Chondromalacia induced by patellar subluxation in the rabbit

Bjarne Nue Møller, Flemming Møller-Larsen and Lars Henrik Frich

A unilateral patellar malalignment was induced in 20 young and 20 mature rabbits by lateral displacement of the tibial tuberosity, the other knee serving as osteotomized in situ control.

At 6 weeks, all the knees appeared macroscopically normal, but histologically definite cartilage degeneration was found on the experimental side. At 3 months, macroscopic changes occurred in 5 of 10 mature rabbits, and histologic cartilage degeneration was found in all the experimental knees, most pronounced in mature animals, and particularly in joint facets submitted to high pressure.

This experimental model produces changes resembling chondromalacia patellae and early arthrotic changes suggesting the importance of malalignment in the development of patellofemoral cartilage degeneration.

The term chondromalacia of the patella is frequently used to describe the anterior knee pain syndrome, but also to describe cartilaginous changes in the patella. There is still much disagreement on the relation between the two definitions and on the etiology of the chondral lesions of the patellar articulation[1–3].

We have produced subluxation of the patella in rabbits and found degeneration of the articular cartilage analogous to chondromalacia patellae.

Material and methods

Twenty immature rabbits (weight 2,058 ± 209 g) (mean ± SD) and 20 mature rabbits (3,310 ± 127 g) older than 9 months[4] were operated on bilaterally under Immobilon (etorfin and acepromazine) anesthesia administered in i.m. doses of 0.06 mL/kg. Osteotomy of the tibial tuberosity was performed on both sides without opening the knee joint. On the right side the tuberosity was displaced laterally increasing the Q-angle, and a sagittal small-fragment AO screw was anchored in the posterior tibia to prevent the tubercle from sliding medially (Figure 1). On the left side the osteotomy was fixed in situ by a similar screw. On both sides the tuberosity was further secured by an extraarticular wire. The position of the patella was controlled by radiographs in lateral and tangential views (Figure 2). After skin closure the anesthesia was reversed by Revivon (diphenorfin) 0.05 mL/kg, and the animals were caged.

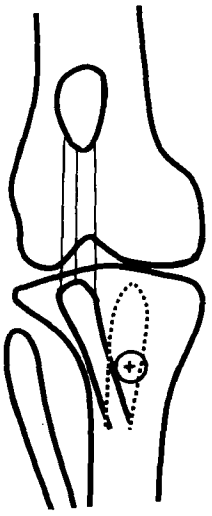

Figure 1. Lateral transposition of the tibial tubercle. The dotted line indicates the original position. The encircled cross indicates the screw inserted between the tuberosity and the medial cortex of the tibia.

The Orthopedic Hospital, University of Århus Institute of Experimental Clinical Research, Århus, Denmark

Correspondence: Dr. Bjarne Nue Møller, Department of Orthopedics, Haderslev Hospital, DK-6100 Haderslev, Denmark

Figure 2. Tangential view of the patellar articulations showing lateral patellar subluxation in the right knee.

Half the rabbits were killed at 6 weeks and half at 3 months. The macroscopic appearance of the joint surfaces was recorded. The distal part of the femur and the patella were removed and placed in 4 percent neutral buffered formaldehyde. After decalcification in EDTA and double embedding in paraffin, transverse sections 6–7 μm thick were taken from the patella and the femoral groove while the lateral and medial condyles were cut sagitally. At least 5 different specimens were obtained from each location; and each specimen was stained with safranin O, fast green, and iron hematoxylin for semiquantitive histologic-histochemical grading according to Mankin et al.[5] (Table 1).

Specimens were also taken from the synovium of the suprapatellar bursa and the synovium attached to the patella, and were stained with hematoxylin-eosin.

For statistical analysis the Pratt[6] and Mann-Whitney rank sum tests were used.

Table 1. Median values of the Mankin[5] score in 40 immature rabbits following experimental patellar subluxation of the right (R) knee, and compared with the sham-operated on left (L) knee joint. The groups contained 10 rabbits each

Weeks	Mature rabbits	Patella		Femoral groove		Lateral condyle		Medial condyle	
		R	L	R	L	R	L	R	L
6	–	1	0	1	0	1	0	0	0
	+	5	0	1.5	0	1	0	1	0
12	–	2	0	1	0	2	0	2	0
	+	7	0	5	0	5	0	3	0

Mankin score. Semiquantitive histologic–histochemical grading of the articular cartilage (grade): structure (0–6); cells (0–3); tidemark integrity (0–1); safranin-O staining (0–4).

