Blood Reviews 30 (2016) 401–409

Contents lists available at ScienceDirect

Blood Reviews

journal homepage: www.elsevier.com/locate/blre

REVIEW

Musculo-skeletal manifestations of haemophilia

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ARTICLE INFO

Keywords:
Haemophilia
Musculo-skeletal manifestations
Orthopaedic surgery

ABSTRACT

Haemophilia left untreated or treated on demand destroys the joints at a very young age. Primary haematological prophylaxis, currently the gold standard for the treatment of haemophilia, is not completely effective. Moreover, it is only available for 25–30% of patients worldwide. Advances in haematology, combined with the advances in orthopaedic surgery and other disciplines (physical medicine and rehabilitation, physiotherapy, specialised nursing, etc.), have made it possible to improve the musculo-skeletal manifestations of haemophilia in these patients through orthopaedic surgical interventions. These interventions are safe, even in the most complex cases, such as patients who develop inhibitors (antibodies to clotting factor) or are HIV + and HCV +. The risk of bleeding in surgical interventions is higher for people with haemophilia than for other patients and there is also a greater risk of infection. Both these factors increase the risk of a poor outcome. Whatever the surgical procedure, adequate surgical haemostasis must be achieved by infusion of concentrate of the deficient factor (factor VIII or factor IX), either in recombinant or plasma-derived form, at the correct doses (ideally for 10–14 days). In patients with inhibitor there are also the aPCCs (activated prothrombin complex concentrates) and rFVIIa (recombinant activated FVII). Surgical orthopaedic interventions that are commonly required by haemophilia patients include synovectomy (open or arthroscopic), osteotomy, arthroscopic joint debridement, tendon lengthening, arthrodesis of the ankle, total joint replacement, resection or percutaneous treatment of pseudotumours, fasciotomy for compartment syndrome, neurolysis of the ulnar nerve, and other orthopaedic interventions.

1. Introduction

In patients with haemophilia, orthopaedic (musculo-skeletal) problems can affect the joints or the muscles [1–3]. Virtually 90%, however, involve the joints and they normally begin in childhood. Haemarthroses (bleeding into the joints) tend to recur in spite of the synovial membrane's capacity to reabsorb the blood. When there is a lot of blood in the joint, the synovial membrane becomes hypertrophied because the cytokines and angiogenic factors from the intra-articular haemorrhage stimulate the synovial cells to replicate [3]. Then, the hypertrophic synovium is more prone to bleed again (it becomes very friable and hypervascularised), ending up in a vicious circle of haemarthrosis–synovitis–haemarthrosis. In addition, the blood in the joint can directly cause apoptosis of the chondrocytes in the joint cartilage [3].

The joint pain caused by the above processes can lead to an antalgic flexion deformity of the affected joint which is initially reversible, but will eventually become permanent (fixed deformity). The hyperaemic reaction caused by the haemarthrosis leads to asymmetrical hypertrophy of the epiphyseal growth plates which can go on to result in axial deviation of the affected limbs (Fig. 1). This all leads to joint damage, which progresses within only a few years to destruction of the joint (haemophilic arthropathy) (Fig. 2) [4].

The non-joint-related musculo-skeletal problems in haemophilia, which account for over 10% of orthopaedic lesions in the patient with haemophilia, are essentially soft-tissue haematomas, muscle haematomas and pseudotumours [4].

With adequate prophylaxis, at least from the age of 2 to 18 (ideally lifelong), it is possible to convert severe haemophilia into a moderate condition, considerably reducing (although not totally preventing) the associated musculo-skeletal problems [5–7].

The main benefit of orthopaedic surgery in haemophilia is that it markedly improves the patient's quality of life [8,9]. This is achieved by appropriately managing the joint problems (haemophilic arthropathy) and the muscle haematomas and their complications, that is to say haemophilic cysts and pseudotumours [10,11], nerve paralysis caused by compression [12] and compartment syndrome [7,13].

The level of evidence of haemophilia literature is very low. In fact, no study on the musculo-skeletal complications of haemophilia has been included in the Cochrane Library so far. The aim of this review article is to discuss the management of the musculo-skeletal manifestations of haemophilia.

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http://dx.doi.org/10.1016/j.blre.2016.04.008
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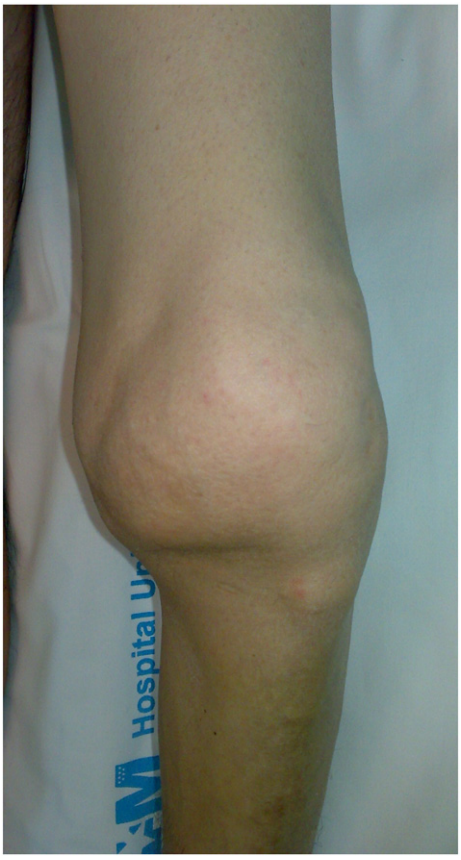

Fig. 1. Clinical view of severe haemophilic arthropathy of the knee with severe varus deformity.

