia (1%-5% factor VIII). C-reactive protein (CRP) increases slightly in two cases with but erythrocyte sedimentation rate (ESR) was normal. Two patients had negative results in bacterial culture of fistula secretions.

The dosage of recombinant coagulation factor VIII for replacement therapy was calculated in preoperation, which based on the patient's weight and preoperative factor VIII concentration. The coagulation factor was given 1 h preoperatively as a single bolus infusion, and the dosage was adjusted to maintain a peak factor level of approximately 80–100% on the day of surgery, 80% on postoperative days 1 to 3, 60% on postoperative days 4 to 6, and 30% thereafter. Factor substitution was maintained for 14 days. The factor VIII level was monitored during surgery and the postoperative.

Surgical procedure

All operations were performed by one group surgeons. The method of operation depends on the origin and the extent of pseudotumor involvement. Four intra-muscular pseudotumors were removed completely including thick fibrous capsule. The deep fascia tissue should be sutured tightly as much as possible to reduce the residual cavity. Patient 5 was intra-muscular pseudotumor with skin ulceration and fistula, who suffered three times operations including debridement and skin grafting. For patient 6, his pseudotumor was found growing in the iliac fossa, who had surgery two years ago, part of the ilium suffered from distrution, complete resection may be difficult because the internal side of pseudotumor was close to the internal iliac vessel and nerve, partial resection was chose. Patient 7 showed pseudotumour invaded tibia, after complete resection, bone graft and supplementary internal fixation were performed. Patient 8 was an intraosseous pseudotumour with a fistula in the distal femur and ipsilateral haemophilic arthritis of the knee. We removed the pseudotumour in the distal femur, performed joint replacement, and implanted a knee mega-endoprosthesis in a one-stage procedure. Patient 9 had pseudotumor in the distal femur, combined with serious destroy of quadriceps femoris and patella, we choose resection of pseudotumour, arthrodesis and bone graft will be performed the second stage.

Six patients had drainage tubes and remained for 2 days .Postoperatively the patients were closely monitored and received prophylactic antibiotics for 2 to5 days.

Results

In our series, the average intraoperative blood loss volume was 710 ± 35 ml(range, 240–2100 ml). Six patients received blood transfusion during perioperative period. The average duration of surgery was 136 ± 12 minutes(range, 110–240 min).The average length of hospital stay was 16.3 ± 2.6 days (range, 12–25 days). All wounds healed smoothly, no infection or chronic sinus formation. There is no iatrogenic vascular nerve injury in our series.

Complete follow-up was performed in all patients. Mean follow-up duration was 14.5 months (range, 6–26 months). One patient (Patient 2) with pseudotumor in the thigh had a recurrence of one year after operation, then secondary operation was performed, no recurrence was found in the last follow-up.

Discussion

In China, standardized diagnosis and treatment of hemophilia lags behind developed countries. The investigation in the 1980s confirmed the prevalence of hemophilia in China was 2.73/100,000 [9], There is a lack of systematic statistics for morbidity in recent years. At present, clotting factor substitution therapy is considered as the most effective way to reduce complications of haemophilia[10], but significantly increase medical costs. Preventive treatment was difficult to realized in the past in China, therefore, the incidence of complications may be more higher in the hemophilia patients in China. With the improvement of national medical insurance policy, many patients from remote and economically undeveloped areas came to orthopaedic clinic for treatment. Our hospital is the main institution for the suigical treatment of hemophilia patients in Anhui province in China. That's why we could receive these patients with pseudotumors in such a short period. In the past three years, our team performed orthopedic operations for 45 haemophilia patients, of those, ten patients suffered from pseudotumor and received surgical resection. Except for one case of postoperative recurrence, most patients have achieved satisfactory results.

The patients with pseudotumour often have multiple clinical symptoms, including pain, swelling, deformity, joint dysfunction and others. The treatment of pseudotumours varies and is associated with the patient's age and the type and progression of the pseudotumour. Distal pseudotumours in children may be treated primarily with long-term replacement therapy or local

radiotherapy[11–13]. Surgical removal is the primary treatment for large proximal pseudotumours or when conservative management fails[11, 14]. Several case reports and retrospective analyses have shown that surgical resection is an effective and reasonable treatment for pseudotumours when the patient is covered by factor replacement therapy [12, 15, 16, 17, 18]. Other therapeutic methods described in the literature include puncture and aspiration of the pseudotumour as well as aspiration and refilling of the pseudotumour with coralline hydroxyapatite [19,20]. The cases described in this group belongs to proximal pseudotumors, two cases appeared skin and bone destruction, the operational indication was clear.

The choice of surgical procedure must be individualized according to the localization and the progress of pseudotumor. In the present cases, four patients with intra-muscular pseudotumors underwent resection completely. For the patient with the recurrent pseudotumor in the iliac fossa, even if the incidence of recurrence will increase, cytoreduction surgery was performed to prevent iatrogenic neurological and vascular injuries[17]. If the bone was involved, after resection of pseudotumor, the reconstruction of bone defect by autogenous or allogeneic cancellous may be necessary. If combined with hemophilic osteoarthritis. one-stage arthroplasty remains an optional method.

Perioperative blood loss, pseudotumor recurrence and infection were also important matters that the surgeons concerned. Though uncontrolled perioperative bleeding is a less serious problem for surgeons with therapeutic clotting factors became available, The perioperative blood loss hemophilia patients still be higher than that of non hemophilia patients in the same kind of operation[21, 22]. There also has a high blood transfusion rate in our series. Standardized application of coagulation factors, precise operative procedure and antifibrinolytic agents are all important steps to control bleeding. For large size of the pseudotumor, in order to control bleeding, many reports suggested the method of arterial embolization can be used to minimize the vascularization of the pseudotumour[23]. In our series, we didn't choose this method because of inexperience. Pseudotumor recurrence may be a tricky problem. He, et al [17] retrospectively reviewed eighteen pseudotumor patients underwent surgical treatment. over a 40-year period in China, Of those, fifteen patients received resection or resection and reconstruction, two recurrence was observed. Whereas, Panotopoulos, et al[24] analysed six patients with a haemophilic pseudotumour who were treated through surgical treatment, at the latest follow-up after 8.4 (range,4–24) years, no recurrence was observed. In our series, follow-up time is shorter, one case showed recurrence. There is no clear reason for recurrence, we speculate recurrence may relate to incomplete resection and late bleeding. The risk of infection was higher in patients with haemophilia than in the normal population [25, 26]. There is no widely accepted explanation for the high incidence of infection in patients with haemophilia. Infection may be associated with self-injection of coagulation factor concentration with skin contamination, human immunodeficiency virus, and hepatitis C[27, 28].

In conclusion, surgical resection for haemophilic pseudotumours is an effective and safe method. The choice of surgical procedure must be individualized according to the localization and the progress of pseudotumor. As relatively few cases and shorter follow-up time in our series. The long-term effects of these patients need further follow-up. Clinical experience in the treatment of haemophilic pseudotumour also needs further improvement.

Declarations

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Availability of data and materials

The datasets used during the current study are available from the first author on reasonable request.

Authors' contributions

Yunfeng Yao was responsible for the study concept and design and drafting of the manuscript. Juehua Jing lead for the work and was involved at all stages of the paper. Yunfeng Yao, Juehua Jing, Jingcai Niu, Chenxi Xue, Wang Fang and Pengde Kang participated in the operation, data collection and analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

An ethics approval for this study was obtained from the Ethics Committee of the Anhui Medical University, and each patient signed an informed consent.

Consent for publication

All authors provided their consent for this publication.

Competing interests

The authors declare that they have no competing interests.

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Figures

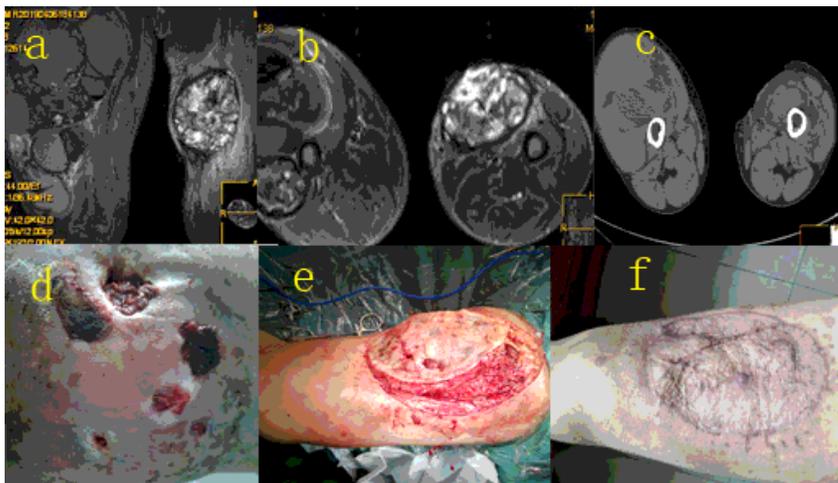


Figure 1

A 51-year-old man, who had hemophilic pseudotumor in both thigh for 6 years, skin ulceration and fistula formation in the left thigh for 2 years. (a,b) The pseudotumors were shown in the coronal and transverse views by MRI examination, Heterogeneous

signal intensity was present on T2-weighted image. (c) The computed tomography (CT) scan showed Skin and soft tissue defect, but no bone destruction. (e) skin ulceration and fistula formation in the left thigh before operation .(f,g) The patient suffered from three times operations including debridement and skin grafting ,the wound healed and no recurrence at 9 months postoperatively

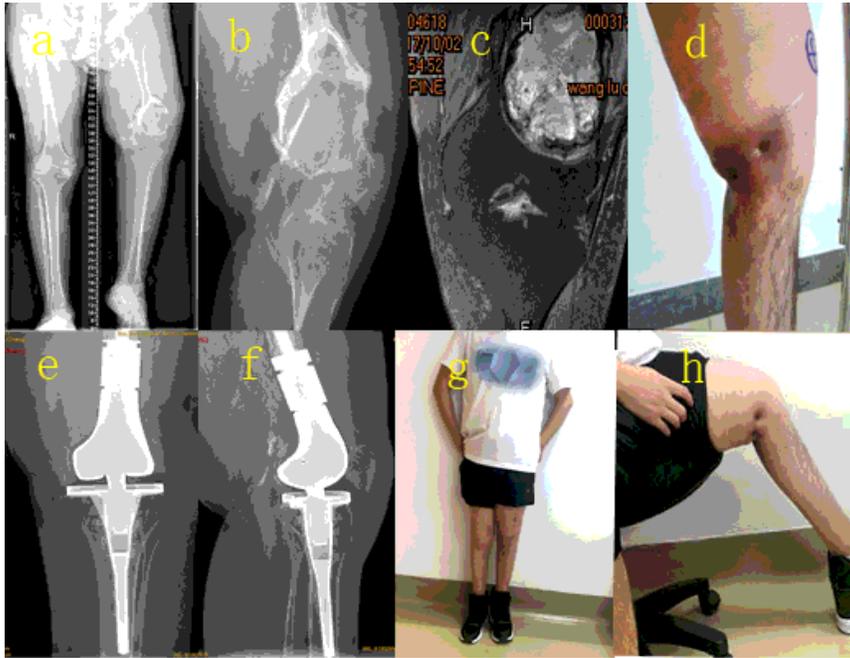


Figure 2

A 23-year-old man. He had a 3-year history of left distal femoral pain and progressive swelling he diagnosis was a haemophilic pseudotumour with severe haemophilic knee arthritis. (a) Double lower-limb full-length standing radiograph showed that the left lower limb was 12.0 cm shorter than the right lower limb. (b) Lateral radiograph of the left knee. The film showed expansile osteolytic destruction of the distal femur extending to the articular surface. Multiple bone septa were present in the lesion area. (c) MRI examination,T2-weighted image. Heterogeneous signal intensity was present. The margin of between the lesion and adjacent area tissue was clear. (d) Preoperative physical examination of left lower limb showed distal femoral swelling and two fistulas. (e,f) Radiographic examination at 24 months postoperatively. Anteroposterior and lateral radiographs of the left knee showed that the implants were stable.(g,h) at 24 months postoperatively,the left knee could flex to 40° and extend to 0°. The fistulas had completely disappeared