Results (Table 1)

Immature rabbits

After 6 weeks of patellar malalignment, no pathologic changes were found macroscopically. Microscopic examination revealed Grades 1–3 cartilage degeneration of the patellar articulation joint in 8/10 rabbits, frequently as a reduction of the glycoaminoglycans in the intermediate zone (Figure 3) of the cartilage as the only change or in association with surface fibrillation and/or hypercellularity. These changes occurred on the experimental side ($P < 0.01$, Pratt test). On the

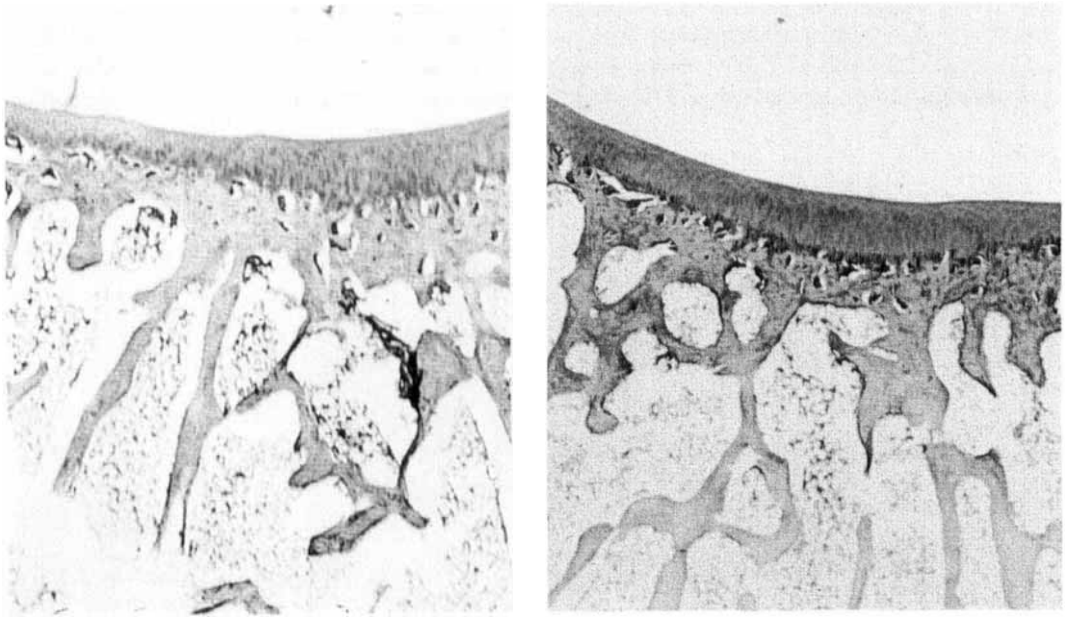

Figure 3. A. Articular cartilage from the right femoral groove of an immature rabbit following 6 weeks of patellar subluxation. The surface and the cell architecture is intact, but the glycosaminoglycans within the superficial and intermediate zones are depleted. Safranin-O staining, x100.
B. Normal appearance of cartilage from the left (control) femoral groove of an immature rabbit 6 weeks after osteotomy of the tibial tubercle. Safranin-O staining, x100.

control side, only slight depletion of the safranin-O stain was noticed in the superficial cartilage zone in 2 rabbits.

At 3 months, additional clefts extending to the intermediate zone occurred, but chondrocyte cloning was not observed. No signs of cartilage degeneration were found on the control side.

The synovial membrane showed no macroscopic or histologic changes in the control knees, whereas a slight synovial reaction—evidenced by thickening of the synovial intima, the presence of plasma cells, and polymorphonuclear leukocytes—was noticed on the experimental side in 3 rabbits followed for 3 months.

Mature rabbits

In the adult animals the macroscopic examination of the experimental knee joint appeared normal at 6 weeks, but at 3 months the normal shiny appearance of wet cartilage had changed to a bluish color in 5 rabbits. Histologically, the cartilage degeneration after 6 weeks was increased compared with controls ($P < 0.01$, Pratt test) and with the 6-week immature experimental group ($P < 0.01$, Mann-Whitney test).

