CLINICS IN SPORTS MEDICINE

Clin Sports Med 21 (2002) 335–347

Sources of anterior knee pain

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The anterior part of the knee consists mainly of structures belonging to the patellofemoral joint (PFJ), which includes a variety of tissues, such as cartilage, subchondral bone, synovial plicae, infrapatellar fat pad, retinacula, capsule, and tendons (Fig. 1). Each of these structures, alone or in combination, can be a source of anterior knee pain (AKP). Unphysiologic load or changed metabolic activities can lead to structural failure with loss of homeostatic conditions.

Physiology of pain

Pain occurs whenever tissues are being damaged [1]. It is a protective mechanism for the body and causes the individual to react to eliminate the pain stimulus. Two major types of pain are fast pain and slow pain. Fast pain, which is felt within 0.1 second after the stimulus is applied, is described also as sharp pain, acute pain, or electric pain. Fast pain is not felt in most of the deeper structures of the body. Slow pain, also described as burning pain, aching pain, or chronic pain, normally is present with tissue destruction. It can lead to prolonged suffering and occurs in the skin and the deep tissues, such as the structures of the PFJ.

Pain is elicited by different types of stimuli: mechanical, thermal, and chemical [1,2]. Fast pain is elicited by mechanical and thermal stimuli, whereas all three types can cause slow pain. Some of the chemical agents that excite pain include histamine, serotonin, and bradykinin. Additionally, prostaglandins and substance P (SP) enhance the sensitivity of pain endings but do not directly excite them [1]. These chemical substances are especially important in stimulating the slow type of pain (chronic, suffering pain) that occurs after tissue injury.

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PII: S0278-5919(02)00026-1

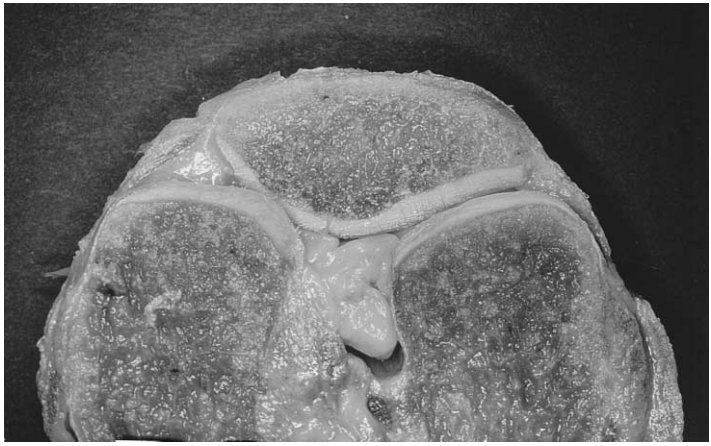

Fig. 1. An axial section through the patellofemoral joint shows the different structures.

Pain receptors adapt very little and sometimes not at all. Under special conditions, excitation of pain fibers becomes progressively greater, resulting in chronic aching pain. The increase in sensitivity of the pain receptors is called hyperalgesia. This may explain the prolonged, unbearable suffering in patients presenting with chronic AKP. The intensity of pain correlates with the rate of tissue damage from chemical stimuli, tissue ischemia, tissue contusion, and increased or decreased pressure. These considerations play an important role in the general understanding of articular and periarticular pain.

Pain receptors are in all free nerve endings (FNEs). These endings use two separate pathways for transmitting pain signals to the central nervous system: the fast-sharp pain pathway and the slow-chronic pain pathway. These pathways correspond to the two types of pain. The fast-pain signals are transmitted in the peripheral nerves to the spinal cord with higher velocities (6 and 30 m/second) than the slow pain signals (0.5 and 2 m/second). This double system of pain innervation gives a double pain sensation: a fast pain that is transmitted to the brain (A fibers) followed by a slow pain (C fibers). The fast pain makes the person react immediately to remove himself from the stimulus, for example impingement of a plica. The slow pain becomes more painful over time, eventually becoming the intolerable suffering of long-continued pain (eg, chronic irritation of synovial membrane).

