Anitschkow Cells in Experimental Autoimmune Myocarditis

Having read the instructive article about experimental autoimmune myocarditis by Kodama et al,¹ I was intrigued by a characteristic of the nuclei visualized by the authors¹ in their excellent Figures 3B and 5A and B. Besides rare clearly identifiable Anitschkow cells, there are numerous nuclei the chromatin of which forms lamellae oriented at a right angle to the long axis of the nucleus. These lamellae are so regularly oriented that an artifact such as a shrinkage of chromatin during histopathological procedures may be excluded. I consider the cells containing these nuclei to be the “forms frustes” of Anitschkow cells. Those who disagree with this proposition will undoubtedly recognize that inflammatory cells with such nuclei have never been described. It is rational, therefore, to identify them as local cells. Again, Anitschkow cells become the most suitable candidates.

The present conventional view considers Anitschkow cells to be the fibroblast-like mesenchymal cells modified by tissue factors unique to the heart.² The problem is that Anitschkow nuclei have been described as inherent to myofibers, and it is easier to explain their migration from myofibers into the interstitial space than vice versa.³ For me, the most striking feature of Anitschkow nuclei is the fact that a periodicity of their lateral chromatin projections from the central bar corresponds to the periodicity of heart myofiber cross-striations.⁴ Even without complicated mathematics, one can easily imagine that the probability of a coincidence in this case is null and that this fact needs a rational explanation. The most plausible hypothesis is that the myofibers affected either by hyaline degeneration or colliquative myocytolysis lose most of their myofibrils and start to be perceived as interstitial cells by light microscopy. The remaining myofibrils, now invisible, continue, nevertheless, to exercise their force and impose their periodicity on nuclear chromatin. These cells would form a majority of cells in a muscle granuloma and in experimental autoimmune myocarditis.¹

If the above hypothesis is true, it must explain why Anitschkow nuclei may be present in intracardiac metastases but not in the corresponding primary lesions.² In this case, it may be argued that Anitschkow nuclei are present not in metastatic cells but rather in the interstitial cells of heart muscle origin.⁷

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References

Reply
The comments raised by Dr. Beranek are relevant, and we thank him for his attention to this model. He states in his letter that the majority of cells in the lesions of experimental autoimmune myocarditis may be Anitschkow cells and that Anitschkow cells probably derive from myocardial fibers by losing their myofibrils.

Various kinds of mononuclear cells and multinucleated giant cells were observed in the lesions of this myocarditis. Some of the mononuclear cells had large ovoid nuclei with nodular accumulation of chromatin,¹ but they were different from typical Anitschkow nuclear structures.² ³ We have immunohistochemically investigated the characteristics of mononuclear cells in the lesions of this myocarditis.⁴ The majority, about 70%, of mononuclear cells were composed of macrophages. The above-mentioned cells that had ovoid nuclei with peculiar accumulation of chromatin were also stained with a macrophage marker.⁵ Another 20% of nuclear cells in the lesions were T cells, about 15% were CD4+ T cells, and about 5% were CD8+ T cells. The remainder were composed of neutrophils, fibroblasts, endothelial cells, and degenerated myocardial fibers. These characteristic subsets of mononuclear cells were constant findings among the sites of the lesions, namely, in the center of the large lesions with massive myocardial necrosis, in the margins of the large lesions, and in interstitial cell infiltrations without myocardial necrosis.⁶ We have also demonstrated the absence of inflammatory cells derived from myocardial fibers by use of muscle-specific monoclonal antibodies.⁷ We could not detect transforming cells that had morphological aspects such as mononuclear cells having muscle cell markers in their cytoplasm.⁸

The origin and characterization of Anitschkow cells remain controversial. Specific markers for Anitschkow cells have not been discovered. Therefore, we are not able to completely deny the possibility of the appearance of Anitschkow cells in the lesions of experimental autoimmune myocarditis. Because the method of induction of this experimental autoimmune myocarditis is quite simple and very easy, we appreciate the fact that many other investigators can resolve various problems of individual interest using this model.

We thank Dr. F. Masani, Kuwana Hospital, Niigata, Japan, for his excellent comments concerning pathological examinations.

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Circulation. 1992;86:1659-1660
doi: 10.1161/01.CIR.86.5.1659

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/86/5/1659.citation

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