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The role of osteophytic growth in hip osteoarthritis

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Abstract We studied the appearance and frequency of the medial epiarticular osteophyte in human femoral heads. Specimens were sampled from 24 men and 31 women who underwent total hip arthroplasty. On radiography, medial epiarticular osteophytes were present in two thirds of the cases. However, histological examination revealed endochondral ossification in all. Presumably, the bone formation was preceded by the formation of canals and cavities containing vessels. Due to the ossification around these canals and cavities, the histological picture frequently featured two layers of cartilage with bone in the middle. Also in the marginal osteophytes, bone was formed by endochondral ossification. However, this bone appeared more irregular. The new bone formation most likely indicates a reactivated growth as an attempt to repair the osteoarthritic lesions rather than a process of degradation.

Résumé Nous avons étudié l'apparence et la fréquence de l'ostéophyte épiarticulaire médial dans les têtes fémorales humaines. Les spécimens ont été prélevés chez 24 hommes et 31 femmes qui ont subi une arthroplastie totale de la hanche. Sur les radiographies, ces ostéophytes étaient présents dans deux cas sur trois et l'examen histologique a révélé de l'ossification endochondrale dans tous les cas. Vraisemblablement la formation de l'os a été précédée par la formation de canaux et cavités qui contiennent des vaisseaux. A cause de l'ossification autour ces canaux et cavités, l'image histologique a fréquemment montré deux couches de cartilage entourant une couche osseuse. Dans les ostéophytes marginaux, l'os a aussi été formé par ossification endochondrale. Cependant, cet os a paru plus irrégulier. La nouvelle for-

mation osseuse indique très probablement une croissance réactivée comme une tentative pour réparer les lésions arthrosiques, plutôt qu'un processus de dégénération.

Introduction

Femoral-head osteophytes in coxarthrosis are mainly seen on the mediodorsal surface from the rim of the femoral neck and up to and sometimes including fovea capitis [13, 15, 17, 18]. These are known as medial epiarticular osteophytes. Marginal osteophytes are those on the marginal surface along the peripheral border of the articular cartilage. Frequently, osteophytes also occur in the acetabulum or around the fovea centralis on caput femoris. Accordingly, osteophytes are located at areas of low joint stress rather than at the joint surface where the cartilage is depleted [13, 15, 17, 18]. As a result, decreased range of motion with regard to rotation and abduction develops in coxarthrosis.

Increased bone remodeling as an early phenomenon in osteoarthritis (OA) has been suggested by increased alkaline and acid phosphatase activity in the subchondral bone, and by increased distribution of ^{99m}Tc -polyphosphate as assessed by scintigraphy in subchondral bone and osteophytes [2, 6, 7, 10, 16]. Furthermore, animal OA models have shown an early general subchondral growth [5, 9], and in human OA, the subchondral bone is thicker [1, 12, 21]. It is still debatable whether this increased osteogenesis precedes the cartilage changes or if it is secondary to these changes [2, 3, 5, 6, 10, 16, 19]. The role of osteophytes in the OA process is unclear. They may be part of an upregulated general bone growth in OA as an attempt to repair the joint. However, in rheumatoid arthritis (RA), another disease that includes progressive degradation of the articular surface, there are no OA pathognomonic signs, osteophytosis, or subchondral thickening.

In order to obtain a better insight into bone formation and repair potential in OA, this study describes, by histology and radiography, the extent of endochondral bone formation in the medial and marginal osteophytes of the

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Fig. 1 A frontal 5-mm-thick section of an osteoarthrotic femoral head demonstrating a medial epiarticular osteophyte at a nonpressure area. It reaches up to fovea centralis with a doubling of the cortex (*a*). Inside the osteophyte is a translucent area with bone marrow and sparse bone trabeculae. The depressed area superolateral on the loaded part of the head shows two great translucent pseudocysts (*b*)

femoral head. Furthermore, bone formation in the osteophytes is compared with that in the loaded areas of subchondral bone.

Material and methods

In 17 men with an average age of 70 years, and in 16 women with an average age of 68 years, 34 deformed arthrotic femoral heads were consecutively taken at operation for total hip arthroplasty and stored frozen at -70°C . From each specimen, two midcoronal slices with an approximate thickness of 5 mm were made by sawing the femoral head from the medial to the lateral side (Fig. 1). The slices were radiographed using a mammography apparatus. From one of the two slices, OA cartilage and underlying bone were chiseled off from the superior-lateral and the inferior-medial surface of the femoral head. After formaldehyde fixation, decalcification with ethylene dinitro tetraacetic acid (EDTA) and subsequent paraffin embedding, 7- μm -thick sections were stained with hematoxylin/eosin and safranin O (stains cartilage red, bone and connective tissue green) and examined by histology.

