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Arthrosis

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Editor's note: Dr. Be'ly presents an excellent description of the pathologic processes in degenerative arthritis and a report on experimental osteoarthritis produced in rats by sodium fluoride. The relation of fluoridated water to the human disease is under further investigation in Hungary.

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Osteoarthritis is a degenerative process leading to progressive damage of the articular cartilage and secondary disintegration of the articular surface of bones. Several factors are known to have a role in the pathogenesis of the disease in secondary arthrosis. If the etiologic factor is unknown, the term idiopathic or primary arthrosis is used.

The degenerative process takes place in the articular cartilage, consisting of chondrocytes and intercellular matrix. The intercellular matrix is formed by a structure of collagen fibrils embedded in a proteoglycan matrix. The collagen fibrils have a characteristic orientation. Originating in the border-line between bone and cartilage, the fibrils run vertically upward to the surface of the articular cartilage, there bend and run further parallel with the surface, forming a dense layer, the so-called lamina splendens. The fibrils of the tangential zone, that run tangentially to the chondrocytes, are named "interterritoreal fibrils." The other part of the collagen fibrils — the territoreal fibrils — are organized circularly around the chondrocytes. The territoreal fibrils form sequences of linearly arranged microspheres.

This particular collagen structure provides the special biomechanical characteristics of the articular cartilage. The vertical fibers ensure resistance against twisting, tracting shearing stress, the lamina splendens serves as a shield, the linearly arranged microspheres resist against pressing forces. The lower zone of the articular cartilage is sclerosed, so the physio-chemical properties of this zone are similar to the characteristics of the subchondral bone tissue, providing firm connection between bone and cartilage.

Four zones can be distinguished from each other in the articular cartilage according to the orientation of collagen fibrils:

IV: Lower, sclerotic zone.

III: Vertical zone.

II: Zone of bending.

I: Zone parallel with the surface.

The other constituent of the intercellular material is the so-called matrix. The matrix consists of aggregates, composed by proteoglycans bound to molecules of hyaluronic acid. The proteoglycans are mucopolysaccharides (new name: glycosaminoglycane) bound to carrier proteins. Binding proteins bind the proteoglycans to molecules of hyaluronic acid. the mucopolysaccharides — strongly hydrophilic due to their negative charge — have a main role in the biomechanical properties of the cartilage. Their great water binding capacity (they can bind as much as 10,000 times larger amounts of water than their own) provides the elasticity and load bearing potential of the cartilage.

The chondrocytes are responsible for the balance of matrix, synthesized by them.

According to a generally accepted principle, the metabolic disturbance of chondrocyte activity is in the center of the pathogenesis of arthrosis in the case of primary arthrosis. The synthesizing activity of chondrocytes decreases, and probably abnormal matrix structures are also generated. A part of chondrocytes becomes degenerated, so enzymes, further damaging the structure of matrix get released:

— mucopolysaccharidase, splitting the mucopolysaccharides off from their carrier proteins;

— protease, breaking up the carrier and binding proteins;

— hyaluronidase, decomposing the molecules of hyaluronic acid, that keep the proteoglycane aggregates together;

— collagenase, damaging the bridges of collagen fibrils, that collapse after all.

The fragments of articular cartilage cause synovitis; the enzymes, released during the inflammatory process further increase the enzymatic destruction of chondroid tissue. Because of the damage of chondroid tissue, the surface of the articular cartilage becomes incongruent, so the remaining congruent surface gets relatively overloaded (unchanged load presses a smaller intact surface). The relative overload further increases the destruction of the articular cartilage. The degenerative process is a so-called vicious circle. The cause that starts the vicious circle is known in secondary arthrosis.

For example, in the case of syringomyelia, or tabes dorsalis, the vicious circle is started by the overload of articular surface due to the disturbance of bathyesthesia of joints. In the case of haemarthrosis, positive ions accumulate in the joint, so the negative charge of mucopolysaccharides becomes neutralized. The mucopolysaccharides, therefore, lose their water-binding capacity, so the elasticity and load-bearing potential of the articular cartilage decreases.

In the case of ochronosis, a pathologic metabolite, the homogentisine acid destroys the chondrocytes, the synthesizing potential of chondrocytes decreases, and enzymes further damaging the matrix get released.

Four clinical-radiological stages of arthrosis are distinguished:

Stage I: Mild clinical symptoms appear. Discrete sclerotization of the cotyloid cavity can be seen on the X-ray picture of the affected joint, the articular space and the condyle remain intact.

Stage II: The movability of the joint decreases because of the pain at the start of a movement, and the rigidity of the joint. There appear small cysts in the cotyloid cavity, and fine osteophytes on the X-ray picture.

Stage III: The movability of the joint becomes significantly limited. Secondary inflammation may occur. Cysts can be observed either in the cotyloid cavity or in the condyle on the X-ray picture. The articular space becomes irregularly narrowed.

Stage IV: The joint is more or less stiff, immobile. Secondary inflammation often takes place, signs of muscle decompensation are observable. Severe deformation of the joint can be disclosed on the roentgenogram: deformation of the condyle and acetabulum, cystic degeneration, detritus in the articular cavity, bizarre osteophytes, extremely narrow articular space.

