## Supplementary data

### Appendix I:

### Differences among PM, DM & IBM (5):

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IBM</th>
<th>Polymyositis</th>
<th>Dermatomyositis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>&gt;50 yrs</td>
<td>&gt;18 yrs</td>
<td>Adulthood &amp; childhood</td>
</tr>
<tr>
<td><strong>Connective tissue diseases</strong></td>
<td>10-15% cases</td>
<td>Yes</td>
<td>Scleroderma &amp; MCTD.</td>
</tr>
<tr>
<td><strong>Co-existent auto-immune diseases</strong></td>
<td>Infrequently</td>
<td>Frequently</td>
<td>Infrequently</td>
</tr>
<tr>
<td><strong>Malignant conditions</strong></td>
<td>No</td>
<td>7-8%</td>
<td>Probably</td>
</tr>
<tr>
<td><strong>Viruses</strong></td>
<td>Unproved, occasionally HIV &amp; HTLV-1</td>
<td>HIV, HTLV-1; possibly others</td>
<td>Unproved</td>
</tr>
<tr>
<td><strong>Positive Family History</strong></td>
<td>In some</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Immunology</strong></td>
<td>CD8+ to MHC class 1</td>
<td>CD8+ to MHC class 1</td>
<td>CD4+ (humoral)</td>
</tr>
<tr>
<td><strong>Muscle strength</strong></td>
<td>Muscle weakness with typical early involvement of distal muscles</td>
<td>Myopathic muscle weakness</td>
<td>Myopathic muscle weakness</td>
</tr>
<tr>
<td><strong>EMG</strong></td>
<td>Myopathic with mixed potentials</td>
<td>Myopathic</td>
<td>Myopathic</td>
</tr>
<tr>
<td><strong>Muscle Enzymes</strong></td>
<td>&lt; 12 times normal</td>
<td>Elevated (up to 50–fold)</td>
<td>Elevated (up to 50–fold)</td>
</tr>
<tr>
<td><strong>Muscle-biopsy Findings</strong></td>
<td>Diagnostic</td>
<td>Diagnostic</td>
<td>Diagnostic</td>
</tr>
<tr>
<td><strong>Muscle involvement</strong></td>
<td>Asymmetric (quadriceps, wrist &amp; finger flexors)</td>
<td>Symmetric</td>
<td>Symmetric</td>
</tr>
<tr>
<td><strong>Rash or calcinosis</strong></td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>
Appendix II:

Theories of pathogenesis of sporadic inclusion body myositis:
Some of the theories given to describe the pathogenesis are as follows:

1) Oxidative stress: Free radicals such as super oxides may be involved in its pathogenesis(2) as evidenced by an increase in super oxide dismutases in cells and mitochondrial abnormalities, including respiratory chain dysfunctions and generation of reactive oxygen species.

2) Muscle ageing: In s-IBM, there are 3 aspects of muscle fibre destruction.
   
   • Attack by CD8+ (cytotoxic T cells) directed against the MHC class I antigens. This is prominent early in the disease and less evident later on. It is similar to Polymyositis.
   
   • Vacuolar degeneration, more evident in the later stages.
   
   • Muscle fibre atrophy (which often resembles denervation atrophy), also more prominent in the later stages.

In aged muscle fibres, cellular defence mechanisms are diminished leading on to accumulation of unknown toxins.

3) Viruses: Viruses may remain dormant for years in aged cells and could get activated due to decreased defence mechanisms. Paramyxoviruses were implicated in the past but this has not been confirmed.

The pathogenesis is best described in the flow chart shown depicted in Fig II:
Appendix III:

MUSCLE-SPECIFIC NUCLEAR MATRIX ALTERATIONS (4)
(GENETIC OR ACQUIRED – AGE RELATED)

Myonuclear disintegration  
Nontolerant (altered) Matrix protein expression at cell surface  
Abnormal(aberrant)gene expression

Myonuclear Attrition  
Rimmed vacuoles  
Over expression of "gene" molecules  
Perturbed mtDNA replication

Cytotoxic T-lymphocyte reactions against muscle fibres

Muscle fibre atrophy  
Muscle fibre damage  
Muscle fibre damage

Under expression of essential molecules(?)  
mtDNA deletion

Muscle fibre damage

Muscle fibre loss
Appendix IV:

Diagnostic criteria for s-IBM:

Mendel’s Diagnostic Criteria for s-IBM (6):

1. **Characteristic features:**
   - **Clinical features:**
     - a) Duration of illness > 6 mths
     - b) Age of onset > 30 yrs
     - c) Muscle weakness in proximal and distal muscles of arms and legs which must include one of the following:
       - Finger flexor weakness
       - Wrist flexor >wrist extensor weakness
       - Quadriceps weakness, often asymmetric.
   - **Laboratory Features:**
     - a) Serum Creatinine kinase < 12 times normal.
     - b) Muscle biopsy:
       1) Mononuclear cell invasion of non-necrotic muscle fibres.
       2) Vacuolated muscle fibres.
       3) Either: intracellular amyloid deposits or 15-18nm tubulofilaments by EM.
     - c) Electromyography consistent with features of inflammatory myopathy
       (Increased insertional and spontaneous activity, but may also show large polyphasic or ‘neurogenic’ potentials as mild axonal neuropathy is seen in up to 30%)
   - **Family history:** Rarely, s-IBM may be observed in families, which is different from h-IBM.

2. **Associated Disorders:**
   An associated disorder does not preclude IBM if the criteria are fulfilled.
   - **Diagnostic Criteria:**
     - Definite IBM: Patients must exhibit all the muscle biopsy features B (a, b, c.)
     - Possible IBM: Invasion of non necrotic muscle fibres by mono nuclear cells and clinical features
       A (a, b, c.) with lab features B (a, c).
Appendix V:

**European Neuromuscular Centre Diagnostic Criteria: (17)**

**Clinical:**
1) Presence of muscle weakness.
2) Weakness of forearm muscles (finger flexors or wrist flexors more than the wrist extensors)
3) Slowly progressive course
4) Sporadic disease

**Histopathological:**
5) Mononuclear inflammatory infiltrate with invasion of non necrotic fibres
6) Rimmed vacuoles.

Definite: 1,2,3,4,5,6. or 1,3,4,5,6,7.
Probable: 1,2,3,4,5. or 1,3,4,5,6.
Appendix VI:

References: