Long-term preserved structure of myofibers and vessels of the latissimus dorsi after Dynamic Cardiomyoplasty

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Evidences of myofiber abnormalities and replacement with fatty and fibrotic tissue have been described experimentally in electrostimulated latissimus dorsi muscle (LDM) transposed for Dynamic Cardiomyoplasty, and clinically such changes were related to the long-term diminished effectiveness of the procedure in patients. Clinically, just a few reports have been addressing direct inspection of LDM after long-term cardiomyoplasty, but only recently some studies described histological and molecular muscle changes at more than one year after the procedure. We had the opportunity to perform three autopic studies in study three LDM after long term cardiomyoplasty (1, 2, and 8 years). In these cases we observed several features of muscle damage, but in substantially normal muscles. Our results show that the LDM present normal aspect with moderate and non specific changes in muscle fibres. Arterial and venous vessels and peripheral nerve fascicles are normal in structure. In particular, endothelial cells and smooth muscle cells of the media do not reveal pathological aspects.

Atrophy and focal degeneration/regeneration which result in variation in fibre size is present in some fascicles. Grouped fibres with centrally located nuclei occupying sarcolemma tubes suggest a recent occurrence of myofiber necrosis/regeneration events, possibly related to terminal events. Real pathological aspects, summarized in fibre atrophy and degeneration and/or myofibre with centrally located nuclei (an accepted morphological marker of fiber damage and regeneration), are confined in the region between the electrodes. The eutrophic state of the LDM was confirmed by its total protein concentration, myosin/actin ratio, and collagen content. Interestingly the isomyosin analysis by SDS PAGE revealed that gene expression was homogeneously changed in all samples taken from the proximal portion till the peripheral part of the pedicled graft. These cases show that the muscle architecture of the prepared LDM stimulated up to eight years is well preserved, in spite of some variation in fibre size and hypernucleosis and in myofiber transformation.

In conclusion, our casuistry, though limited, shows that the degenerative changes described in some cases of cardiomyoplasty are not obligatory events, so that the LDM could assist a failing heart at list for 8 years.

I. INTRODUCTION

Sport scientists and physiatrists are well aware that spontaneous exercise per se could be a trauma to muscle fibers [1]. Indeed muscle pain and leakage of myoglobin, troponin and CPK are well known markers of exercise-induced muscle damage [14].

Dynamic cardiomyoplasty is a surgical procedure in which a pedicled latissimus dorsi muscle (LDM) flap is transposed into the chest, wrapped around the ventricles of a failing heart, and then electrically stimulated to contract in synchrony with ventricular systole [2]. With the actual clinical protocols the flap stimulation is gradually increased over a period of several weeks to achieve full conversion of its myofibers from type 2 (anaerobic, fatigue prone, fast) to type 1 (aerobic, fatigue resistant, slow) [7, 12, 15]. An important issue in dynamic cardiomyoplasty is if muscle damage is induced by the chronic abnormal stimulation, in particular when a muscle-to-heart contraction ratio of 1 : 1 is applied, since there are reports explaining long-term ceased effect of the procedure with indirect evidence of major muscle atrophy, fibrosis and fat infiltration; furthermore, direct histological evidence of muscle damage had been collected in sheep and goat experiments [6,8, 9]. On the other hand, we have shown that these are not obligatory events. We here review results of morphological studies on LDM flap from three subjects deceased 1,2 and 8 years after cardiomyoplasty [3, 4, 7].

II. METHODS

In the first case the patient died after 15-month cardiomyoplasty and at autopsy several specimens were collected from right normal and left trosposed LDM. The second case pertain to a LDM graft stimulated more than two years. In the last case the LDM was studied more than 8 years after cardiomyoplasty. In all cases, some LDM specimens were fixed in formalin, embedded in paraffin and stained with hematoxylin-eosin and Gomory trichrome. Other specimens were cooled in liquid nitrogen and cryostat sections were treated for myosin ATPase at pH 9.6 and 4.6. The intramuscular capillaries were studied on transverse sections stained with Gomory-silver impregnation for reticulin and reported as capillary density for mm2 (CD) and as number of capillaries/muscle fibre (C/F). In a case, myosin heavy chains, myosin/actin ration, total protein and collagen contents were analyzed according to [13].

III. RESULTS AND DISCUSSION

Contralateral normal LDM, as seen in the 1-year cardiomyoplasty case, was composed by fascicles of fibers with a mean diameter of 40 µm. These results are in agreement with those seen in LDM from middle-aged subjects normal and with chronic heart failure [5, 11, 16, 17]. After electrostimulation the grafted LDM showed a slight reduction in fibre diameter (36 µm), while only near the site of electrode implantation there was a marked reduction of fibre diameter (28 µm) [4]. In all cases, histological aspects with moderate,
degenerative non-specific changes were observed. Centrally located nuclei were the most frequent aspect of muscle damage. It is worth stressing that peripheral nerve fascicles and blood vessels were normal in structure [3, 7].

Fat and collagen contents, though increased, did not change the overall aspects of the studied LDM specimens. In two cases [4, 7], it was evident by myosin ATPase staining that the LDM flap was transformed in an almost pure slow (type 1) muscle. In one case [4], the result was substantiated by SDS PAGE of myosin heavy chains. We would like to stress that the LDM flap we studied were stimulated either every two or four cardiac cycles, and that the clinical results were satisfactory. On the other hand, it is known that the LDM flap shown to be heavily atrophic and/or fat infiltrated were stimulated every systole. Whatever the possible explanation of discrepancies among results of our morphological and molecular approaches and those obtained using NMR evaluation [9], we have evidence that muscle damage is not a compulsory consequence of the unusual pattern of muscle activity imposed to LDM by electrostimulation protocol for Dynamic Cardiomyoplasty.

To many authors, cardiomyoplasty is a clinical reality, which founds its basis on a girdle effect which limits or even reverse the progressive dilatation of a failing heart. Indeed load independent measurements demonstrate a real amelioration of the heart energetic when analyses are compared before and after cardiomyoplasty [10, 18]. Besides these results, our morphological studies support the hypothesis that a transformed skeletal muscle could perform long-term a cardiac-like work to sustain a failing heart.

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REFERENCES