Int J Clin Exp Med 2017;10(4):7279-7284
www.ijcem.com /ISSN:1940-5901/IJCEM0047003

Case Report

Total femoral replacement for treatment of a massive femoral hemophilic pseudotumor: a case report and review of the literature

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Received December 20, 2016; Accepted January 25, 2017; Epub April 15, 2017; Published April 30, 2017

Abstract: Hemophilic pseudotumor (HP) is a rare complication of hemophilia, which occurs in a wide spectrum of bones and soft tissues. A case of a massive femoral HP in a Chinese adult is reported. With adequate infusion clotting factor VIII replacement therapy in the perioperative period, the patient had a radical resection of HP and reconstruction with a custom total femoral prosthesis. The patient was followed up for 4 years, he resumed walking with crutches and there was no evidence of recurrence. Various treatment strategies have been used to treat HP, however, there is no agreement about the first-line therapy. The choice of therapy depends on many parameters, such as the size and location of the pseudotumor, the age of the patient, and the relation with underlying organs. We reviewed the current treatment options reported in the literature as well in order to provide valuable suggestions in management of this rare but complicated pathological trouble.

Keywords: Hemophilic pseudotumor, surgery, total femoral replacement

Introduction

Hemophilia is a rare inherited bleeding disorder transmitted by the X chromosome with a recessive trait that is characterized by clotting factor (VIII or IX) <1% of normal level (moderate to severe hemophilia) [1]. Clinically, it manifests itself by a hemorrhagic syndrome that may occur on any location. A rare complication of hemophilia is the hemophilic pseudotumor (HP), also called hemophilic cyst, which described firstly by Starker in 1918 as a slow progressive subperiosteal hemorrhage [2]. Essentially, HP is a collection of encapsulated blood caused by recurrent extraarticular hemorrhage in bone or soft tissue. When left untreated, it grows and causes increasing compression of adjacent structures [3, 4]. Various treatment strategies including clotting factor replacement, local radiation and surgical therapy have been used to treat HP [5, 6], however, because of its rarity, no standardized and defined treatment protocol has been developed until now. In this paper, a massive femoral HP treated with radical resection and reconstructed with a custom total femoral prosthesis was reported and current treatment modalities for HP was reviewed as well.

Case report

Informed consent has been obtained from the patient for publication, including the necessary photographs. A 45-year-old Chinese man with moderate hemophilia type A (factor VIII <5%) was referred to our orthopedic department for the swelling and pain of his right thigh by the hematologist. 22 years ago, he had a femoral hematoma after an injury and was observed uncontrollable bleeding during the incision and drainage surgery for hemophilia. Then, he was diagnosed as hemopilia A for deficiency of clotting factor VIII. He suffered infrequent femoral hematomas in the following several years and was treated symptomatically with analgesics and rest. He suffered a trauma again 15 years ago with serious pain on the right thigh. Plain radiographs confirmed the presence of a fracture of the femoral shaft. A non-operative treatment of rest and skin traction was applied. A