The second coronal slice from these femoral heads was embedded in methylmethacrylate and sectioned by microtome to 5- μm sections without prior demineralization, stained with hematoxylin/eosin, safranin O, Goldener (in undecalcified tissue, stains bone exclusively green, cartilage and connective tissue get different red nuances) and von Kossa (stains undecalcified bone and other calcified tissues black).

To study the marginal osteophytes, femoral heads from seven men, average age 65 years; and from 15 women, average age of 71 years, were taken at total hip arthroplasty. The marginal osteophytes were chiseled off and sectioned frozen into 6- μm sections, and stained with hematoxylin/eosin, safranin O, and toluidine blue for histological examination.

Fig. 2 *a* Magnification $\times 10$ ocul. $\times 10$ obj. Safranin O. *b* Magnification $\times 10$ ocul. $\times 20$ obj. Safranin O. Endochondral ossification with formation of primitive bone with lamellarly appearance around the small canals containing vessels or bone marrow (*a*). Multiple tidemarks (*b*) in the basal cartilage becoming more calcified in the progress of the disease. The subchondral bone plate is thick and unregular, with heavy lamellarly bone trabeculae (*c*)

Results

Generally, the radiographic pictures showing osteophytosis, sclerosis, and cysts corresponded well to histological findings. Endochondral ossification of cartilage and osteophytes was a common finding in the vast majority of cases.

Radiography

Twenty-three of 34 specimens had medial epiarticular osteophytes reaching up to the fovea capitis (Fig. 1). These showed an irregular thickening of the cortical bone in four cases, a partial medial bone duplication in nine cases, and a total bone duplication in ten cases (Fig. 1). Marginal osteophytes occurred in 30 of the 34 slices from the femoral heads.

On the weight-bearing areas, there was substantial subchondral compression in 20 cases. In 29 of the 34 slices, the superior part of these areas showed pseudocysts (Fig. 1).

Fig. 3a–c Three stages of endochondral ossification with doubling of the cartilage. Magnification $\times 10$ ocul. $\times 2.6$ obj. Safranin O. A cartilage with endochondral bone formation in the middle zone of the original cartilage. The upper part of the cartilage is stained red by safranin O, indicating glucosaminoglycan biosynthesis (a). Magnification $\times 10$ ocul. $\times 2.6$ obj. Safranin O. A double cartilage with further bone production and bone trabeculae between the two cartilages. The upper, but not the lower, part of the cartilage is stained red (b). Magnification $\times 10$ ocul. $\times 1$ obj. A doubling of the cartilage with bone marrow and small trabeculae in between. Weak red staining by safranin O. The lower cartilage mineralized but maintained chondrocyte-like cells. The distance between the two cartilages is approximately 3.5 mm (c)

Histology

Medial epiarticular osteophyte

These osteophytes showed endochondral ossification around cavities in the cartilage and subchondral plate thickening (Fig. 2a, b). At the ossification sites, the cartilage was almost completely mineralized and contained sparse hypertrophic chondrocytes. These islands of formed bone mimicked primitive haversian systems with a lamellar appearance (Fig. 2a, b). Histology also revealed that endochondral ossification occurred around the cartilage cavities in eight of 11 cases, without radio-

graphic medial epiarticular osteophytes. Subchondral thickening and advancing calcification, often with multiple tidemarks, were always present in the deeper parts of the joint cartilage (Fig. 2a and b). von Kossa staining showed that in all 34 specimens, the joint cartilage was calcified in patches to about half of its thickness. We were not able to detect bone formation without calcified cartilage adjacent to vessels and bone marrow.

As the ossification process mostly occurred around the canals and cavities in the central parts of the cartilage, the cartilage appeared “doubled” in 14 of 31 cases, as shown by two layers of cartilage with bone in the middle (Figures 3a, b, and c). Fig. 4 shows growth of a total medial epiarticular osteophyte in a slice stained by toluidine blue. The same doubling of the cartilage is also illustrated on Fig. 3c.

Only in cases with a rather intact cartilage is a complete doubling of the medial cortex and cartilage possible (Fig. 4 and Fig. 3c). The number and thickness of trabeculae differed in the osteophytes, as seen in Fig. 3b and c. Multiple tidemarks were often observed when the bone formation occurred more superficially in the medial epiarticular osteophyte (Fig 2a and b).