Innervation of the knee joint

Current understanding of the specific pattern of innervation of the human knee is summarized best by Kennedy et al [3], who describe two groups of articular nerves. The posterior group consists of the prominent articular nerve (as a branch of the tibial nerve) and a terminal branch of the obturator nerve. The anterior group

consists of articular branches of the femoral, common peroneal, and saphenous nerves. The posterior articular nerve supplies the posterior capsule and cruciate ligaments [4]. This nerve arises in the popliteal fossa and penetrates the posterior capsule [5]. The lateral articular nerve innervates the lateral and posterolateral parts of the knee, whereas the recurrent peroneal nerve supplies the middle and anterior portions of the lateral joint capsule. Anteriorly, the capsule is innervated by terminal branches of the femoral, common peroneal, and saphenous nerves. The femoral nerve divides into the vastus lateralis, medialis, and intermedius muscles; it also contributes branches to the anterior medial joint capsule. The saphenous nerve contributes a branch to the anterior medial capsule and also provides sensory branches to the patellar tendon [6].

The nerve supply of the patella is studied in detail by Fontaine [7]. He finds that nerves travel to the entire medial side and to the proximal half of the lateral side. The medial branches are most important and originate from the nerve of the vastus medialis muscle. The lateral branches originate from the nerve of the biceps femoris muscle (caput breve) and the nerve of the vastus lateralis muscle.

The complex innervation of the structures of the PFJ may explain the variety of clinical findings in patients suffering from AKP.

Anatomy of pain

Morphologic studies reveal that joint receptors (mechanoreceptors) can be classified into four categories—Ruffini endings, Pacinian corpuscles, Golgi tendon organ-like endings, and FNEs [3,6,8].

Free nerve endings

Type IVa FNEs (Fig. 2) detect crude touch, pressure, pain, heat, and cold. Primarily, they constitute the articular nociceptive system. They transmit information on pain and inflammation and are therefore sources of AKP [3,9]. They remain inactive during normal circumstances but become active when they are subjected to abnormal mechanical deformation or special chemical agents [9,10]. Type IVb FNEs function as efferent vasomotors [9].

In a comprehensive histologic study of neurologic receptors in 19 static and dynamic knee structures, the authors record the qualitative and quantitative incidence of type IVa FNEs [9]. FNEs are stained by the hematoxylin-eosin (H-E) and Masson's trichrome methods. The immunohistochemical tests were performed using S-100 and synaptophysin [9].

Different structures of the PFJ show high FNEs counts. The tendon of the quadriceps muscle has the highest density, and the retinacula and patellar tendon had the second-highest FNEs count. This is not surprising, because they control acceleration, deceleration, and rotation of the knee joint, and therefore need a high proprioceptive capability for coordinating these conditions. It also indicates their importance in balancing the patella during the gliding mechanism. The

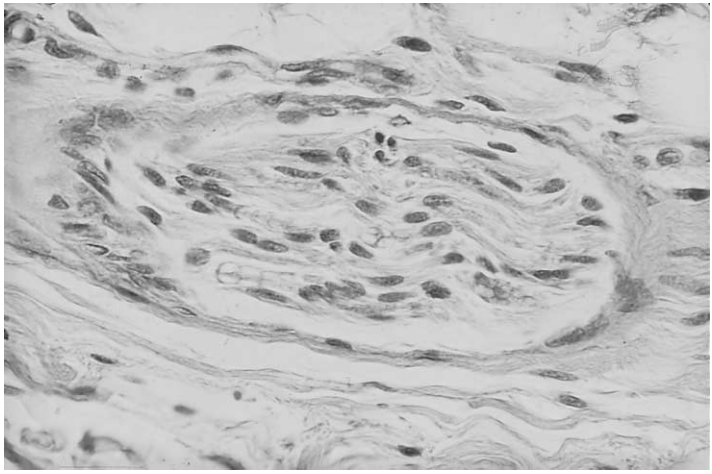

Fig. 2. Type IVa free nerve ending stained by hematoxylin-eosin and Masson's trichrome methods.

correlation between these histologic findings, the AKP, and the clinical pathology is described later in this article.