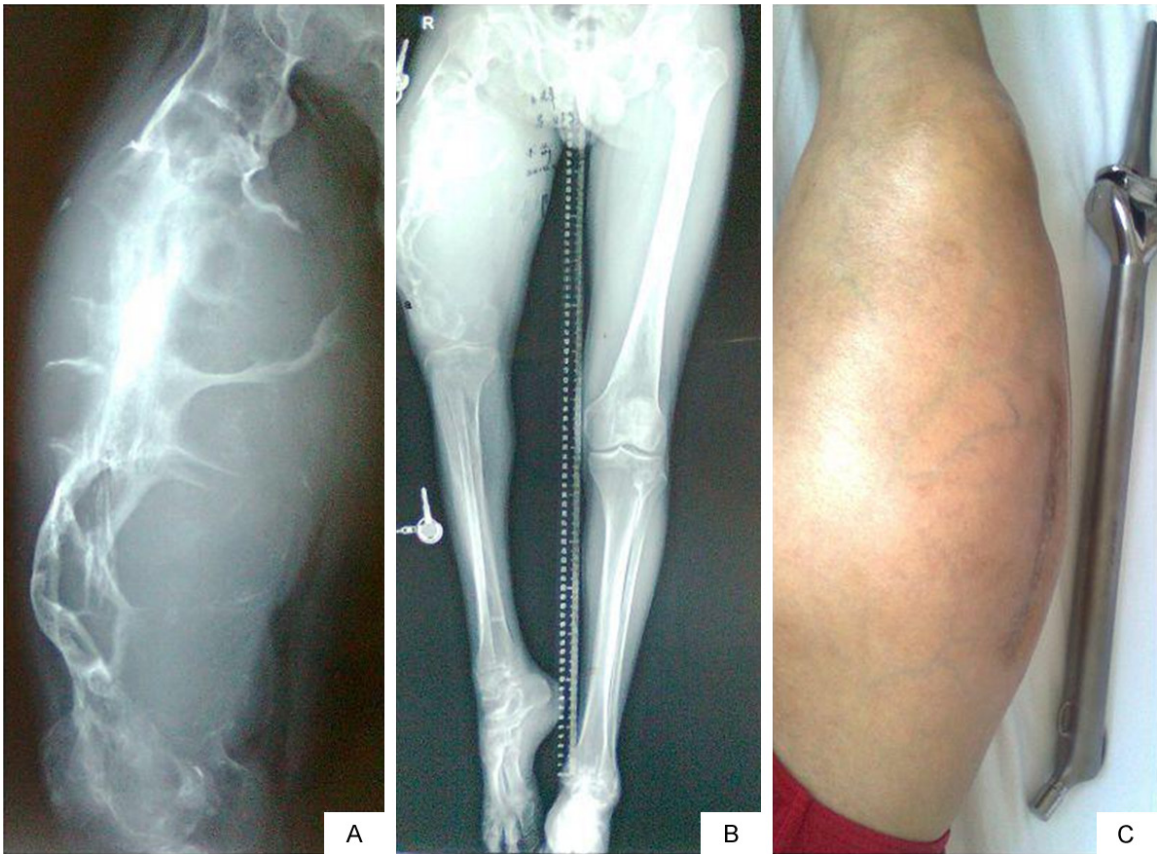

Figure 1. Plain radiograph of the right femur shows radiolytic lesions with bubbly cortical thinning, expansion and destruction (A). Plain radiograph of the lower extremity shows the leg suffered pseudotumor is shorter than the collateral side (B). The clinical photograph shows substantial right thigh swelling and the custom total femoral prosthesis (C).

progressive swelling of the right thigh started to grow 3 years before presentation, but only during the last year has the growth been rapid. The primary complaint was disabling pain in his right thigh and severe limitation of knee function.

A routine physical examination revealed the following status. The patient had a very pale complexion due to anemia. Soft tissue fullness in the whole right thigh that was tender to palpation and cutaneous dilated veins were seen. His right thigh circumference was measured to be 12 cm greater than the contralateral side and the right lower extremity length was 10 cm shorter (**Figure 1**). The range of motion of his right hip was satisfactory. However, his right knee showed markedly impaired movement and was restricted to 5 degree of flexion, which was thought to be secondary to hemophilic arthropathy. The activated partial thromboplastin time (APTT) was 58.90 s, 15 s prolonged than the normal value. His clotting factor VIII level was less than 5% of normal, and screening test for factor VIII inhibitors were negative. An x-ray of the femur showed extensive osseous destruction with erosion of bone cortex, residual bone cortical sclerosis, saccular osteolytic lesion and large expansile lytic lesions in soft tissue (**Figure 1**). A diagnosis of HP was hence established.

A treatment project of HP and the involved tissue resection combined with total femoral construction, followed by continuous clotting factor VIII infusion was scheduled, based on the huge size of the pseudotumor, extensive one destruction and the patient's will. The surgery was performed in left lateral position under general anesthesia. The entire femur and proximal tibia were exposed through a long, direct lateral incision. Marked cystoid changes were observed at the whole femur with great amount of blood clot filled in the capsular spaces. The femoral

