PERICARDIAL CELLULAR DEATH IN VIBROACOUSTIC DISEASE

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Introduction Pericardial thickening in the absence of an inflammatory process and with no diastolic dysfunction is the hallmark of vibroacoustic disease (VAD) [1]: a whole-body pathology caused by long-term (years) exposure to low frequency noise (LFN) (≤500 Hz, including infrasound) [2]. In previous studies concerning pericardial thickness in VAD [3], images of cellular death were impressive with cellular debris scattered throughout all layers. Pericardial cellular death in the VAD patients is the focus of this report.

Methods *Pericardial Fragments.* Pericardial fragments were removed from 11 VAD patients (LFN-exposed professionals for >10 yrs), with their informed consent, at the beginning of cardiac surgery (for other reasons), and always from the same location: anterior, ventral portion of the parietal leaflet. No visual adherences or inflammatory aspects were observed. Fluid amounts were normal and pericardia were grossly thickened. Fragments were divided in two and pinned in dentist wax with serosal surface facing up. *Transmission Electron Microscopy* (TEM). Pericardial sections were fixed at room temperature in an aldehyde mixture, washed in buffer, postfixed in ferricyanide-reduced osmium solution, dehydrated through graded ethanol series, and embedded in Epon. Samples were sectioned in a LKB ultramicrotome, stained with uranyl acetate and lead citrate, and viewed with a JEOL 100C electron microscope.

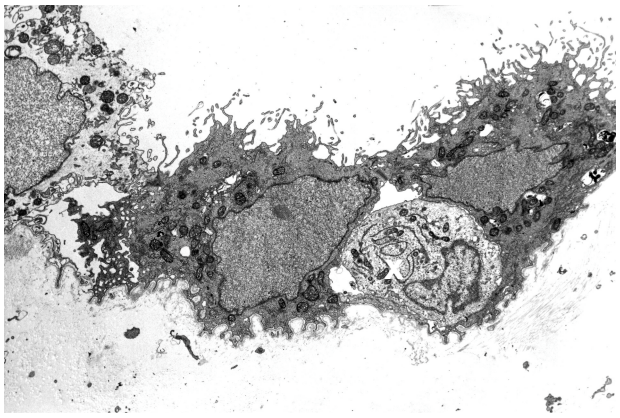

Fig. 1. (TEM) VAD patient parietal pericardium. Mesosthelial layer cell (X) under death process and phagosytosis. In the submesothelial layer there is a large amount of small cellular debris. (x2800)

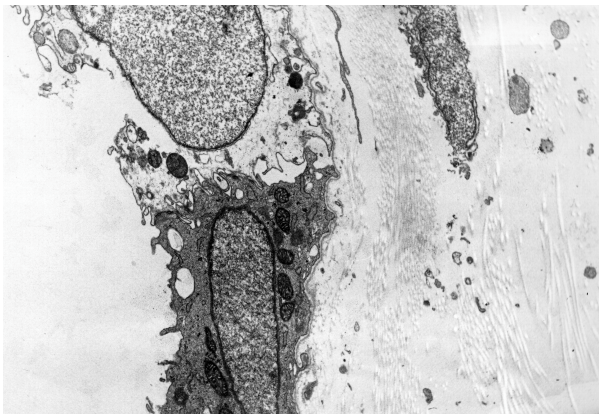

Fig. 2. (TEM) VAD patient parietal pericardium. Mesothelial cell with ruptured membrane and partial loss of cytoplasm. Burst cell in submesothelial layer with large amount of small debris. (x4000)

Results In the mesothelial layer, simultaneous images of several cellular life-cycles were frequently captured. In most images, young cell nuclei are irregularly shaped reflecting a stress situation, and cytoplasmic extensions protude into the pericardial sac, under herniation

processes. As cellular aging progresses, cytoplasmic electronic density decreases, nuclei become rounded or oval with chromatin condensation along membrane borders, and organelles become swollen (Figs 1,2). Older cells swell until organelles are spewed into the pericardial sac after rupture (Fig. 1). Deep in the mesothelial layer (no contact with the pericardial sac), phagocytosis was frequently seen. In all remaining layers, 3 major situations can be easliy identified: Cell and organelles are a) gathered together, but not contained by a cytoplasmic membrane; b) scattered, but still within the vicinity of each other, with nuclei fragmentation and empty cytoplasmic membranes; c). no longer in each other's neighborhood, appearing fragmented and scattered throughout all fields, with significant concentration around and inside lymphatics or near elastic fibers. No layer exhibited inflammatory cellular inflitration. In the fibrotic and loose tissue layers, macrophages and vascular hyperplasia, including in the lymphatic vessels, were seen.

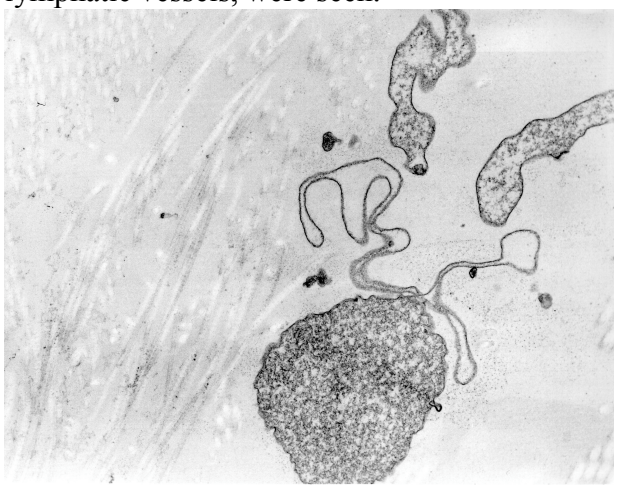

Fig. 3. (TEM) VAD patient parietal pericardium. Within the loose tissue layer, cell membrane surrounded by three fragments of nuclear material. (x5300)

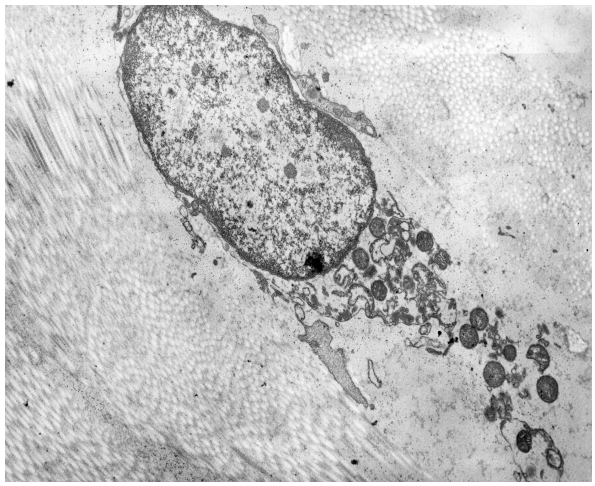

Fig. 4. (TEM) VAD patient parietal pericardium. Deep within a fibrosa layer: a burst myofibroblast near a small elastic fiber surrounded by collagen bundles. (x4000)

Discussion The observed cellular death was not necrotic. The apoptotic process was not evident except for the phagosytosis processes that were seen deep in the mesothelial layer. Cell life cycles seem accelerated but the final images of programmed cell death were not evident. Instead, "old" ruptured mesothelial cells and burst myofibroblasts are pecularly frequent. The presence of macrpohages and the abundance of lymphatics is an expected and natural feature in this situation. Special immunohistochemical studies are underway to study cell proliferation (KI-67), cell death (Bcl2), and inflammatory cell population (LCA).

Keywords: low frequency noise, fibroblasts, collagen, elastin, electron microscopy

References

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