Eight-Year Human Dynamic Cardiomyoplasty: Preserved Structure of Myofibres and Vessels of the Latissimus Dorsi

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Abstract

We here present a case report of a latissimus dorsi muscle (LDM) used for cardiomyoplasty eight years after operation. Clinically just a few reports have been addressing direct inspection of muscle at autopsy, but no study described histological and molecular muscle changes at more than two years after cardiomyoplasty. Evidences of myofibre abnormalities and replacement with fatty and fibrotic tissue have been described experimentally and clinically in electrostimulated latissimus dorsi muscle transposed for Dynamic Cardiomyoplasty. Such changes were related to the long-term diminished effectiveness of the procedure in patients. The results here reported show that the muscle shows 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 myofibre necrosis/regeneration events, possibly related to the terminal episode of right heart failure. In conclusion, this case shows that the muscle architecture of the grafted LDM stimulated over eight years is well preserved, in spite of some variation in fibre size and hypernucleosis, and that muscle damage is not a compulsory consequence of the unusual pattern of muscle activity imposed to LDM by electrostimulation protocol for Dynamic Cardiomyoplasty.

Key words: cardiomyoplasty, circulatory assist, eutrophic state, heart failure, latissimus dorsi muscle.

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Evidences of myofibre abnormalities and replacement with fatty and fibrotic tissue have been described experimentally [8] and clinically [7] in long-term electrostimulated latissimus dorsi muscle (LDM) transposed for Dynamic Cardiomyoplasty. Such changes were related to the long-term diminished effectiveness of the procedure in patients. Clinically, just a few reports have been addressing indirect evaluation by magnetic resonance imaging [3] or direct inspection of muscle histology [4]. Among them a study showed that two years after cardiomyoplasty, at necropsy, the LDM flap was adherent to ventricular myocardium, and sections of the flap showed preservation of muscle structure without fibrosis. Histochemical analysis revealed a considerably higher percentage of type I fibres than in the contralateral muscle, from 35% to 97%, respectively.

We here present a case report of a latissimus dorsi used for cardiomyoplasty eight years after operation.

Patient died on December 21 1995, 8 1/2 years after cardiomyoplasty. The patient was a frenchman aged 52 years at the moment of surgery, who presented ischemic cardiomyopathy following three myocardial infarcts. Clinically the patient was in NYHA functional class 4, the LV ejection fraction (radioisotopic) was 16%, and the cardio-thoracic ratio of 54%. Associate diseases were: nephrectomy in 1983 for renal cancer and insulin-dependent diabetes. Cardiomyoplasty was performed on July 23, 1987. The patient was assisted postoperatively with intra aortic balloon pump (IABP). The patient developed a postoperative cholecystitis, resolved with cholecystectomy. The clinical outcome was excellent, the patient improved to NYHA functional class 1, and he underwent

an "enjoyable" social and working life. Chronic latissimus dorsi muscle electrostimulation was performed using mean pulse amplitude of 4.5 volts, with a muscle-to-heart ratio of 1:2. In 1993, a left colectomy was performed due to colonic cancer. In 1995, the clinical status deteriorated. The patient died on December 21, 1995, following severe renal insufficiency, bilateral bronchopneumopathy, and right heart failure.

Muscle fragments were collected from the myocardium, and from the grafted LDM, which appeared well wrapped and trophic, taking care of including neurovascular branches. Muscle morphology was studied on paraffin em-