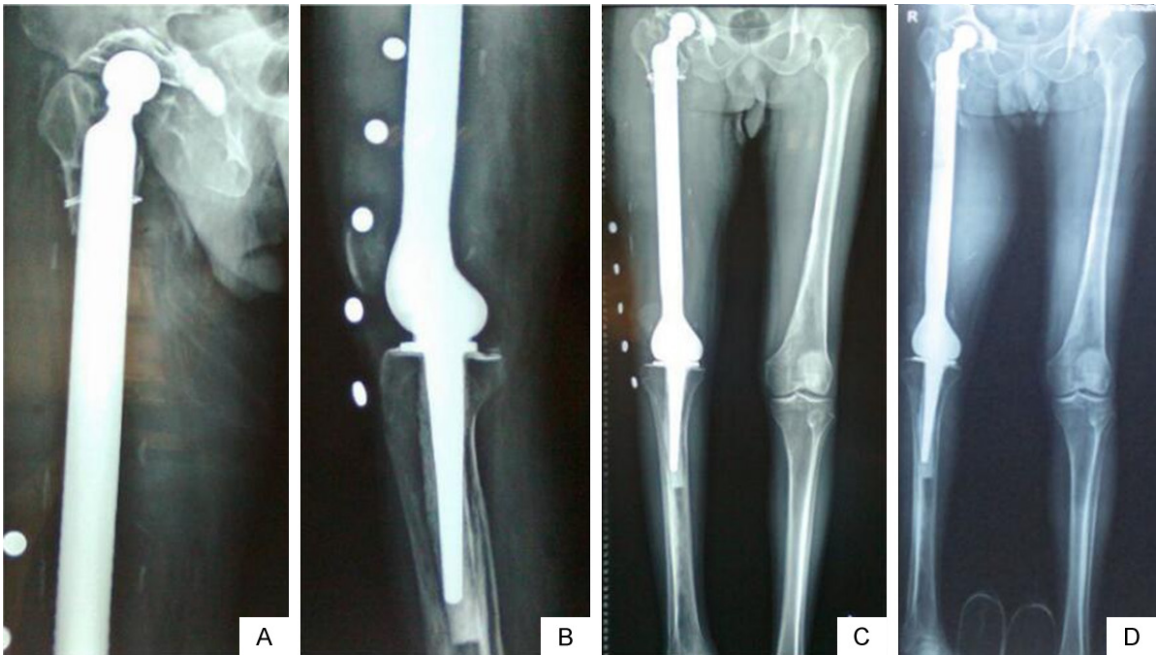

Figure 2. Postoperative plain radiographs, including an anteroposterior view of the pelvis (A), a lateral view of the right lower extremity (B) and a full length of lower limb view (C) showed resection of the hemophilic pseudotumor and femur, and reconstruction with a custom total femoral replacement. No abnormal signs were detected 4 years after surgery through a full length of lower limb view (D).

shafts just beneath subtrochanteric and above the supracondylar ridge were osteomized to facilitate resection of the femur. After en bloc resection of the pseudotumor with affacted soft tissue, the proximal and distal femurs were removed subperiosteally while the great and small trochanters were reserved. After debridement of the acetabulum, a matched cement acetabular component was inserted in proximally. The proximal tibia received a stemmed rotating hinge prosthesis after osteotomy and trim of the tibial plateau. A trial reduction was done, and the tibial component was fixed with cement. The femoral component was assembled and reduced into hip while both the great and small trochanters were fixed on the femoral prothesis by steel-wire. Deep drains were placed at site of hip and knee, and repair the tensor with interrupted absorbable suture and then close the subcutaneous tissues and skin.

The entire procedure was covered with clotting factor VIII replacement therapy. A bolus dose was applied to raise the clotting factor level up to 100% during the operation, and maintained 75% above the first week after surgery, then 40%~50% in the second week, and 30% above during the following 8 weeks of rehabilitation period. The postoperative course was uneventful: daily clotting factor VIII concentrate was administered after determination of the blood levels of clotting factor VIII. Only one minor bleeding complication occurred on the 10th postoperative day, when the patient started partial weight-bearing exercise. This was controlled by additional factor VIII administration and rest. The patient resumed walking with crutches after leaving hospital. There were no abnormal signs such as infection or recurrence have been detected by radiography postoperatively (**Figure 2A-C**) and at the 4 years of follow-up examinations (**Figure 2D**).

Discussion

HP is an uncommon and severe complication occurring in a wide spectrum of bones and soft tissues in patients with hemophilia. A retrospective single-centered study reported that the incidence of HP was 1.12% in Chinese patients [7]. HP is recognized as a collection of chronic encapsulated blood initiated in most cases by a minor traumatic injury, followed by recurrent extra-articular haemorrhage either into muscle or periosteum or intraosseous spaces and development of a tough surround-

ing fibrous capsule [7, 8]. The mass usually grows in size over months or years resulting in compression of adjacent structures and increasing destruction of bone and causing severe pain and deformity. Gilbert distinguished HP into two subdivisions: proximal HP occur primarily in the pelvis and femur and appear mainly in adults, where repeated and unresolved hematomas of the muscles lead to subsequent erosion of the adjacent bone; distal HP are located primarily in the small bones of the hands and feet, occur most commonly in children after injuries, and tend to have a better prognosis [9].

HP was diagnosed according to the clinical and radiological manifestation described previously [1, 4]. The radiographic findings of a soft tissue mass with areas of calcification and adjacent bone destruction in a patient with underlying haemophilia is usually sufficient to make the diagnosis of a HP. It may be misdiagnosed as tumor of bone by only local signs and radiography, especially in those who do not have established hemophilia diagnosis [7, 10]. Magnetic resonance imaging (MRI) and computed tomography (CT) are of great value in diagnosis. CT is useful in showing the size and location of the HP, reflection of trabeculae, cortical change, and periosteal reaction. The property of the focus can be identified by quantitative CT value: fresh hemorrhage 50~80 hounsfield unit (HU), stale hemorrhage 10~20 HU, clot 30~60 HU, calfication zone 80~100 HU or above. MRI is useful in evaluation of intramedullary bone and adjacent soft tissue as well as monitoring the therapeutic response [11]. Therefore, it is important for a surgeon to inquire the history of bleeding and perform the basic biochemistry including APTT, prothrombin time (PT), fibrinogen, and thrombin time to make final diagnosis.