Substance P

Other studies focus on the nociceptive afferent nerve supply in the knee joint using SP or calcitonin gene-related peptide (CGRP) immunoreactivity. They suggest that SP and CGRP are neurotransmitters of nociceptive sensation [11–14].

Fibers containing SP are isolated in the lateral retinaculum, the fat pad, synovial membrane, periosteum, and the subchondral plate of patellae affected with degenerative disease [11,12,14–16]. Nerve fibers immunoreactive for SP are not observed in the articular cartilage of the patella [14]. Examination of subchondral bone, however, shows the presence of SP-positive nerve fibers in the erosion channels, which are present in patients with degenerative joint disease [14].

The results of the studies by Witonski et al [14] and Sanchis-Alfonso and Roselló-Sastre [12] demonstrate that SP-immunoreactive nerve fibers are widespread in the soft tissues around the knee joint. These tissues include, especially, the retinacula, synovium, and fat pad. These investigators conclude that AKP depends not only on mechanical factors (ie, elevated subchondral pressure, jumper's knee), but also on neural factors (nerve damage in affected lateral retinaculum) that are involved in this process. SP-positive fibers often are associated with blood vessels [14]. Here, SP functions as a vasodilator that can produce inflammation [14].

Clinical implications

AKP is one of the most common knee complaints in sports medicine. AKP can be experienced by the patient as a sharp, acute, or chronic pain. It can be

aggravated by prolonged activity with increased patellofemoral compressive forces (eg, climbing stairs, squatting, or kneeling) or by prolonged inactivity (eg, prolonged periods of sitting in knee flexion, cinema sign, or driving) [17,18]. Also, the duration of pain (seconds, hours, or weeks) as it relates to specific activities or movements (eg, patellar subluxation) is important. A clear understanding of the localization, duration, and type of pain is necessary for exact diagnosis and for determining the required therapy. This includes also a precise clinical examination.

Cartilage

AKP often is associated in patients with chondromalacia of the patella or trochlea. Thus, it is surprising that patients with normal-appearing cartilage can experience pain and that others with extensive chondral damage can be pain-free [19,20]. Hyaline cartilage is completely free of nerve fibers [14,17,19]; therefore, the aneural cartilage cannot be the source of pain alone. Also, defects in the surface are not believed to produce pain. Dye [21] does not feel any pain during arthroscopic palpation of his extensive lesion of the patellar cartilage without intraarticular anesthesia.

Abnormal biomechanical configuration (maltracking patella) is described as an important cause of the development of patellar chondromalacia [14,22]. Here, the sources of pain are chemical synovitis [23] with effusion and mechanical factors (Fig. 3) [11,19].

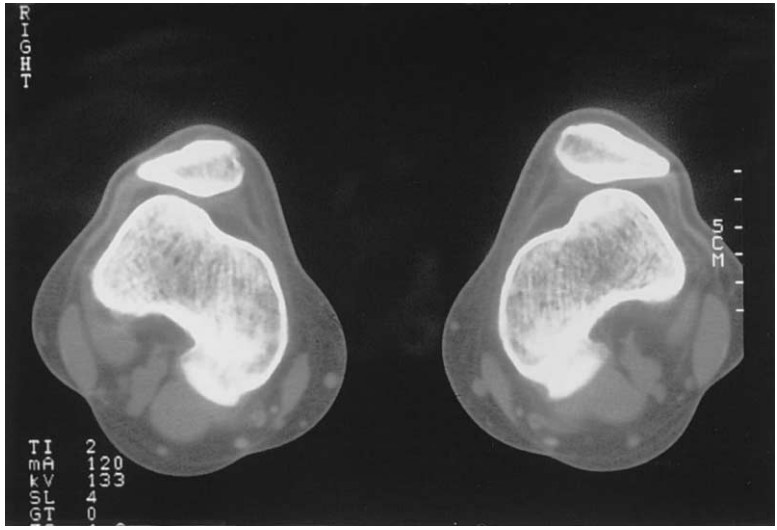

Fig. 3. Axial CT scan with lateral patella subluxation causing damage to the retropatellar cartilage and the lateral retinaculum.