A combined analysis of the medial epiarticular sections gave an impression that bone formation was preceded by formation of matrix cavities frequently contain-

Fig. 4 Growth of a total medial epiarticular osteophyte in an osteoarthrotic femoral head. A slice stained by toluidine blue demonstrating the occurrence of cartilage on the double cortex medially. The doubling of the cartilage is also illustrated on 3c

ing vessels (Fig. 2a and b). It also appeared as if primitive lamellarly bone was initially formed around these vessel-containing cavities. In cases with more severe OA, more endochondral bone was formed, as shown by radiography (Fig. 1).

Marginal osteophytes

As in the case of the medial epiarticular osteophytes, the specimens with marginal osteophytes contained subchondral calcified cartilage with cavities and bone-marrow-like tissue lying relatively close together. Osteoblasts occurred in most cases at the interior margin of the cavities (Fig. 5a and b). The new bone was mostly uneven and irregular, as woven bone without lamellar features seen in the medial epiarticular osteophytes. Most of the formed bone was calcified, as shown in black by von Kossa staining.

Loaded superolateral area of caput femoris

In contrast to the specimens with osteophytes, the cartilage of the weight-bearing part of the femoral head demonstrated a much higher degree of osteoarthrotic injuries, as shown by the extended loss of cartilage. Generally, the area consisted exclusively of sclerotic bone with coarse trabeculae or necrotic bone and without bone formation. No osteoblasts were identified. Pseudocysts occurred frequently in the weight-bearing part of the femoral head; however, these were mainly empty and showed no vessel formation. Occasionally these cysts contained a fibrous mass or necrotic tissue.

Fig. 5 **a** Magnification $\times 10$ ocul. $\times 4$ obj. Safranin O. **b** Magnification $\times 10$ ocul. $\times 40$ obj. Hematoxylin/eosin. Marginal osteophyte with cysts in the subchondral calcified cartilage. The basal part of the cartilage is unevenly becoming mineralized without any clearly visible tidemark. Mineralized cartilage is stained green. As a consistent finding, osteoblasts (a) were located at the interior rim of the cysts

Discussion

OA is a disease that affects all joint structures. In OA cartilage, a metabolic imbalance where cartilage degradation processes outscore repair mechanisms has been implicated [22]. Accordingly, as OA progresses, the joint cartilage is gradually lost. A cartilage repair potential has been suggested by the increased biosynthesis of type-two collagen [20]. Others have shown increased metabolic activity in the subchondral bone [2, 6, 7, 10]. The present study confirms the occurrence of new bone formation, as shown by the endochondral ossification in osteophytes and subchondral bone in coxarthrosis.

Indicative of a reactivation of bone-growth processes in OA is the resemblance between the endochondral ossification in the examined femoral heads and the ossification of the epiphyses in prenatal life. In contrast to the normal joint cartilage, the osteophytes and the subchondral plate in OA have cavities with bone marrow and also some smaller canals containing blood vessels. The same situation with vascular canals, necessary for endo-

chondral bone formation, occurs at ossification of prenatal epiphyses [4]. TGF- β and b-FGF are expressed in the osteophytes of the human femoral head in OA, as shown by Uchino et al. [23]. The same growth factors are expressed in developing human bone and cartilage [11]. Furthermore, a glycoprotein showed high expression in the secondary ossification center in developing fetal cartilage and in diseased human OA cartilage and osteophytes but not in nondiseased cartilage [8].

In aging, the subchondral bone grows with an increasing number of vessels perforating the calcified cartilage into the uncalcified cartilage, with endochondral ossification between the vessel and the cartilage [18]. However, these changes are not as profound as in OA, and no osteophytes and cysts are formed [14, 18]. The exponentially increasing incidence of OA with age may, in some cases, be a result of uncontrolled vessel formation.

There were histologic differences between medial and marginal osteophytes. In the marginal osteophytes, cavities occurred in the calcified cartilage. The margins of these cavities showed osteoblasts, and less lamellarly looking bone was formed in these cartilages, whereas the newly formed bone in the epiarticular osteophytes mimicked primitive haversian systems with a lamellarly appearance. The marginal osteophyte growths in a relatively free space adjacent to both collum and caput femoris is contrary to the medial epiarticular osteophyte that grows in the cartilage and subchondral bone. This may influence osteophyte development. Consequently, the histologic differences may reflect different phases of osteophyte development or different kinds of osteophytes.

In conclusion, our study shows an active bone remodeling in coxarthrosis, as shown by the endochondral ossification in osteophytes and cartilage together with the subchondral thickening. With regard to OA pathogenesis, this supports the contention that osteophytic growth is more likely a repair attempt than an expression for degeneration.

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