The Haemophilic Joints
New Perspectives

Edited by

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Dedicated to my wife Hortensia
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There are new perspectives in the treatment of intra-articular complications of haemophilia that I have tried to clarify in this book with the help of clinicians and academics who have a high degree of expertize in the field. The patient with haemophilia presents a particular challenge for those providing musculo-skeletal care. Haemophilia is a lifelong inherited bleeding disorder characterized by spontaneous bleeding resulting in painful joint deformities.

Unfortunately 70% of those with haemophilia worldwide have no access to adequate haematological care. Many of those individuals are untreated, and therefore suffer enormously. Often, expert orthopaedic care cannot be provided to the haemophilia patient because of the constraint of lack of clotting factor provision for economic reasons.

In the so-called ‘developed world’, the availability of safe and effective clotting factor concentrate has enabled the orthopaedic surgeon to approach the patient with haemophilia with almost the same security as a patient without a bleeding disorder. The development of high-purity concentrates has enabled peri-operative delivery of clotting factor by continuous infusion, giving added safety during the period of surgery and the possibility of more intensive physiotherapy and rehabilitation postoperatively. The newer recombinant clotting factor concentrates are particularly easy to deliver by continuous infusion.

Today, synoviortheses, synovectomies, joint debridements, tendon lengthenings, osteotomies, joint fusions, removals of osteophytes and haemophilic cysts, joint arthroplasties and other orthopaedic procedures can be performed to relieve pain. Furthermore, these procedures are now available for the patient with an inhibitor (alloantibodies against infused exogenous factor VIII or IX).

I have tried to provide an in-depth analysis of the new perspectives involved in the treatment of those with haemophilia, and I hope that this book will provide information that will be helpful for those treating the articular manifestations of haemophilia. My experience as Editor of this book has been rewarding and challenging. I am indebted to my colleagues who have contributed chapters.

Editor: E.C. Rodriguez-Merchan
Introduction

The management of orthopaedic problems in haemophiliacs requires a haematologist, whose function is to control haemostasis, an orthopaedist, physical therapist, orthotist and occupational therapist, all of whom concentrate on the preservation and restoration of function to the musculoskeletal system. The clinical severity of haemophilia is usually related to the plasma level of factor VIII or factor IX. Patients are classified as having mild, moderate or severe haemophilia depending on the level of the deficient factor, which can be > 5% of normal in mild cases and < 1% of normal in severe haemophilia. This is reflected in the frequency and causes of bleeding. Whereas a patient with mild haemophilia will bleed rarely, usually only after significant trauma or surgery, those with severe haemophilia may have several episodes per month, and typically bleed spontaneously as a result of minimal trauma or activities of daily living. Over 90% of bleeding episodes in haemophilic patients occur within the musculoskeletal system and, of these, 80% occur within the joints.

Management of intra-articular bleeds

The vast majority of bleeding episodes in haemophiliacs occur within the joints (haemarthrosis). Of these haemorrhages, the ankles, elbows and knees account for almost 80%. The involved articulation is usually held in flexion, and active and passive motion is painful and very restricted. With the early provision of the missing coagulation factor, haemorrhages can be controlled and conservative orthopaedic management can usually terminate the episode without any long-term complications.

Should the haemorrhage persist or a re-bleed occur, the synovium begins to hypertrophy (Fig. 1.1) and a vicious circle of chronic synovitis develops, leading to joint destruction and classical osteoarthropathy. The hypertrophic synovium is characterized by villous formation, markedly increased vascularity and the chronic presence of inflammatory cells. Synovitis causes hypertrophy of the epiphyseal growth plates [1].

Bone hypertrophy may lead to leg length discrepancies, angular deformities and alterations of contour in the developing skeleton.

If the synovitis is not controlled, cartilage damage will follow. The synoviocytes disintegrate and release lysosomal enzymes, which not only destroy articular cartilage but also further inflame the synovial tissue. Blood breakdown products also affect the chondrocytes. The haemosiderin staining of the synovium and cartilage bears testimony to the destructive elements of proteolytic enzymes. Symptoms of chronic arthropathy typically develop by the second or third decade. As the joint cartilage progressively degrades, deterioration in joint function occurs.

Continuous prophylactic clotting factor replacement (prophylactic therapy)

Prophylactic therapy has been reported to slow the natural course of haemophilic arthropathy. Swedish authors were the first to report that continuous prophylaxis from ages 2 to 18 years prevented the development of haemophilic arthropathy if
the concentration of the patient’s deficient factor was prevented from falling below 1% of normal [2]. This can be achieved with administration of 25–40 units/kg factor VIII three times weekly in patients with haemophilia A and 25–40 units/kg factor IX twice weekly in patients with haemophilia B.

