Cardiovascular manifestations of myofibrillar myopathy

Miyofibriller miyopatinin klinik göstergeleri

Ayman A El Menyar, MD, Abdulbari Bener, PhD*, Jassim Al Suwaidi, MD

Department of Cardiology and Cardiovascular Surgery, *Department of Medical Statistics & Epidemiology, Hamad Medical Corporation, Hamad General Hospital Doha, State of Qatar

ABSTRACT

Myofibrillar myopathy (MFM) is a rare autosomal dominant disorder characterized by cardiac and skeletal myopathy. Either of these can dominate in the clinical picture. It is associated with cardiomyopathy, arrhythmia and/or atrioventricular (AV) conduction defects. Myofibrillar myopathy is often an overlooked disorder because of its variable clinical presentation. We highlight the various cardiovascular manifestations of MFM that have been reported in the literature and address the importance of considering this syndrome in young patients presenting with idiopathic cardiomyopathy and /or AV conduction defects. (Anadolu Kardiyl Derg 2004; 4: 336-8)

Key words: Myofibrils, desmin, cardiomyopathy

ÖZET


Anahtar kelimeler: Miyofibril, desmin, kardiyomyopati

There are few reported families with myofibrillar myopathy (MFM) worldwide (1-4). Clinically this disorder is characterized by cardiac and skeletal myopathy, either of these can dominate in the clinical picture. Histologically, it is characterized by non-hyaline lesions (foci of myofiber destruction) and hyaline lesions (myofibrillar residues) on light electron microscopy. However, because there is considerable clinical and pathological heterogeneity, the gene-phenotypical correlations are expected to be very difficult in MFM (5-6). Both neurological and histological evidences from skeletal muscle tissue in the presence of cardiomyopathy and/or atrioventricular (AV) conduction defects are usually sufficient to diagnose the disease even without endomyocardial biopsy (1). Myofibrillar myopathy and desmin related myopathy (DRM) are synonymously applied to a combination of familial myopathy and cardiomyopathy disorder (7). Application of immunohistochemical techniques has contributed to the term "desmin-related myopathies". Desmin is not the only protein that can be abnormally expressed with immuno-staining in patients with myopathy (8). However desmin is the main intermediate filament of skeletal and cardiac muscle fibers and certain smooth muscle cells; it plays an essential role in the maintenance of cyto-architecture by anchoring neighboring Z discs (9). Quantitative or qualitative abnormalities of Z-disk-associated proteins especially desmin causes abnormal mitochondrial behavior, disruption of muscle architecture, ends with fibre degeneration and fibrosis (10-12), excessive desmin (1,4), lacking of desmin (10-12), or mutation of desmin (13) and has been associated with different types of cardiomyopathy and variable degrees of myopathy. Mutation in desmin gene interferes with the normal assembly of desmin, it may be the cause of sporadic forms of MFM/DRM as 45% of patients do not report previous family history of the disease. Immunohistochemical evidence of desmin storage in either skeletal or cardiac muscles is available only in a minority of cases with this MFM/DRM. Three subgroups of MFM/DRM have been encountered and electromyography demonstrates myopathic features in each of the three types (11) as shown in Table 1. It preferentially affects distal skeletal muscles with variable degrees of severity, muscle group involvement and the age of presentation.

Cardiac features in MFM/DRM

Cardiac involvement is commonly present in the type I MFM. Different types of cardiomyopathies have been reported in association with DRM/MFM: 17 cases have been reported with restrictive cardiomyopathy (1,3,4,8,11,12,14-16) and three cases with hypertrophic cardiomyopathy (17-19). Arrhythmogenic right ventricular cardiomyopathy was found in one case.
reported in patients with MFM/DRM (8). Other muscle of intramural coronary blood vessels have also been recognized in eleven cases (1,3,8,19). The early manifestation of ventricular tachycardia (2,8) is the most frequent arrhythmia in MFM/DRM. Three out of six cases with conduction system (18,21). Atrial fibrillation (AF) is the most frequent arrhythmia in MFM/DRM (1), it has been applied specifically when certain criteria are fulfilled. It entails the presence of restrictive cardiomyopathy, disturbance of AV conduction and skeletal myopathy in the presence of granulofilamentous and desmin-immunoreactive material. In the state of Qatar we reported a Qatari family (21) with myofibrillar myopathy consisting of one brother and three sisters. The brother has restrictive cardiomyopathy and severe skeletal myopathy at the age of 16 years. One sister underwent heart transplantation for severe hypertrophic cardiomyopathy at the age of 15 years, the other sister had implantation of permanent pacemaker for complete heart block at the age of 21 years, and she has nearly normal echocardiographic findings. This is an unique family that presented with two different types of cardiomyopathy (restrictive and obstructive) in two young members of one family of the same generation. The progressive deterioration in clinical course is more commonly reported in affected males than females. Desmin inclusions have been recognized also in vascular smooth muscle (8) and smooth intestinal muscle (1), this underscores the systemic nature of this rare myopathy.

Arrhythmia and conduction system involvement in MFM/DRM

Atrioventricular block (AVB) of variable degrees has been recognized in eleven cases (1,3,8,19). The early manifestation of desmin accumulation may be atrioventricular conduction defects that were attributed to the depositions of desmin in the conduction system (18,21). Atrial fibrillation (AF) is the most frequent arrhythmia in MFM/DRM. Three out of six cases with arrhythmia had chronic AF in addition to history of recurrent ventricular tachycardia (2,8).

Coronary artery involvement

Cytoplasmic granulofilamentous inclusions within the smooth muscle of intramural coronary blood vessels have also been reported in patient with MFM/DRM (8).

Table 1. Subtypes of DRM / MFM

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
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</thead>
<tbody>
<tr>
<td>Genetics</td>
<td>Autosomal dominant</td>
<td>Autosomal dominant</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>Onset</td>
<td>Adulthood</td>
<td>Adolescence</td>
<td>Childhood</td>
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<tr>
<td>Desmin pattern</td>
<td>Granulofilaments</td>
<td>Cytoplasmic inclusions</td>
<td>Mallory body like inclusions</td>
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<tr>
<td>Distribution of deposits</td>
<td>Disseminated</td>
<td>Focal</td>
<td>Focal</td>
</tr>
<tr>
<td>Cardiac involvement</td>
<td>Constant</td>
<td>Occasional</td>
<td>Rare</td>
</tr>
<tr>
<td>Progression</td>
<td>Slow</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Skeletal myopathy</td>
<td>Distal muscle</td>
<td>Distal/proximal</td>
<td>Proximal/facial</td>
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<tr>
<td>Cause of death</td>
<td>Sudden cardiac death</td>
<td>Respiratory failure</td>
<td>Rapid death</td>
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<td>Association</td>
<td>Smooth muscle disease</td>
<td>Dysphagia</td>
<td>Short course</td>
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</tbody>
</table>

**Conclusion**

Myofibrillar myopathy is a rare genetic disorder that should be considered in the differential diagnosis of idiopathic cardiomyopathy. Whether this condition is commonly overlooked or a rare condition is unknown and requires further epidemiological studies. High index of suspicion is needed for early diagnosis.

**References**


