The Role of Synovectomy in the Management of a Target Joint

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The primary goal for all musculoskeletal health practitioners is to prevent joint bleeds (hemarthroses) and subsequent damage to synovial tissue, so that children with hemophilia reach adulthood with optimal joint health, said Dr. Adolfo Llinás.

Repetitive joint bleeds trigger synovial activation, which over time can lead to the development of a target joint. However, the exact point when a joint has become a target joint is the subject of some controversy. Sometimes parents, patients, and even healthcare workers are hesitant to confirm the existence of a target joint, Dr. Llinás said. However, investigations have shown that even a joint that returns to normal between bleeds can become a target joint.

"A lot of data now show that joint injury happens a lot earlier than previously thought," he stated. "It is clear that musculoskeletal joint bleeds must be kept to a minimum to prevent permanent inflammation of the synovial tissue." Moreover, he said, "we should be treating target joints expeditiously, but in reality we have a tendency to wait and to delay considering the fact that it has become a target joint."

Although people generally think that when fluid is removed from a joint, it returns to normal , the synovial lining under the skin may remain thickened and inflamed, adding volume to the joint. A joint that does not return to normal between bleeds has become a target joint and is in a state of chronic synovitis, Dr. Llinás said.

Synovitis is deleterious and harmful to the joint in many ways. The inflamed synovial lining has a greater tendency to bleed, with the blood in the joint space producing large deposits of iron. The presence of blood inside the joint causes synovial proliferation (the multiplication of cells in synovial tissue), angiogenesis (the growth of new blood vessels), release of inflammatory cytokines (which causes pain and swelling), and proto-oncogene expression (the production of potentially cancer-causing proteins), all known to contribute to cartilage destruction and bone and ligament injury, Dr. Llinás noted.

A key question is how long it takes for a joint to suffer irreversible damage. Evidence suggests that secondary prophylaxis limits but does not stop the progression of hemophilic arthropathy. Furthermore, delays in starting treatment seem to cause progressive joint damage. A Dutch study by Fischer et al. in 2002 demonstrated 8% deterioration in the Pettersson score in children for every year that prophylaxis was delayed after the first joint bleed.

Dr. Llinás said that individuals with hemophilia are a heterogeneous group. The presence of inhibitors, the age of the person, the stage at which articular bleeds develop, and the date that treatment is started will all affect the severity of synovitis and influence whether a patient will become resistant to treatment.

A 2007 study by Manco-Johnson et al. comparing prophylaxis to episodic treatment for the prevention of joint disease has challenged conventional thinking about when synovitis becomes a problem, Dr. Llinás said. The randomized trial looked at 65 boys with severe hemophilia A,

with one group receiving primary prophylaxis and the other group receiving enhanced episodic treatment. The study's primary objective was to compare the incidence of bone or cartilage damage. Findings showed that at six years of age, 93% of the boys on primary prophylaxis had normal joint health, whereas only 55% of those on episodic prophylaxis were normal in terms of bleeds detected by magnetic resonance imaging (MRI).

More surprisingly, said Dr. Llinás, even though clinicians have been using X-rays as the standard of care for decision-making, the study revealed that more than half of the positive results found by MRI were not seen on the X-rays. Furthermore, a number of clinically relevant hemarthroses found by MRI were not noticed on physical examination.

A change from our current way of thinking is needed to recognize that even if joint damage isn't clinically detectable, that doesn't mean the joint is healthy, Dr. Llinás said. In young mice, irreversible damage occurs after 17 weeks and only three bleeds, he noted. Delaying prophylaxis for a year or more comes with a high price in terms of the Pettersson score. Sub-clinical synovitis is evident in patients even while they are on high-compliance prophylaxis, and irreversible damage occurs rapidly, he said.

Synovitis is generally classified in four stages:

- Grade I: Transitory synovitis, when the joint returns to normal between bleeds
- Grade II: Chronic synovitis, when the joint does not return to normal between bleeds
- Grade III: Chronic arthropathy, with formation of axial deformities and rigidity
- Grade IV: Formation of bony or fibrous ankylosis

Synovectomy (surgical removal of the synovial tissue) can successfully deactivate the synovium in grade I and II synovitis — deactivation stops the bleeding, reduces the volume of the synovium to normal, and allows the patient to pursue physical therapy to recuperate joint range of motion, strength, and speed, Dr. Llinás said. However, synovectomy is unlikely to return the joint to normal function in grade III synovitis, and is not successful for grade IV synovitis.

Chronic synovitis is a complex clinical situation that affects each person with hemophilia differently. Dr. Llinás said individuals who need treatment for synovitis can be classified in three groups:

- Patients with bleeding while on primary prophylaxis
- Patients without primary prophylaxis and not responding to treatment with secondary prophylaxis
- Patients receiving neither primary nor secondary prophylaxis

Orthopedic surgeons tend to expect everyone who has a synovectomy to have the same outcome — to deactivate the synovium, to help the patient regain range of motion, muscle strength, and joint speed, and to return a joint to a state where prophylaxis is effective in preventing articular bleeds and chronic synovitis, Dr. Llinás said. However, the prognosis is more likely to vary for each group, he emphasized.

Two main synovectomy approaches can prevent recurrent hemarthroses:

- Induce synovial fibrosis by chemical synovectomy (with osmic acid or rifampin) or radiosynovectomy (yttrium, chromic phosphate, or rhenium).
- Remove the synovium by arthroscopic synovectomy.

For many years, synovectomy was performed using chemical agents. However, there is now a strong preference for radioisotopes, because chemical agents are believed to be 30%–44% inferior to radioisotopes, said Dr. Llinás.

Radioactive and chemical synovectomy are the simpler, safer, and more convenient procedures. Both can be administered using local anesthesia and do not require overnight hospitalization. Radioactive synovectomy generally involves fewer doses than chemical synovectomy. However, a number of practical and logistical issues account for the many different types of procedures used around the world, Dr. Llinás said. Regional availability, the cost of factor concentrate compared with the cost of isotopes, the complexity of the institution, and the accessibility of the treatment centre for the patient all influence the method and type of agent that is used.

Arthroscopic synovectomy is recognized as an effective method of synovial deactivation, but it is generally considered as a second level of defense. The procedure requires surgical expertise and meticulous execution, surgical amounts of factor replacement, hospitalization, and extensive physiotherapy, Dr. Llinás said. There are advantages, though, including access to the majority of the joint, few external incisions, the removal of osteophytes, treatment of chondrial lesions, and remodelling of miniscal tears.

From the musculoskeletal perspective, the consensus is that synovitis is a destructive state for the joint and, once diagnosed, should be treated, Dr. Llinás concluded. “Our patients are young, impatient, and busy, and do not have time to waste with us in the clinic,” he said.