Pathomorphological Changes in Hyaline Cartilage during Focal Persistent Infection

I. P. Zhurakovskii, A. I. Ryzhov, and N. I. Komandenko

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 134, No. 10, pp. 477-480, October, 2002
Original article submitted June 10, 2002

We studied morphological changes in hyaline cartilages of different localization in adult male rabbits with focal persistent infection produced by *Staphylococcus aureus* strain 209. Local chronic inflammation produced systemic atrophic and degenerative changes in the cartilage tissue. The severity of pathological changes depended on genetically determined repair and metabolic activity of the cartilage tissue.

Key Words: *hyaline cartilage; chronic inflammation; Staphylococcus aureus; experimental modeling*

Much attention is now given to the role of infections in the pathogenesis of joint diseases. Previous studies showed that streptococci, yersiniae, salmonellae, borrelias, klebsiellas, and chlamydiae are involved in the development of rheumatism [2,3,5,7], reactive arthritis [6-13], Lyme disease [8,9], ankylosing spondylitis [4], and Reiter's disease [1,10]. The concept regarding the influence of infectious agents on macroorganisms was formulated. However, the interaction of macroorganisms with potentially pathogenic bacteria, whose aggressiveness depends on the immune state, received little attention. At the same time, changes in the economic environment, industrialization, ecological problems, and other factors impair adaptive capacities in humans.

Here we studied the type and dynamics of changes in the hyaline cartilage accompanying chronic bacterial infection.

MATERIALS AND METHODS

Chronic osteomyelitis of the tibia was produced in adult male Chinchilla rabbits using *Staphylococcus aureus* strain 209.

Tomsk Research Institute for Health-Resort Treatment and Physiotherapy; Siberian State Medical University, Tomsk. Address for correspondence: referent@niikf.tomsk.ru. Zhurakovskii I. P.

We examined cartilages of the joint surface in knee and intervertebral joints, incomplete rings of cartilage in the trachea, and hyaline lamina limitance of intervertebral discs. Morphological characteristics were evaluated 1, 2, 3, 5, and 8 months after modeling of bacterial infection. Samples taken from intact animals of the same age served as the control.

The samples were taken from experimental animals immediately after decapitation, fixed in 12% neutral formalin and 96% alcohol, and embedded in paraffin. Serial sections were stained with hematoxylin and eosin or with picrofuchsin (method of van Gieson). In detailed analyses we studied nucleic acids (reaction with methyl green and pyronin, method of Brasche), neutral glycoproteins (reaction with Schiff iodic acid, method of MacManus), and glycosaminoglycans (toluidine blue staining with metachromatism).

RESULTS

In the early stage (months 1-2) of chronic inflammation the hyaline cartilage had a well-defined external layer. Chondrocytes with similar shape and size were stained with acid and basic staining agents. Cell nuclei, cytoplasm, and membranes were characterized by strong staining. By contrast, in the deep layers of the joint cartilage we revealed large and light anuclear cells with very small layer of the cytoplasm. The inter-

0007-4888/02/1344-0414$27.00

cellular space was weakly stained with hematoxylin and eosin (similarly to chondrocytes) and areas with different metachromatism were seen (Fig. 1, *a*). In single chondrocytes and isogenic groups nuclei underwent considerable deformation and pyknosis and, therefore, had unusual shape. Chromatin granules in individual cells were localized at the periphery of the karyoplasm or appeared as small hyperchromic particles at one of the poles.

The count of isogenic groups containing 3-8 cells and having round shape increased, particularly in the hyaline limiting lamina of intervertebral discs. Chondrocytes in isogenic groups retained their structure and functional activity.

Three months after modeling of chronic infection the deep cartilage layer included cells differing by their size and shape. We found relatively large, intermediate, and small chondrocytes. In these cells, nuclei had normal shape or were enlarged, deformed, and shifted toward one of the poles (Fig. 1, *b*). In most cells chromatin was hardly detectable. In individual aggregates the cell cytoplasm contained optically dense eosinophilic inclusions. In other chondrocytes the cytoplasm displayed high affinity for eosin and had no