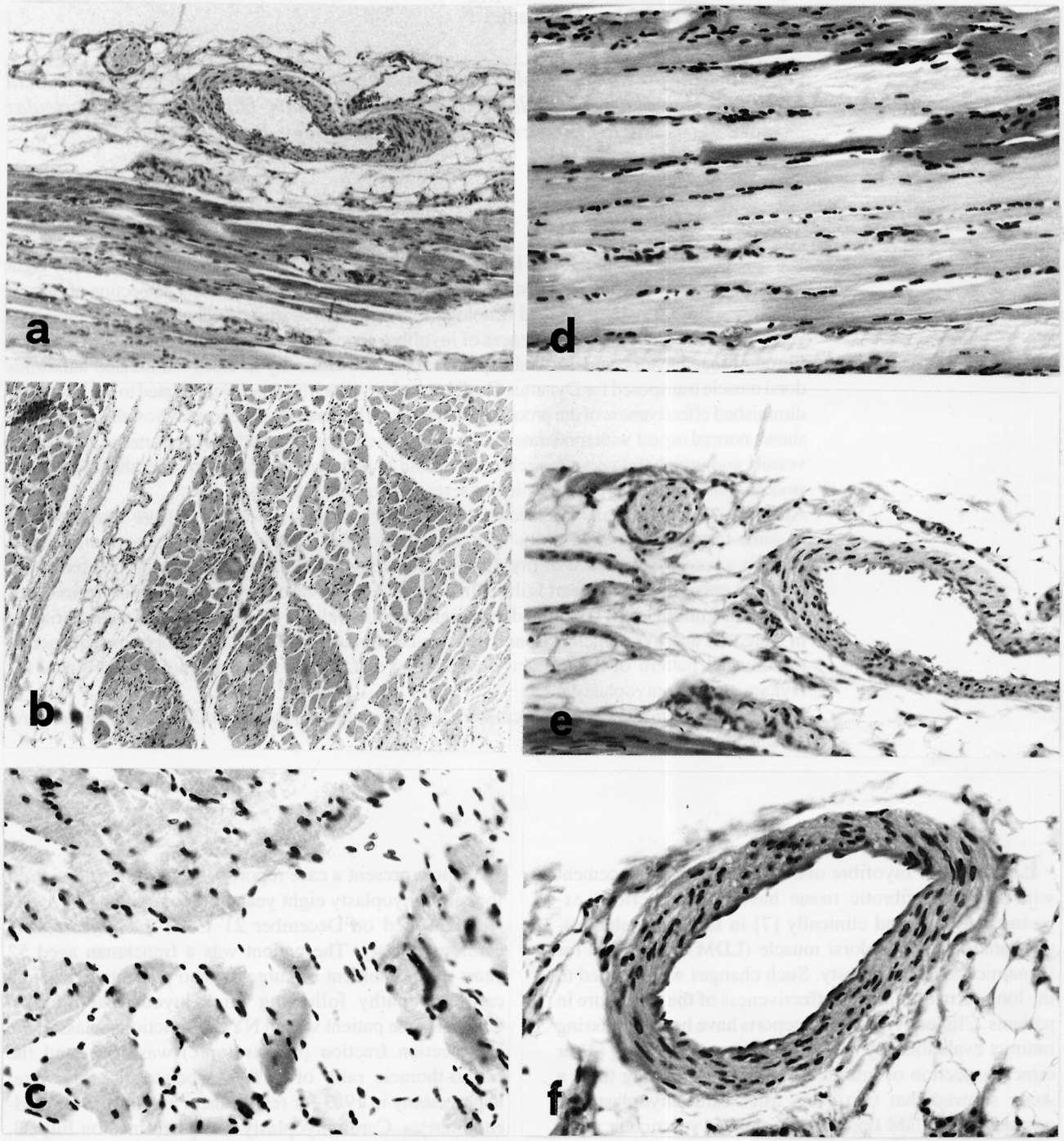

Figure 1. Histology of the left LDM 8 years after cardiomyoplasty. Hematoxylin and eosin. a, Perimisial and subfascial neurovascular structures are normal; b, c, d, the muscle architecture of the grafted LDM stimulated over eight years is well preserved, in spite of some variation in fibre size and hypernucleosis; e, f arterial and venous vessels and peripheral nerve fascicle are normal in structure. In particular, endothelial cells and smooth muscle cells of the media do not reveal pathological aspects.

bedded sections, stained with H-E.

