Severe and early heart disease in Duchenne Muscular Dystrophy: example of three families with symptomatic female carriers

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Introduction: Cardiac involvement in the Duchenne Muscular Dystrophy (DMD) consists of dilated cardiomyopathy (DCM) with steadily increasing incidence from teenage to adulthood. This may also be observed in rare cases of female carriers. DCM leads to end stage heart failure and is the cause of death in about 20% of DMD cases. We report three families with a severe and early cardiac involvement either in DMD patients and/or in four relative female carriers.

Case reports: In the first family, a female carrying an out-of-frame duplication of exons 53-54 in the *DMD* gene was diagnosed with end-stage heart failure without myopathic features at the age of 49 years. She required HeartWare Ventricular Assist System as an alternative to heart transplant. In the second family, a frameshift small deletion (c.9887-9908del) in exon 68 of the *DMD* gene was identified in two brothers. The elder one showed cardiac symptoms since the age of 10 years and died from end-stage heart failure at 13. His affected 11-year-old brother still has normal cardiac evaluation. Moreover, the maternal aunt (mother of another affected boy), and the maternal grandmother were both heart transplanted at the age of 32 and 61 years respectively. In the third family, the proband carrying an out-of-frame exon 19 deletion in *DMD*, died at 17 years from the disease. His mother was diagnosed with a rapidly progressive DCM at 51 years requiring heart transplant at 59 years. Heart histological studies showed a decreased dystrophin immunostaining.

Conclusion: These observations of early and severe heart disease leading to premature death of DMD boys and end-stage heart failure in female carriers highlight the possibility of rapid course and severity of cardiac

involvement in some DMD families. It raises the question of an early identification and a specific management of these patients.