Cause of cardiac disease in a female carrier of Duchenne muscular dystrophy: myocarditis versus genetic cardiomyopathy without skeletal myopathy?

Anca Florian[1], Anna Ludwig[2], Peter Ong[2], Karin Klingel[3], Reinhard Kandolf[3], Antje Bornemann[4], Udo Sechtem[2], Ali Yilmaz[1]

1 - Department of Cardiology and Angiology, University Hospital Münster, Münster

2 - Division of Cardiology, Robert-Bosch-Krankenhaus, Stuttgart

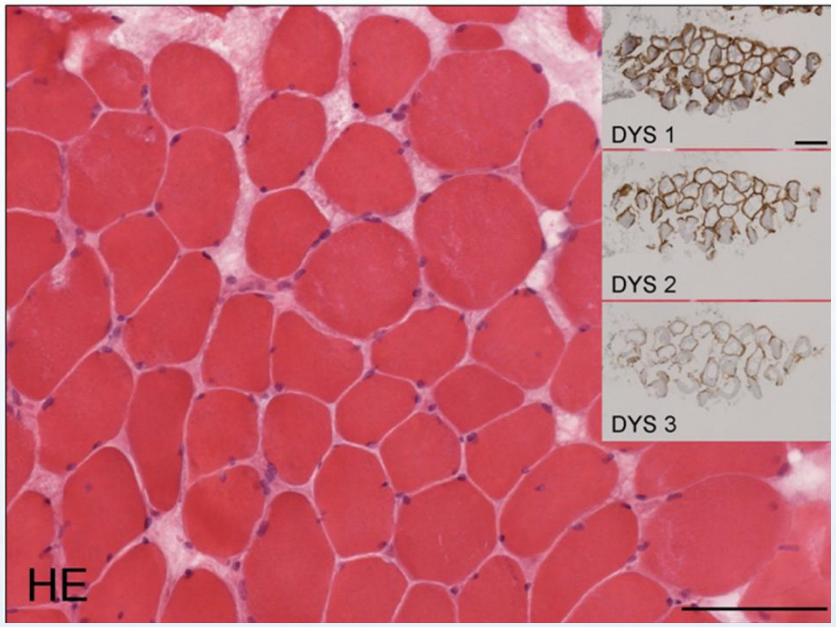
3 - Department of Molecular Pathology, University of Tübingen, Tübingen

4 - Department of Neuropathology, University of Tübingen, Tübingen

Background

- F, 51yrs, with prolonged fatigue and muscle pain after respiratory tract infection
- Family history: 30-year-old son with Duchenne muscular dystrophy (DMD; deletion in the dystrophin gene), wheelchair bound
- Blood analysis: elevated total CK (479 U/l, normal <190 U/l) with normal CK-MB (17 U/l, normal <25 U/l)

- Calf muscle biopsy:
  "normal" histopathological findings – no signs of structural abnormalities / inflammation / dystrophin deficiency*