2. Management of muscle haematomas and their complications

2.1. Compartment syndrome and compression neuropathy

Muscle haematomas can occur in any part of the body although the most common sites are the iliopsoas muscle and the flexor compartment of the forearm [4,14]. If not adequately dealt with, they can lead to compartment syndrome and a possible need for urgent surgical decompression of the compartment. Iliopsoas haematomas are often associated with paralysis of the crural nerve. It is important to remember that a right iliopsoas haematoma can be confused with appendicitis. The diagnosis of iliopsoas haematoma should be confirmed by ultrasonography (US) and/or computed tomography (CT) ad/or magnetic resonance imaging (MRI). Crural nerve paralysis often requires rehabilitation for as long as 18 months before it fully resolves. Electromyography (EMG) is useful for the diagnosis and for assessing progress. Periodic US is essential to confirm that the haematoma has been completely reabsorbed and with the appropriate haematological treatment, this does usually occur. New bleeding, however, is common and the treatment must therefore be continued for several weeks or months, until complete reabsorption is certain.

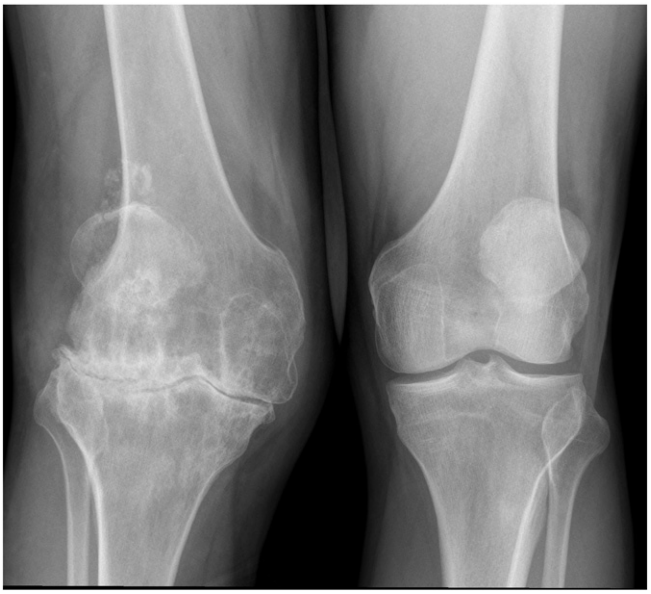

Fig. 2. Severe right knee arthropathy (X-rays) in a patient with haemophilia.

In the forearm, surgical opening of the entire flexor compartment may be necessary, since once compartment syndrome is established, it has a considerable effect on the function of the upper limb [4]. In some patients (particularly the immunosuppressed), a soft-tissue haematoma can become spontaneously infected and turn into an abscess. Diagnosed early, this can generally be resolved with treatment based on intravenous antibiotics and surgical drainage.

2.2. Haemophilic pseudotumours

Although rare, pseudotumours are a serious complication of haemophilia. They are progressive cyst-like inflammations that affect the muscles, caused by recurrent bleeding and associated with radiographic evidence of bone involvement [10,11]. Most pseudotumours are seen in adult patients and occur near the proximal ends of the long bones. However, they can occur distally in the wrist and ankle in young patients before skeletal maturity. If left untreated, proximal pseudotumours may destroy the soft tissues, erode the bone and cause serious vascular and/or nerve damage.

Despite having a mortality rate of 20%, the treatment of choice for proximal pseudotumours is surgical removal [10]. This mortality is primarily due to surgery. Regression, although not true cure, has been reported with long-term treatment with the deficient clotting factor and immobilisation. This treatment should only be used in inoperable cases, such as patients with inhibitors who are poorly controlled. Percutaneous evacuation of the pseudotumour followed by filling with fibrin glue and/or cancellous bone and/or bone cement can at times provide satisfactory results. Preoperative embolisation of large pelvic pseudotumours may help to reduce intra-operative bleeding when removing surgically.

Distal pseudotumours can be controlled with haematological treatment and immobilisation. It is important to be aware of the possibility of pseudotumours when one or more masses are detected in the limbs or pelvic region of a person with haemophilia. However, chondrosarcoma and liposarcoma have been confused with haemophilic pseudotumours in these patients [15]. US, CT and MR will help to confirm the diagnosis in each case.

3. Management of haemophilic arthropathy

Haemophilic arthropathy is polyarticular (knees, ankles, elbows, hips, shoulders) and affects the patients from early childhood. Haemarthroses are accompanied by severe pain and an initially reversible antalgic flexion contracture. The blood within the joint alters chondrocyte (cartilage cells) proteoglycan synthesis, causing their death (apoptosis).

3.1. Haemarthrosis

Proper treatment of haemarthrosis should include early diagnosis, adequate haematological treatment, evacuation of the blood in the joint (arthrocentesis) (Fig. 3), rehabilitation and physical medicine,