Management of haemarthroses

If prophylactic therapy is not feasible because of expense or lack of venous access, then a major haemarthrosis must be aggressively treated to prevent progression to synovitis, recurrent joint bleeds and, ultimately, end-stage arthritis. These joint bleeds need the following:
1. transfusion to 50%);
2. aspiration (arthrocentesis) to debulk the joint blood;
3. short-term splinting for 48 h; and
4. transfusion every 48 h until the joint is fully rehabilitated and there is no evidence of synovitis. This requires 10–30 days of transfusion.

Management of synovitis

If left untreated, synovitis followed by degenerative changes within the joint will occur and a stiff or painful joint will result. Both surgical synovectomy and radioactive synoviorthesis are procedures for synovial destruction used in a number of haemophilia centres for the management of chronic haemophilic synovitis. Taking into account the risk of infection after surgical procedures in human immunodeficiency virus (HIV) positive patients, synoviorthesis is recommended first. Radioactive synoviorthesis is also of particular interest in patients with haemophilia caused by factor inhibitors, who otherwise are difficult to treat. No complication related to radiation synovectomy has been reported to date. For the treatment of chronic haemophilic synovitis, synoviorthesis should always be indicated as the first procedure. It is an easy procedure with a number of satisfactory results [3].

With $^{198}$Au synoviorthesis there is an expected 75% success rate, while with $^{90}$Y synoviorthesis there is an expected 85% or more success rate. It is important to emphasize that no more than three synoviortheses can be repeated with a 3-month interval between them. If, after three procedures, synoviorthesis fails, a surgical synovectomy is indicated. Rifampicin is expected to produce similar results to $^{90}$Y in the small joints (elbows and ankles), but several weekly, painful injections are needed; in addition, rifampicin synoviorthesis is not recommended for the knee joint. Surgical synovectomy generally achieves similar results to $^{90}$Y synoviorthesis; however, as it is a surgical procedure under general anaesthesia, it is accompanied by a certain number of complications common to surgical procedures.

When surgical synovectomy is indicated for the knee, arthroscopic synovectomy is recommended because of the lower risk of infection and lack of postoperative mobility; however, there are no true comparative studies to conclude which type of synovectomy is most efficient. For the elbows and ankles, open surgical synovectomy is advised. It is possible that the way forward is to use radioactive synoviorthesis ($^{90}$Y or $^{32}$P) first, and then up to three times. If this fails for the knee, then arthroscopic synovectomy is indicated. Open surgical synovectomy for the knee should be the method of last resort, after three previous failures with the other procedures. Although difficulties arise when comparing different studies regarding synovitis of the knee, the decreased frequency of haemarthrosis after synoviorthesis is not as great as after operative synovectomy.

From the point of view of quality of life and economy, radioactive synoviorthesis offers advantages in that it is usually almost painless and requires minimum replacement therapy. Open surgical synovectomy of the knee in haemophilic patients who are managed with conventional postoperative therapy has frequently been complicated by a loss of motion, even with prolonged inpatient treatment. Rehabilitation after synovectomy of the knee is particularly difficult for children with haemophilia because they tend to be less motivated and co-operate less with the postoperative physical therapy programme. The rationale behind arthroscopic synovectomy of the knee in haemophilia is to provide a similar decrease in bleeding episodes as open synovectomy, while avoiding the loss of range of motion that can occur.

Personal experience and the general recommendation among orthopaedic surgeons and haematologists is that when three early consecutive synoviortheses (repeated every 3 months) fail to halt synovitis, a surgical synovectomy (open or by arthroscopy) should be immediately considered. Although patients are admitted to hospital for synoviorthesis for haematological preparation, it must be recognized that it is not necessary in every case and the procedure could be performed at the outpatient clinic with minimal risks. Radioactive synoviorthesis should be performed in very young patients, when the amount of synovial membrane is still moderate. Once the degree of synovitis has become severe, the expected results of synoviorthesis are decreased.

Management of flexion contractures (tendon lengthening, extension osteotomy and external fixators)

In those patients with flexion contractures of the knee or ankle, provided the joints are preserved (without haemophilic arthropathy), it is advisable to carry out a tendon lengthening procedure in order to obtain adequate joint extension and to improve articular function. The most frequent tendon lengthening classically performed on haemophiliacs are Z-lengthening of the Achilles tendon (to correct equinus of the foot) and the so-called hamsstrings release (commonly associated with a posterior capsulotomy) for flexion contractures of the knee.