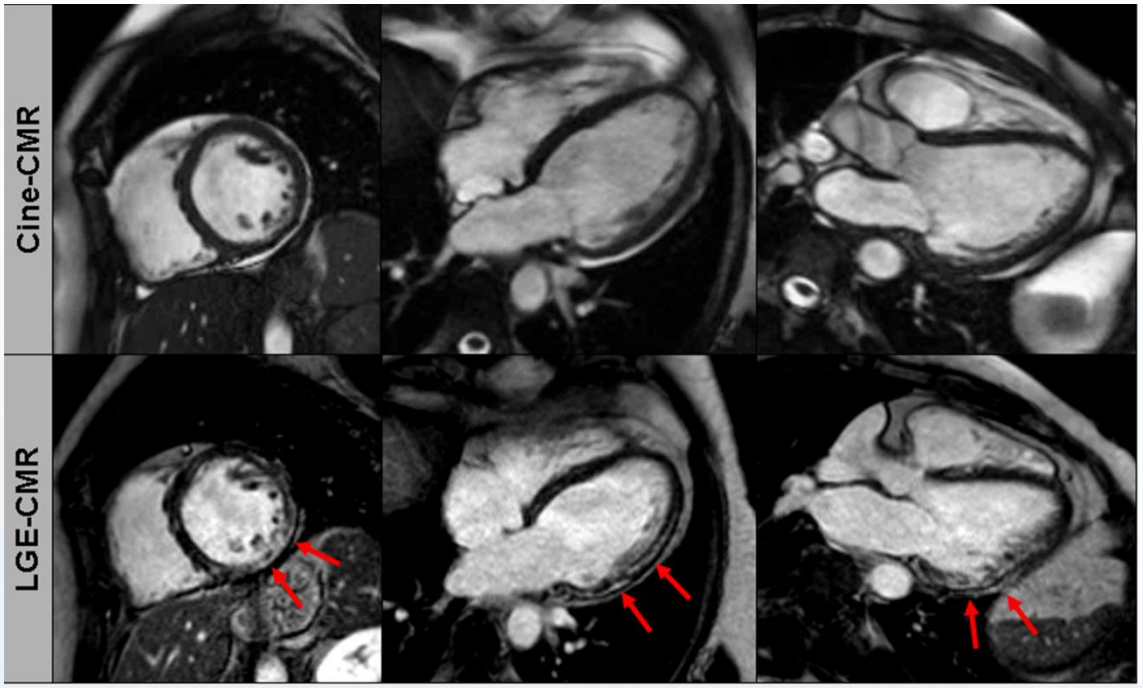


*Immunohistochemical dystrophin stainings (DYS) with 3 different dystrophin antibodies: no signs of dystrophin deficiency.

Genetic analysis:
Heterozygous dystrophin gene mutation
–> **symptomatic DMD carrier?**

Cardiac evaluation

- Due to persistent exertional dyspnea and fatigue -> cardiac work-up
- ECG: SR, no abnormalities
- Coronary artery disease: ruled out by coronary angiography



- CMR (1.5-Tesla):
  - ✓ Cine-CMR: LV-EF 55%, hypokinesia of the inferolateral wall
  - ✓ LGE-CMR: subepicardial, non-ischemic LGE in the inferolateral wall segments - (viral) myocarditis pattern (described also in patients with muscular dystrophy)

Persistent myocarditis after (viral) respiratory tract infection?

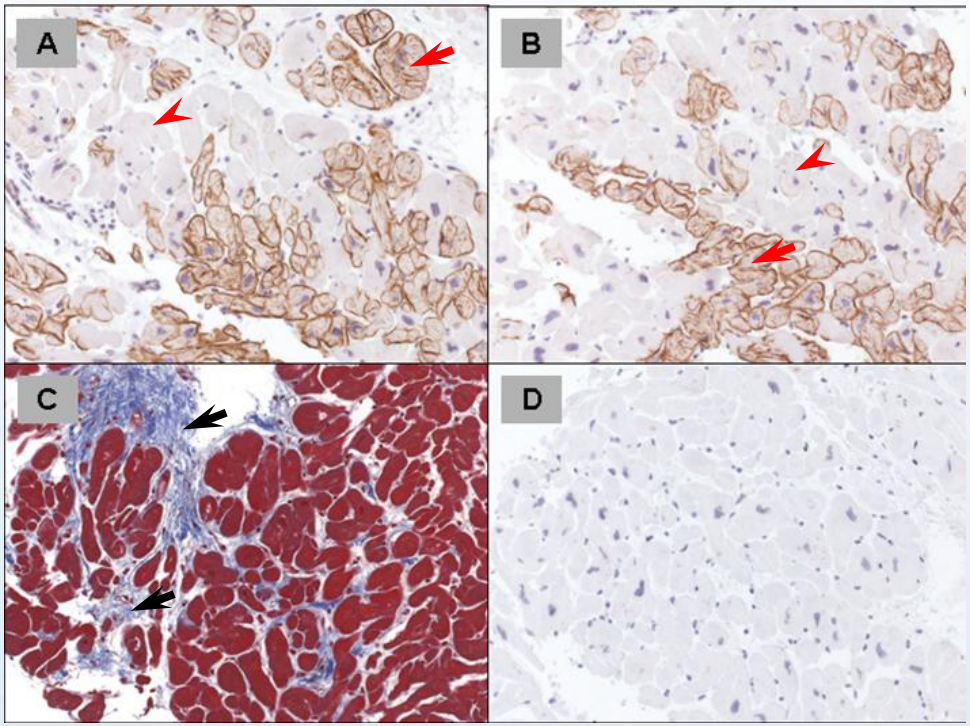
Endomyocardial biopsy

- Clarify diagnosis: persistent (viral) myocarditis vs. cardiac involvement by DMD?