The synovial membrane and cartilage of the joint and the subchondral bone tissue are inseparables [and] form an interdependent functional unit. The above mentioned vicious circle process leading to increasing destruction of the joint is accompanied by reactive synovitis. Secondary changes occur in the subchondral bone tissue too. The incongruence of the surface of the articular cartilage leads to the overload of the intact, congruent parts of the joint. The subchondral bone trabecules may collapse; therefore secondary necrosis of bone tissue in smaller fields may occur. The osteonecrosis increases the incongruence, leading to relative overload of the intact areas.

This process is a vicious circle too. The synovial membrane, articular cartilage and subchondral bone tissue form a functional unit. Injury of any of these components during an illness leads to the impairment of the other structures of this functional unit.

For example, in the case of primary arthritis, secondary destruction of the cartilage and osteonecrosis takes place; or at primary necrosis of the subchondral bone tissue, secondary destruction of the cartilage and reactive synovitis occur.

Cases of primary arthritis accompanied by secondary bone and articular impairment, due to mycosis, metabolic diseases, and autoimmune processes are interpreted.

Cases of aseptic bone necrosis due to trauma or systemic diseases (osteonecrosis due to sickle cell anemia, dysbaric trauma, steroid administration, etc.) are interpreted.

If the aseptic necrosis occurs in the subchondral region, impairment of the articular cartilage and synovial membrane can be disclosed in every case.

The histologic differential diagnosis is very important because the therapy and prognosis is different in osteo-arthrosis of different origins.

Changes in the Collagen Structure of Bone Tissue in Experimental Fluorosis

Introduction

According to experi[ments] in human [physiology], about 10% of the whole preexisting bone tissue is reorganized in a year.[12] This perpetual process of rebuilding, remodeling the bone tissue is due to the action of multicellular functional units (BMU, BRU or BSU), consisting of osteoclasts and osteoblasts. It is generally accepted fact, that sodium fluoride causes enlargement of the whole bone mass. There is no confirmed and generally accepted theory in the literature yet as to how NaF influences bone tissue whether the enlargement of the bone mass is due to increased osteopoesis (stimulation of osteoblasts)[4,5,8,9,13,14,16,18] and/or to decreased bone absorption (blockade of osteoclasts)[1,2,7,10,11,13,15,17,19]. Authors agree that the formed bone is inferior to normal, the matrix is irregular[4,6,10,18] the collagen structure of the newly formed bone tissue differs from normal,[10] and the mineralization is enhanced[4,8,10,11,13,14,18].

The aim of our experiments was the investigation of the changes of collagen structure in experimental fluorosis.

Material and Methods

The experiments were performed on 45 female rats in 3 groups. Fifteen animals were given 0.5 mg, another 15 animals received 5.0 mg of sodium fluoride intraperitoneally, daily, for 3 months. Fifteen animals — the control group — received physiological saline solution in the same way.

X-ray pictures were taken of the killed animals. Histologic investigation was performed on both femurs and on the third, fourth and fifth lumbar vertebra of the animals. The material, fixed in 1% formalin solution was decalcified. The decalcifying agent consisted of 24 ml of 85% formic acid, 50 ml 35% hydrochloric acid, and 125 mg distilled water, (imbedded in paraffin, serially sectioned, and stained with picrosirius red).[2]

The regularity of collagen fibrils of the preexisting bone tissue was measured by a polarization optic method according to Brace-Kohler in 550 nm monochromatic light using an Opton Standard microscope. The measurements were performed on the corticalis and spongiosa of both femurs and vertebrae using 5 visual fields in each case. Ten measurements were made in all fields. The average of retardation values, characterizing the regularity of collagen fibrils was calculated. Analysis of significance was performed between the retardation values obtained according to T and Welch (modified T) tests.

Results

The retardation values measured in the spongiosa and corticalis of the femurs and vertebrae are represented.

The regularity of collagen fibrils in the corticalis and spongiosa of femurs and vertebrae decreased as compared to normal. In the case of daily administration of 0.5 mg NaF, the observed difference is significant.

Administering 5 mg NaF daily for 3 months, the regularity of collagen fibrils significantly decreased as compared to normal in the corticalis and spongiosa either of the femur, or of the vertebrae.

Discussion

The intercellular matrix of bone tissue consists of a collagen structure, embedded in proteoglycan aggregates. The process of formation and mineralization of the inter-cellular matrix are in a close relation. Isolation injury of any of these components is inconceivable. During the recent investigation, irregularity of the preexisting bone tissue's collagen structure could be disclosed by a specific topooptic method.

The investigations disclosed that the regularity of the collagen structure of preexisting, differentiated, lamellar bone decreases, so fluoride exerts its effect not only on the newly generated (newly formed woven) bone tissue, but also changes the collagen structure of the preexisting bone too. In our opinion, these changes can be considered as part of the toxic effect of fluoride exerted on osteocytes. The changes in collagen structure are certainly followed by damage to the matrix (proteoglycan aggregate). We are planning the selective investigation of this field.

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