At 3 months, fibrillation with chondrocyte cloning and disarrangement of the cartilage cell columns were accompanied by a reduction or loss of safranin-O stain on the experimental side (Figure 4), and in one knee the subchondral bone of the lateral patellar facet was exposed. In a few knees, horizontal splitting following shearing[7] was observed at the junction between the calcified cartilage and the subchondral bone. Also reduced nuclear stain and enlarged or empty lacunae were present in the most degenerated parts, typically at the joint facets submitted to hyperpressure, i.e., the lateral aspect of the patellar articulation, in particular the patellar ridge and the lateral facets of the patella. The degeneration of the medial part of the patellar articulation was less severe compared with the lateral part ($P < 0.01$, Mann-Whitney test).

On the control side, 4 rabbits revealed a Grade-1 stainability with safranin-O at the superficial zone of the cartilage.

A slight reduction of the safranin-O and surface fibrillation was found at the weight-bearing areas of the lateral and medial femoral condyles in 4 rabbits followed for 12 weeks.

Osteophytes were not found, although a synovial membrane proliferation associated with a slight inflammatory response was observed, but only in animals with advanced cartilage degeneration.

Discussion

Since the term was introduced by König[8], several theories on the etiology of chondromalacia patellae have been put forward. Among these, trauma[3], changes of the subchondral bone[9,10], and morphologic abnormalities[1] have been reported as important factors. Current studies suggest, however, that abnormal stress on the cartilage, such as patellar malalignment, may be a key factor in the initiation of the cartilage breakdown[11].

The mediator of patellar subluxation is not known, but insufficiency of the vastus medialis muscle[12], patella alta[13], and excentric location of the tibial tuberosity[14] all seem to be predisposing factors leading to an unstable patellofemoral joint. In this study, we induced

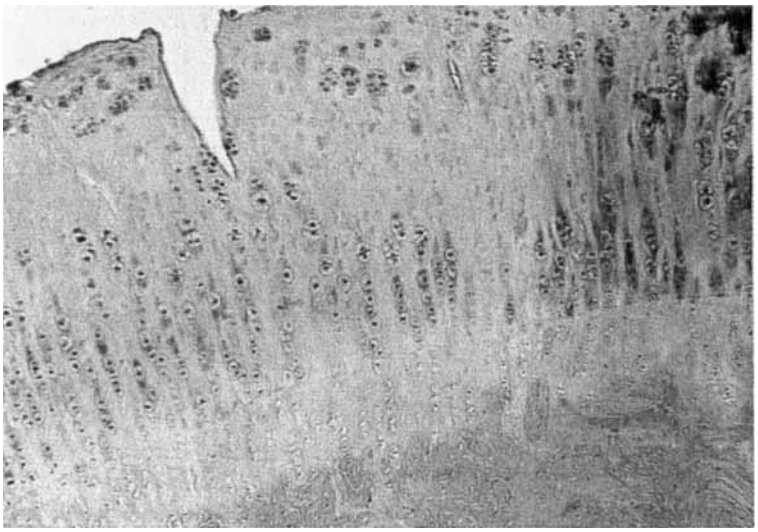

Figure 4. Histologic section from the lateral aspect of the patella of an adult rabbit 3 months after patellar subluxation. The surface is fibrillated, and the cell clusters appear in the intermediate and superficial layers. There are deep clefts and severe reduction of the glycosaminoglycans. Safranin-O staining, x350.

abnormal shearing forces in the patellar articulation by displacing the tuberosity laterally. The cartilage degeneration thus induced was pronounced in adult animals where also histologic evidence of shearing was present, suggesting that mature cartilage is relatively sensitive to abnormal mechanics. The reason for this might be an age-dependent reduction of collagen fibers[15] or disturbances in the proteoglycan synthesis[16] and thereby in the nutrition of the cartilage, which in immature animals partly comes from the underlying bony end plate[17].

The initial lesion of the cartilage was mainly a change in the ground substance of the intermediate and deep zones alone or in association with surface fibrillation, as also described by Goodfellow et al.[18] and others[19].

The most frequently involved area was the central ridge of the patella and the lateral facets of the patellar articulation, where also the greatest potential to progression into arthrosis has been shown to be located[13].

Among the many animal models that have been used to induce arthrosis, only a few have focused on the patellar articulation[14,19–21]. Our model seems suitable for further studies of early cartilage degeneration.

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