✓ Histopathological analysis: some structural abnormalities and areas of fibrosis (black arrows, C), no signs of myocardial inflammation (negative CD3 staining for T lymphocytes, D)

✓ Dystrophin staining: impressive mosaic pattern with clear “absence” of dystrophin in the cell membrane of some cardiomyocytes (red arrow heads, A-B) and coexistent “presence” of dystrophin in neighbouring cells (red arrows, A-B)

⟶ **Typical for a cardiac dystrophinopathy (genetic cardiomyopathy)**



Conclusion

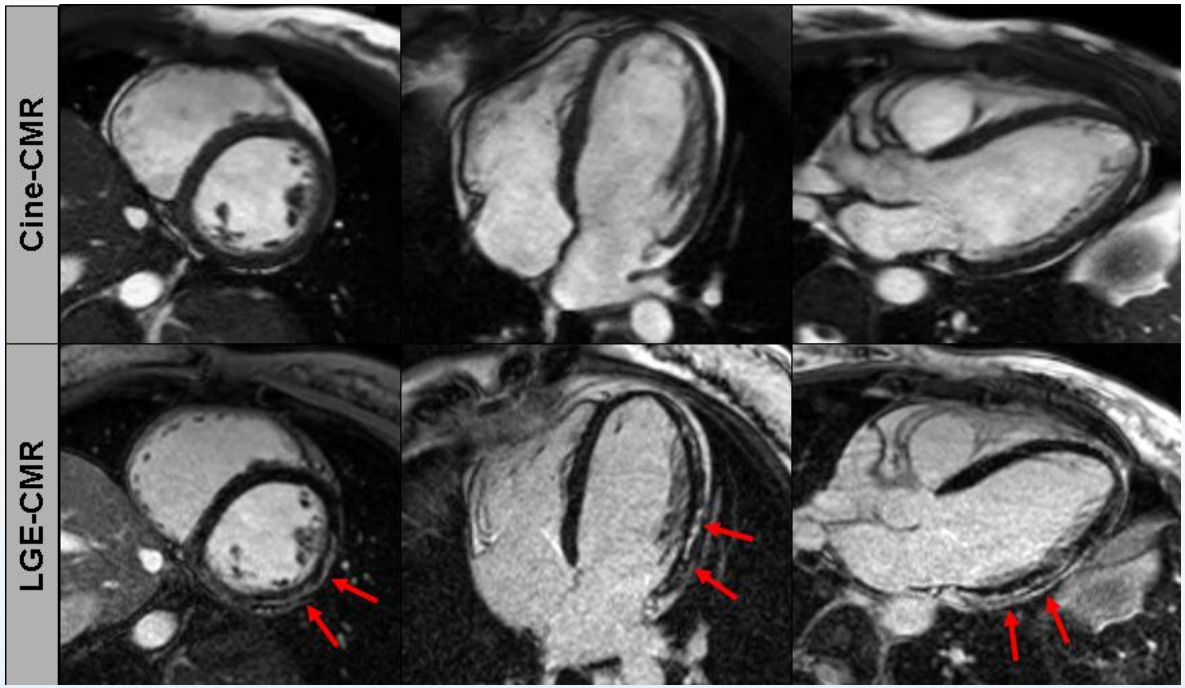
Female Duchenne muscular dystrophy carrier showing:

- ✓ Cardiac involvement by LGE-CMR and a striking mosaic pattern of cardiac dystrophin deficiency and no signs of ongoing myocarditis

- ✓ No skeletal muscle involvement with normal dystrophin expression

The different involvement of skeletal and cardiac muscles found in this patient indicates a need for thorough cardiac investigations even in those DMD carriers who have normal skeletal biopsy findings.

✓ CMR performed in the 25 year-old clinically healthy daughter of the patient – a similar LGE pattern:



✓ Genetic analysis revealed the same heterozygous dystrophin gene mutation as in the mother