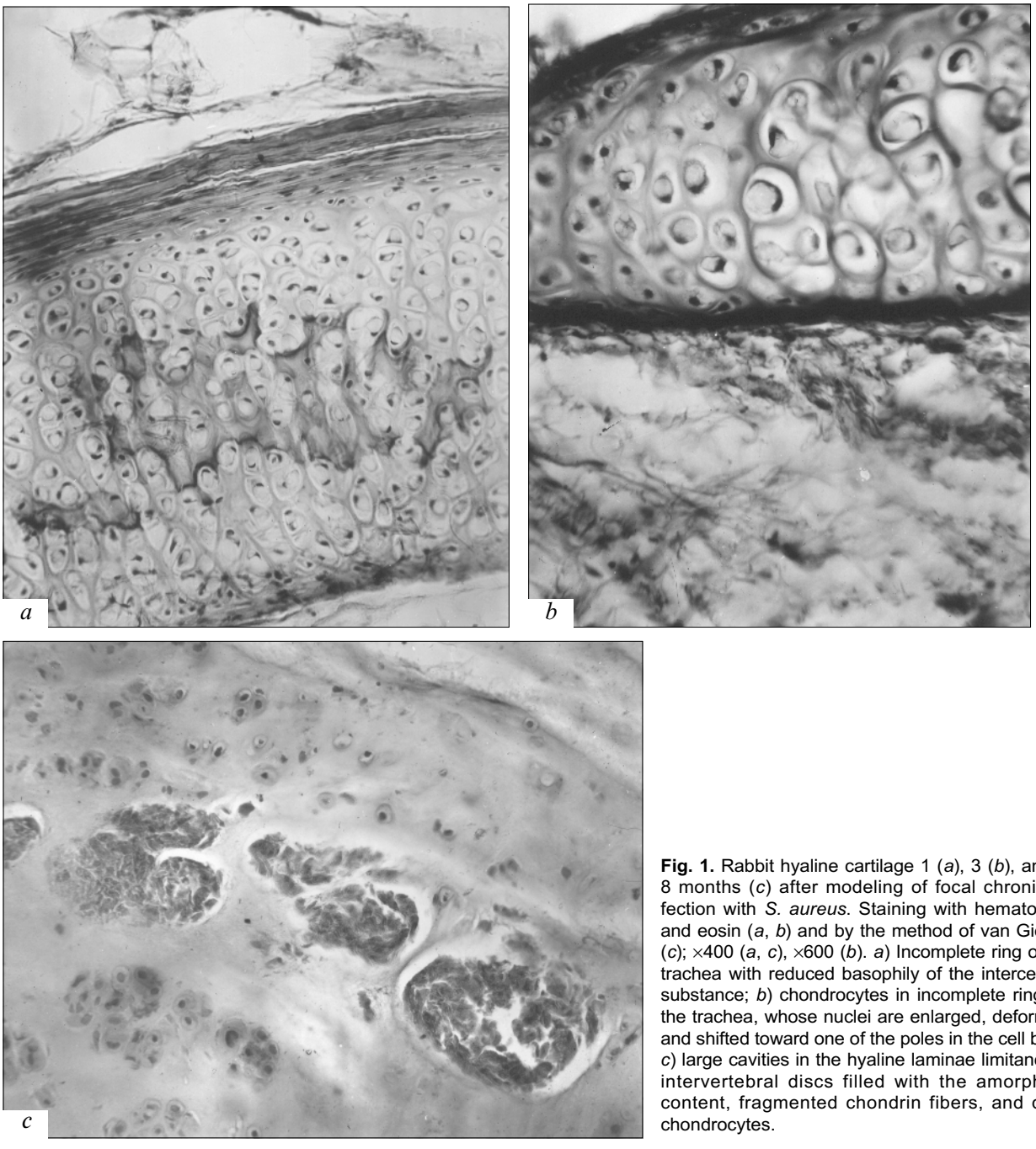

Fig. 1. Rabbit hyaline cartilage 1 (*a*), 3 (*b*), and 5-8 months (*c*) after modeling of focal chronic infection with *S. aureus*. Staining with hematoxylin and eosin (*a*, *b*) and by the method of van Gieson (*c*); ×400 (*a*, *c*), ×600 (*b*). *a*) Incomplete ring of the trachea with reduced basophily of the intercellular substance; *b*) chondrocytes in incomplete rings of the trachea, whose nuclei are enlarged, deformed, and shifted toward one of the poles in the cell body; *c*) large cavities in the hyaline laminae limitance of intervertebral discs filled with the amorphous content, fragmented chondrin fibers, and dead chondrocytes.

inclusions; the nucleus was weakly stained with hematoxylin and localized in the center.

Changes in the matrix correlated with the severity of damage to cartilage cells. Focal destructive lesions were found around modified single chondrocytes or isogenic groups and involved the surrounding intercellular substance (as estimated by staining with toluidine blue).

In individual regions of the deep cartilage layer, the state of cells was similar to that observed during simple division. The capsule of isogenic groups was hardly detectable or absent.

At the late stage of chronic inflammation (months 5 and 8) progressive pathological changes in the deep layer and peripheral regions of the hyaline cartilage were revealed. Large cavities often had different contours and were filled with the amorphous light substance. We found irregular lumps and bodies of necrotized cells (Fig. 1, *c*).

On months 5-8 hyaline laminae limitance of intervertebral discs underwent more pronounced pathological changes than the cartilage tissue of the joint surface and trachea. It should be emphasized that at the earlier stage of observations the hyaline cartilage of different localization was characterized by similar atrophic and degenerative changes. The size and number of focal destructive lesions containing lumps of different shape and necrotized chondrocytes markedly increased. Blood vessels and loosened fibrous connective tissue grew into focal necrotic areas localized in the vicinity of osseous laminae limitance.

Our results show that long-lasting persistent bacterial infection is accompanied not only by the formation of mononuclear infiltrates and local damage to the connective tissue around granulomas, but also by the development of atrophic and degenerative systemic changes. The severity of these changes depends little on the localization and distance between cartilages and primary focuses, but is determined by trophic characteristics of these structures and ability to maintain homeostasis and metabolism at the optimal level.

Morphological assay revealed the following dynamics of the pathological processes and compensatory-and-adaptive reactions: development of atrophic changes in chondrocytes and structural heterogeneity of the intercellular substance; increase in the number and cellularity of isogenic groups; necrosis of chondrocytes (particularly in isogenic groups) and formation of large deformed cavities; and fibrosis associated with ingrowth of the loosened connective tissue from subchondral bone.

Therefore, local chronic inflammation accompanying focal persistent infection produces systemic atrophic and degenerative changes in the cartilage tissue. The severity of pathological changes depends on genetically determined reparative and metabolic activity of the tissue.

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