At the knee, extension supracondylar osteotomy can be used to correct a fixed-knee flexion contracture. It is a major procedure which requires fracturing the femur at its supracondylar
area and then performing bone fixation by means of an adequate internal fixation device. External fixators can not only be used for fixation of fractures, such as those at the distal radius, but also for the treatment of flexion contractures. The aim is to obtain a progressive but efficient straightening of the affected joint, the most common being the circular fixator of Ilizarov.

The implantation of an external fixator is a rather complicated procedure, especially regarding its postoperative care. It has an extension device that allows an extension of 1°/day, up to a maximum of about 30°. Later on, in a second surgical procedure, the external fixator is removed and an orthosis is indicated in order to maintain the extension gained during the procedure. In other words, what an external fixator achieves is a slow but progressive extension of the soft tissues (including tendons, nerves and vessels). An excessively rapid extension will cause nerve paralysis, such as of the peroneal nerve at the knee. These procedures must be carried out when the contractures are only moderate and after the failure of conservative treatment. At the knee, such a conservative treatment entails the use of a extension traction followed by an orthosis of progressive extension together with a rehabilitation programme.

**Management of haemophilic arthropathy**

**General principles**

The orthopaedic complications of haemophilia are patient-specific and treatment protocols often need to be tailored to suit the individual. There are a number of orthopaedic procedures that can be carried out in haemophilic joints when a severe degree of arthropathy is reached.

**Curettage of subchondral bone cysts and cheilectomy**

Some haemophilic patients present with large subchondral cysts on the humeral head or the proximal tibia. When such cysts are symptomatic, curettage and filling with fibrin glue and/or cancellous bone graft is recommended. Other patients present with an anterior osteophyte at the distal tibia (ankle joint) that elicits pain at foot dorsiflexion and when walking. Under such circumstances the surgical removal of the osteophyte (cheilectomy) is indicated. It is commonly performed by open surgery although it can also be carried out by arthroscopy.

**Joint débridement**

Joint débridement is commonly performed on young patients with severe haemophilic arthropathy of the knee, in patients who the orthopaedic surgeon in charge considers are too young to indicate a total joint replacement. In other words, débridement is a procedure that can alleviate articular pain and bleeding for a number of years and delays the need for a total joint arthroplasty. Joint débridement consists of opening the joint in order to remove existing osteophytes, resect the synovium and carry out curettage of the articular cartilage of femoral condyles, tibial plateaus and patella.

Some authors do not believe in the efficacy of débridement and so when facing a severe degree of arthropathy in a young patient they directly indicate a total knee replacement. It should be emphasized that if débridement fails, a joint arthroplasty can be performed by the same approach. Some authors perform joint débridement by arthroscopic means with similar results to open surgery. Often, a synovectomy and débridement are performed together because haemophilic synovitis and early arthropathy commonly coexist. Again, postoperative rehabilitation is paramount to avoid loss of range of motion, and therefore should be associated with adequate haematological control in order to avoid re-bleedings.

**Realignment osteotomy**

Sometimes, during childhood, adolescence or early adulthood, haemophilic joints undergo an alteration of their normal axis. Knees show varus, valgus and flexion deformities, and something similar may occur at the ankle joint. When the malaligned joint is painful, the patient needs an alignment osteotomy. The most common osteotomies performed in haemophiliacs are: proximal tibial valgus osteotomy, supracondylar femoral varus osteotomy, ankle alignment osteotomy and knee extension osteotomy.

In all of these the rationale is to produce a fracture at an adequate place in order to re-align the joint to a normal axis. After the osteotomy it is necessary to obtain an adequate bone fixation by any kind of internal fixation device. (I have sometimes corrected a flexion contracture of the knee at the same time as a spontaneous supracondylar fracture of the femur.) When axial malalignment occurs in a joint with severe haemophilic arthropathy, a total joint arthroplasty is usually indicated and hence both problems can be solved at the same time.

**Arthrodesis**

Joint fusion (arthrodesis) is today used only at the ankle. It is indicated when a severe ankle arthropathy causes intense pain and/or disability, ankle arthroplasty being the alternative. However, ankle replacement has not been proved to be better than arthrodesis (not only in haemophiliacs). Ankle arthrodesis usually requires two approaches in order to remove the involved cartilaginous surfaces of distal tibia and talus. Then it is necessary to compress the surfaces using lag screws, staples or an external fixator. By 10–12 weeks joint fusion is usually achieved and hence all immobilization devices can be removed. Ankle pain is likely to disappear although subtalar pain sometimes appears after arthrodesis. Such pain is a result of the abnormal biomechanics of the foot after ankle fusion. In summary, ankle arthrodesis is an extreme surgical procedure which considerably improves joint pain but sometimes provokes another type of pain, usually not so intense as the primary one.