Synovium

The synovium has a rich nerve supply of type IVa FNEs [9] and fibers containing SP [11]. Synovium can be irritated and produce pain [17,23]. The primary function of the synovium as pain receptor is of great interest [24]. Kennedy et al [3] and Andrade et al [25] report an irritation of FNEs in the synovium in Hoffa's disease and in symptomatic synovial plica, with decreased quadriceps activity produced by only slight synovial effusion resulting from painful stimulation of FNEs. Repetitive impingement of a medio- or suprapatellar plica between patella and femur also can be the underlying cause of AKP (Fig. 4) [9]. Often in such situations, the articularis genu muscle is unable to retract the synovial fold in the suprapatellar pouch whenever the plica is thickened, scarred, or inflamed [26]. Peripatellar synovitis is described by Dye et al [27] as one of the most common causes of AKP (Fig. 5).

Destruction of articular cartilage (Fig. 6) leads to a local tissue response with episodes of inflammation and synovitis [28]. Cartilage damage results not only from overuse (eg, maltracking), but also from active mechanisms in the metabolism of chondrocytes. During inflammation, there is decreased absorption of essential nutrients by the cartilage. Inflammation affects the integrity of the different components of the joint. Polymorphonuclear granulocytes, which are responsible for phagocytosis of damaged tissues, affect cartilage and joint structures [17]. The changes induced by inflammation cause painful stretching of the joint capsule by recurrent episodes of effusion [28]. Additionally, increased inflammation also may irritate the fibrous capsule's richly endowed nerve endings [17]. The increase in pain may also be a result of synovitis or irritation of a synovial plica. Changes induced by inflammation also include alteration of the viscosity of the synovial

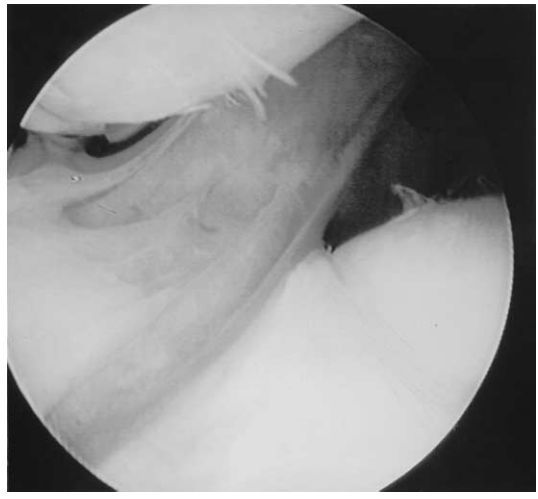

Fig. 4. Arthroscopic view of a left knee showing a big mediopatellar plica between patella (top) and femur (bottom) that can be impinged.

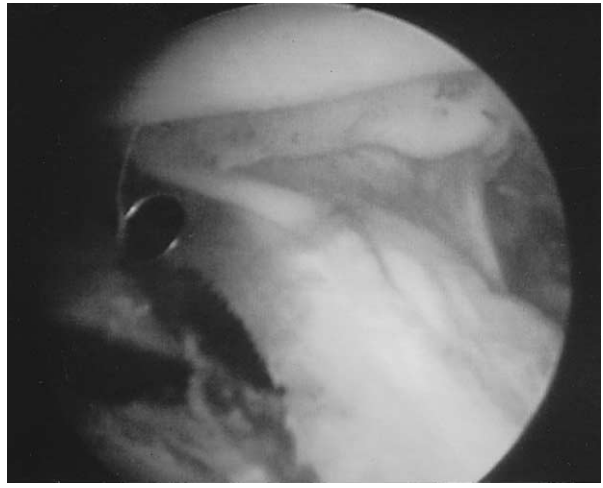

Fig. 5. Arthroscopic view of the suprapatellar pouch showing peripatellar synovitis. Patella (top); water canula (left).

fluid, caused by the elaboration of enzymes or free radicals that degrade hyaluronic acid and lubricin [28]. This breakdown of hyaluronic acid decreases smooth movement of the articular surfaces (crepitations) as a result of a decrease in the viscosity of the synovial fluid. This is important in further choice of treatment.