The managemant of HP are mainly confined to case reports or small case series without a standard protocol [12], and the primarily goals of management are minimizing complications and preserving function of the affected tissues [8]. The consensus is that treatment should take place in a specialized center where the hematologist and the orthopedic surgeon can work in close collaboration [13, 14]. The choice depends on many factors such as the size, location and extent of the tumor, the age and constitution of the patient, and the relation with underlying organs. The different treatment modalities of HP include clotting factor replacement therapy, radiotherapy, surgical therapy (including resection, incision drainage, amputation and joint replacement) and the combination of them.

In most cases of asymptomatic HP, conservative treatment with clotting factor replacement as well as immobilization is recommended [15]. According to the algorithm suggested by Caviglia, every child without inhibitor will require no less than 12 weeks of clotting factor replacement [16]. The purpose is to reduce the size of HP before surgery and to determine the degree of aggressiveness of the lesion. Less aggressive HP are prone to respond to conservative treatment. Repeated MRI scans are carried out 12 weeks later. If the mass has reduced 50% in size, a similar treatment procedure is perfomed for another 6 weeks. If the lesion doesn't show any sign of improvement during the follow-up, surgery is advocated.

Radiotherapy has been recommended by some authors, especially in the presence of factor VIII inhibitor [17], but has generally been reserved for patients who do not respond to conservative treatment or those in whom surgery is contraindicated [6, 18, 19]. Reviews in the literature have documented complete resolution of lesions in a large number of cases, but mainly for small pseudotumours of the distal extremities [6, 18, 19]. Although the exact mechanism of radiation is unknown, it has been proposed that irradiation may cause damage in the feeding vessels of pseudotumours, resulting in fibrosis and leading to eventual healing [18, 19]. Despite the reported successful outcomes, several authors have questioned the efficacy of radiation in the treatment of hemophilic pseudotumor. Jensen and Putman reported that, although some have used irradiation, their own experience indicated this was ineffective in treatment of HP with long-standing bone changes [20]. Till now, there are no randomized trials to support or disapprove its use and clinicians base their decision on individual cases and their own experience. Besides, therapeutic emoblization, alone or combined with radiotherapy has also proved to be an efficient method, especially for HP in the pelvis, to decrease the size of the mass and decrease bleeding during surgery [21].

Surgical excision of HP is the most effective and curative in most patients [22], and has become the standard modality of treatment with a recurrence rate as low as 15% [1]. Surgical resection is curative for most HPs but this modality also includes risks of massive life-threatening hemorrhage, infection, and even possible limb amputation [23, 24]. Indications for surgical excision include large lesions, gradual increase in the tumor size, soft tissue HPs, or when rupture is imminent, or failure of conservative therapy, and also in cases of skin necrosis and neurovascular compression. The key point excision should start in normal tissue for a clearly anatomical identifcation, and the HP should be excised en bloc or as completely as possible [1]. In a multicenter study, Magallon stated that surgery was more successful than nonoperative treatment and that it provided a cure for eight of 14 patients (compared with two of 15 patients who had a successful outcome with nonoperative measures) [8]. A Chinese group also identified surgical therapy is safe and effective when covered with replacement therapy [7]. In this case, the massive HP caused extensive bone and soft tissue destruction, after careful consideration, a radical resection of HP and reconstruction with a custom total femoral prosthesis was performed in order to achieve maximum lower limb function. The main possible postoperative complications included recurrence, infection, fistulization, clotting factor inhibitor formation, and pathological fracture [25]. The recurrence may caused by incomplete resection or postoperative hematoma [1]. Contamination of injection of the coagulation factor, bone grafting or postoperative bleeding may be blamed for high incidence of infection, whose exact explanation remians unkonwn [26]. Fortunately, none of these was occured in our case during the rehabilitation and a satisfied outcome was achieved.

Although there is no general agreement among authors in the management of HP, most authors indicate that therapy is ultimately dependent on a careful individual evaluation. Thus, the choice of therapy, conservative or surgical, must be made taking into account the patient's constitution and requires a coordinated multidisciplinary team to achieve optimum results.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (No. 81402224), the Provincial Science Foundation of Hunan (No. 2015JJ3139 and 2015JJ2190), the Health and Family Planning Commission of Hunan Province (B2014-12), the Administration of Traditional Chinese Medicine of Hunan Province (No. 2015116), the Open-End Fund for the Valuable and Precision Instruments of Central South University (CSUZC201639), China Scholarship Council (student ID: 201606370164 and 201606375101), Clinical Research Foundation of Xiangya Hosptal (2016L01), the Open-End Fund for the Valuable and Precision Instruments of Central South University (CSUZC201733) and the Hunan Provincial Innovation Foundation for Postgraduate (CX2016B060).

Disclosure of conflict of interest

None.

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