Figure 1 a shows that perimisial and subfascial neurovascular structures are morphologically normal. Figure 1, b, c and d illustrate at low and high magnification that the muscle architecture of the grafted LDM stimulated over eight years is well preserved, in spite of some variation in fibre size and hypernucleosis. Panels e and f of Figure 1 confirm that arterial and venous vessels and peripheral nerve fascicle are normal in structure. In particular, endothelial cells and smooth muscle cells of the media do not reveal pathological aspects. These results are of value since experimental observations in goat suggested that severe intimal hyperplasia and proliferation of smooth muscle cells may occur in the arterial wall of wrapped and stimulated latissimus dorsi [5].

Focal damage was scantly present in the LDM specimens. Some microscopic fields show fat infiltration and reduction in size of muscle fascicles (Figure 2a). Figure 2b shows marked variation in myofibre size due to hypothrophy and atrophy of myofibres; some fibres show internalized nuclei. Figure 2c confirms that nuclear internalization is due to previous damage/regeneration of muscle fibres, since several small myofibres fill one sarcolemmal tube. They appear similar to regenerated myofibres present in bupivacaine-induced muscle necrosis-regeneration a week after myotoxic damage [6]. Figure 2d is suggestive of terminal vascular congestion, which could have been responsible for the foci of muscle damage. At electron microscopy, the grouped myofibres could be recognized as early regenerated myofibres by the presence of a doubled layer of basal lamina which surround them. Skeletal muscle fibres, muscle capillaries, renal tubules and nerves are examples of tissues where two layers of basal lamina are commonly present early after a single episode of injury and regeneration [1]. Unfortunately, LDM specimens were neither fixed for electron microscopy nor quenched in liquid nitrogen. This is a severe limitation to muscle analyses, since neither myosin AT-Pase or immunohistochemistry can be used to type muscle fibres, and because electrophoretic analyses are hampered by insolubility of myosin subunits cross-linked during tissue fixation. Myosin heavy chains analysis by mRNA hybridization in situ, suggestive of a fast to slow transformation, is also of limited value in autoptic specimens embedded in paraffin. In summary, LDM shows normal histological aspect with moderate and non-specific changes in muscle fibres. Atrophy and focal degeneration/regeneration which result in variation in fibre size is present in some fascicles, where grouped fibres with centrally located nuclei occupying a unique basement membrane tube suggest a recent occurrence (days) of myofibre necrosis/regeneration events, possibly related to the terminal episode of right heart failure. Nerve structure is normal. Arteries and veins are patent and with normal endothelial and muscular walls.

In conclusion, though based only on histology, this case demonstrates that muscle damage followed by fibrosis