Infrapatellar fat pad

As mentioned previously, SP-immunoreactive nerve fibers and type IVa FNEs are found in the fat pad [9,13,29], demonstrating the rich nerve supply of this

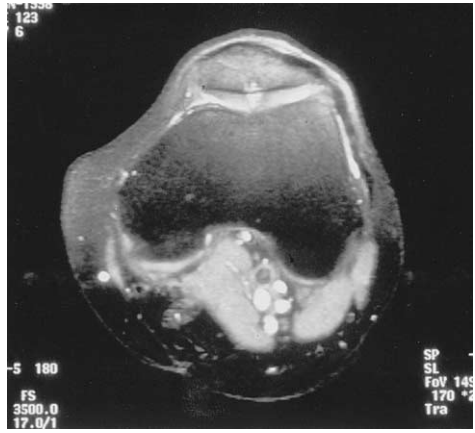

Fig. 6. Axial CT scan demonstrates retropatellar damage of the cartilage with increased signal intensity in the patella. This could be synovial fluid.

structure [9,29]. The heavily vascularized infrapatellar fat pad, with its alar plicae, fills the anterior part of the knee joint. It is held in place by the patellar tendon, the bilateral longitudinal retinacula, and the infrapatellar synovial plica, the central structure that passes posterosuperiorly to the intercondylar roof [30].

The close anatomic relationship to the patellar tendon and the lateral superficial oblique retinaculum make the fat pad a frequent source of pain. McConnell [31] describes 78% of her patients presenting with patellar tendonitis as having an irritation of the fat pad. Impingement of the fat pad is possible especially during eccentric load in jumping or running. Also, straight leg rising can cause pain by compression of the fat pad. In addition, chronic irritation of the synovium with joint effusion leads to swelling of the fat pad, and the risk of impingement behind the patellar tendon increases. A laterally oriented increased tension caused by a tight lateral retinaculum also may create fat pad irritation.

Understanding the biomechanical processes is necessary in order to choose the corresponding treatment. McConnell's [32] taping technique can help relieve the symptoms. Tape is a successful method for restoring tissue homeostasis [33].

Subchondral bone

The subchondral bone has a rich nerve supply [17,34,35]. An elevated subchondral bone pressure is shown to produce pain [11,17]. The best-known cause of hyperpressure is the lateral patellar compression syndrome [17] (Fig. 7). The increase of intraosseous pressure is the result of failure of energy absorption function of the articular cartilage caused by the decreased contact area [17,23]. Abernethy et al [36] and Minns et al [37] state that pain arises from changes in the bone caused by patellar stress patterns and loss of bone stiffness.

Waisbrod and Treiman [38] suggest that pain may originate from increasing venous engorgement in the patella in the presence of an abnormal patellofemoral

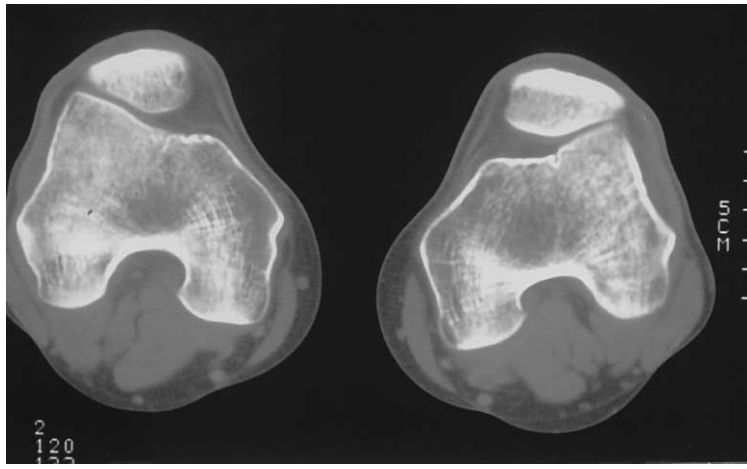

Fig. 7. CT scan demonstrates increased pressure in the lateral patellofemoral joint.