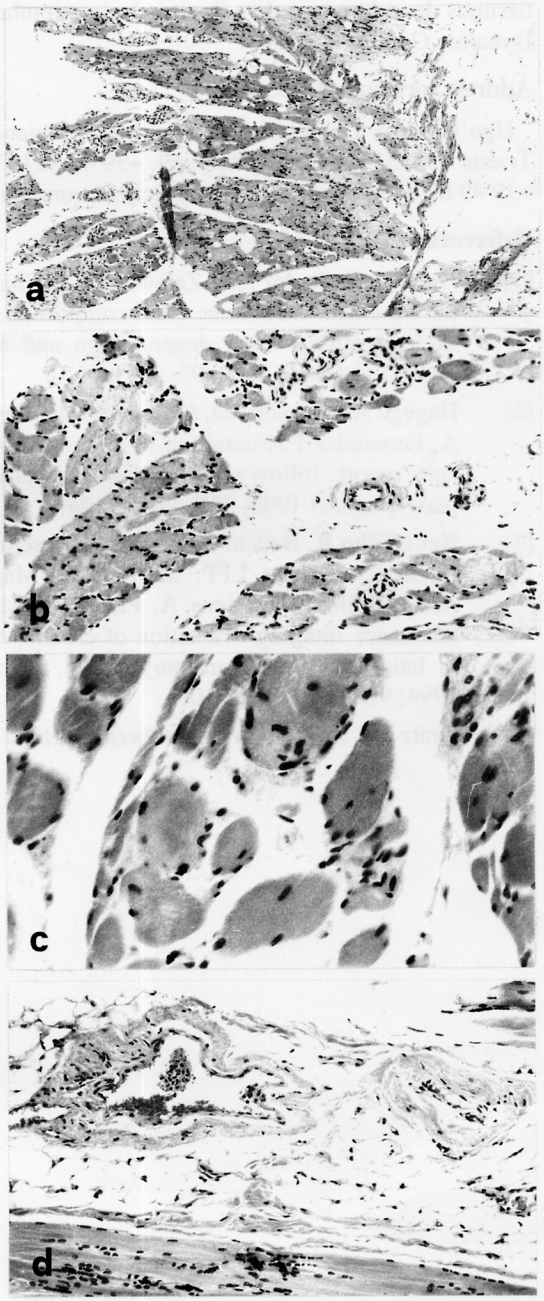

Figure 2. Focal damage is scantly present in the LDM specimens. a, some microscopic fields show fat infiltration and reduction in size of muscle fascicles; b, marked variation in myofibre size due to hypotrophy and atrophy of myofibres; some fibres show internalized nuclei; c, nuclear internalization is due to previous damage/regeneration of muscle fibres, since several small myofibres fill a sarcolemmal tube; d, terminal vascular congestion, which could have been responsible for the foci of muscle damage.

and/or fat substitution is not a compulsory consequence of the unusual pattern of muscle activity imposed to latissimus dorsi by more than 8-year electrostimulation for Dynamic Cardiomyoplasty.

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References

[1] Gulati AK, Reddi AH, Zalewski AA: Changes in the basement membrane zone components during skeletal muscle fiber degeneration and regeneration. *J Cell Biol* 1983; 97: 957-962.

[2] Hagège AA, Desnos M, Chachques JC, Carpentier A, Fernandez F, Fontaliran F, Guérot C: Preliminary report: follow-up after dynamic cardiomyoplasty. *Lancet* 1990; 335: 1122-1124.

[3] Kalil-Filho R, Bocchi E, Weis RG, Rosemberg L, Bacal F, Moreira LFP, Stolf NAG, Magalhaes AAC, Bellotti G, Jatene A, Pileggi F: Magnetic resonance imaging evaluation of chronic changes in latissimus dorsi cardiomyoplasty. *Circulation* 1994; 90 (part 2): 102-106.

[4] Kratz JM, Johnson WS, Mukherjee R, Hu J, Krawford FA, Spinale FG: The relation between latissimus dorsi skeletal muscle structure and contractile function after cardiomyoplasty. *J Thorac Cardiovasc Surg* 1994; 107: 868-878.

[5] Lucas C: The use of the latissimus dorsi muscle for cardiac assist. Universitaire Pers Maastricht, Netherlands, pp 100-121.

[6] Mussini E, Favero G, Carraro U: Maturation, Dystrophic changes and the continuous production of fibres in skeletal muscle regeneration in the absence of nerve. *J Neoropath Exp Neurol* 1987; 46: 315-331.

[7] Schreuder JJ, van der Veen FH, van der Velde ET, Delahaye F, Alfieri O, Jegaden O, Lorusso R, Jansen JRC, van Ommen V, Finet G, Wellens HJJ: Beat-to-beat analysis of left ventricular pressure-volume relation and stroke volume by conductance catheter and aortic modelflow in cardiomyoplasty patients. *Circulation* 1995; 91: 2010-2017.

[8] Van Doorn CAM, Bhabra MS, Hopkinson DN, Barman D, Cranley JJ, Hooper TL: Latissimus dorsi muscle blood flow during synchronized contraction: implications for cardiomyoplasty. *Ann Thorac Surg* 1996; 61: 603-609.