rhythm and pressure. Drill holes or patella osteotomies can decrease the subchondral pressure and improve the articular contact area in the PFJ [39,40]. Either technique can relieve pain.

Pain in the subchondral bone also can be caused by dynamic metabolic adaptations characterized by increased turnover and remodeling [41]. Dye and Chew [41] describe multiple triggers, including mechanical neurovascular and hormonal factors, that may initiate increased osseous metabolic activity. The increased activity is detectable with technetium scintigraphy (Fig. 8). Dye and Chew [41] believe that chronic, supraphysiologic loading or abnormal joint mechanics combine with chronic, excessive periarticular cytokine production to produce the increased remodeling in most patients. They also note that persistently increased osseous metabolic activity of periarticular bone identifies a subgroup at risk for early structural changes [41].

In contrast with the increased pressure in the lateral patellar compartment syndrome, the medial PFJ shows hypopressure of cartilage on the patellar and femoral surfaces [17]. This incongruity also is seen in dysplastic patellae. Hypopressure and disuse of the medial facet may cause malnutrition and early degenerative changes of the articular cartilage [17]. This may explain why early lesions of the cartilage in patients with lateralization of the patella usually are noted on the medial patellar facet and why late lesions on patellar facets and osteoarthritis are more advanced later in the lateral patellar facet [17].

Retinacula

Neuropeptide-containing nerve fibers [12,14,16] and type IVa FNEs [9] are documented in the lateral and medial retinacula. Thus, the retinacula may be an important factor or trigger point in AKP [42]. Fulkerson concludes that the lateral

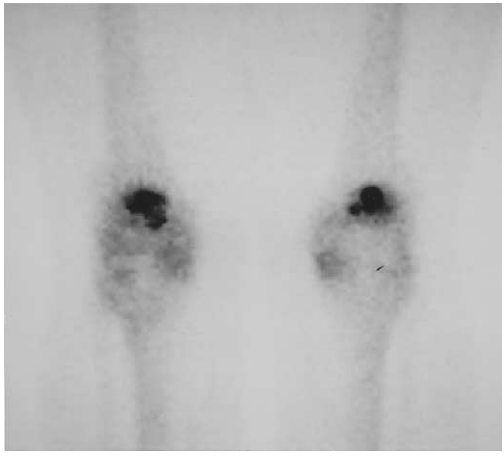

Fig. 8. Anterior technetium scintiscan of a female patient with a five-month history of unspecific anterior knee pain. The study shows marked increase in the activity in both patellae.

retinaculum itself is painful, although it is difficult to distinguish retinacular pain from pain in the underlying synovium [43]. The observations reported by Sanchis-Alfonso et al [11,12] provide a neuroanatomic basis for AKP syndrome in active young patients with patellofemoral malalignment and support the clinical observation that the lateral retinaculum may have a key role in the origin of this pain.

Recently, Sanchis-Alfonso et al [11] conclude that histologic changes in the nerves of the lateral retinaculum may be an important cause of pain in patients with patellofemoral malalignment, as there is a direct correlation between the severity of pain and severity of nerve injuries. Moreover, they believe that instability in patients with patellofemoral malalignment can be explained, at least in part, by the damage of nerves of the lateral retinaculum, which can be related to proprioception (Fig. 9).

Some studies implicate neural damage and hyperinnervation into the lateral retinaculum as a possible source of pain in patients with patellofemoral malalignment [11,12,42,44,55]. In reviewing the literature, the authors note that hyperinnervation is a factor implicated in the pathophysiology of pain in other orthopaedic pathologies [45–47]. The mechanisms by which this neural proliferation is produced in the lateral retinaculum, however, currently are unknown.

Sanchis-Alfonso and Roselló-Sastre [12] observe the presence of neural growth factor (NGF) and SP in the lateral retinaculum of patients with isolated symptomatic patellofemoral malalignment. NGF is a cytokin neurotrophin that is released during axonogenesis and inflammation and stimulates neural sprouting [48]. It is involved in pain mechanisms by means of stimulating the release of neuroceptive mediators, such as SP, and attracting lymph cells and mastocytes, which can potentially release more cytokins, including NGF, thus perpetuating the cycle [12,49]. The authors show that nerve proliferation in patellofemoral malalignment primarily dependents on nociceptive sensory SP-positive nerves in the lateral retinaculum [12]. Moreover, the group of patellofemoral malalignment

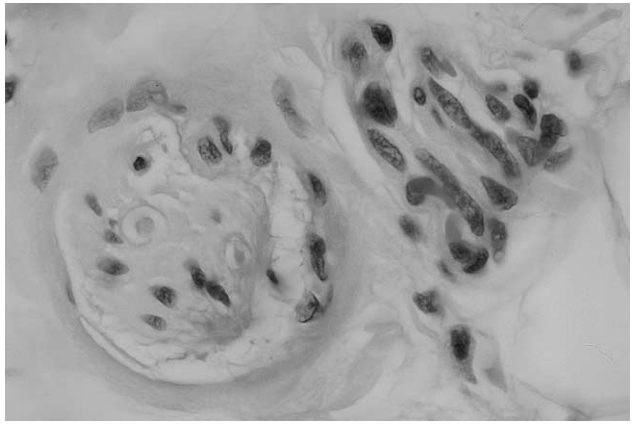

Fig. 9. Nerve bundle showing myxoid degeneration of the endoneurium in a patient with chronic lateral patella subluxation (retinaculum, hematoxylin–eosin; original magnification × 300).

patients with pain as a predominant symptom shows higher levels of NGF than patellofemoral malalignment patients with instability as the main complaint [48]. This NGF is detected primarily in the vessel walls and in the large neural structures and is found as active precursors of 35 kD, which means that the nerve fibers of these lateral retinaculae must still be in a proliferative phase [48].

NGF synthesis can be induced by ischemia [50–52,56]. Moreover, it is observed that NGF hastens neural proliferation in vessel walls [44,53], and it is this pattern of hyperinnervation that is seen in the lateral retinaculum of patients with painful patellofemoral malalignment [43,47].The authors hypothesize that ischemia may be the main problem in painful patellofemoral malalignment [44,48] as a result of a mechanism of vascular torsion secondary to patellar malalignment—medial traction over a retracted lateral retinaculum in contrast with the lax lateral retinaculum in knees with patellar instability; periodic episodes of ischemia are promoted and could trigger NGF release. Once NGF is present in the tissues, it leads to hyperinnervation, SP release, pain, and attraction of mastocytes [12,49], leading to the ischemia-hyperinnervation-pain cycle.

Therefore, the authors [48] suggest that two pathobiologic mechanisms lead to a symptomatic patellofemoral malalignment: (1) pain as the predominant symptom with detectable levels of NGF that provoke hyperinnervation and stimulus of SP release, and (2) instability as the predominant symptom, whereby there is less local NGF release, less neural proliferation, and less nociceptive stimulus.

Damage to these neuroproprioceptive fibers can alter the proprioceptive innervation [11] and stability of the patella [40]. Jerosch and Prymka [54] find a reduction in knee proprioception after patellar dislocation compared with the asymptomatic contralateral knee, which can be explained by proprioceptive loss. This also may explain why elastic knee bandages can improve knee stability by increasing proprioceptive feedback from skin mechanoreceptors.

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