INCLUSION BODY MYOPATHIES

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DISCLOSURE

Relevant Financial Relationship
None
INCLUSION BODY
“MUSCLE DISEASES”

Group of muscle diseases characterized by the presence of vacuoles and inclusions within the muscle fibers

**Inclusion Body Myositis**
- Inflammation in muscle
- Sporadic (sIBM) (not hereditary)

**Inclusion Body Myopathy**
- No inflammation in muscle
- Hereditary (hIBM)
Muscle biopsy

sIBM

Arrow: Inflammation attacking a healthy muscle fiber

Arrows: Rimmed vacuoles

Arrows: Inclusions (= abnormal accumulation of proteins)

No inflammation in hIBM

hIBM

Arrows: Rimmed vacuoles

Arrows: Inclusions (= abnormal accumulation of proteins)
Inclusion Body Myositis (sIBM)

sIBM

• Most common acquired muscle disease after age 50
• Cause unknown: inflammatory + degenerative
• Early weakness of:
  • Finger and wrist flexors
  • Quadriceps
• CK (muscle enzymes): normal or increased < 15-fold
Hereditary Inclusion Body Myopathy (hIBM)

hIBM

• Can affects children and adults

• Distribution of weakness can be of various type, affecting:
  - Forearm and leg muscles
  - Shoulder and leg muscles
  - Shoulder and hip muscles

• Quadriceps is spared in a specific form of hIBM

• Swallowing difficulty can occur

• CK (muscle enzymes): normal or increased
Hereditary Inclusion Body Myopathy (hIBM)

hIBM

• hIBM is a descriptive pathological diagnosis
  (= description of abnormalities seen on muscle biopsy)

• Has a genetic cause

• Several genes can cause hIBM
Hereditary Inclusion Body Myopathy (hIBM)

hIBM

• Depending on the specific gene responsible for the disease:
  - *One mutation (=gene defect) is sufficient to cause disease*
  - *Two mutations are necessary to cause disease*

• The lack of muscle disease in other family members does not exclude hIBM
hIBM: same gene can cause other diseases

- Some of the genes that cause hIBM can cause also other diseases (ALS, dementia or Paget disease of bone)

- Measurement of a bone enzyme, called alkaline phosphatase, may suggest co-existence of Paget disease of bone, if elevated

- Family history is important: muscle weakness? Other diseases possibly caused by the same gene?
IBMPFD: Valosin-containing protein (VCP)

- Paget disease of bone
- Frontotemporal Dementia
VCP- IBM: Clinical Features

Nalbandian et al, J Mol Neurosci 2011

Palmio et al, Neuromuscular Disord 2011
VCP- IBM with Paget Disease of Bone

- Bone radiographs:
GNE-hIBM: Muscle MRI

T1 weighted MRI

Huizing et al, Biochim Biophys Acta 2009
GNE-hIBM: Muscle Biopsy

Nonaka et al, Neuromuscular Disord 1998
GNE-IBM: Therapeutic Hopes

- Sialic acid – clinical trial
- \textit{GNE} gene delivery

\textit{GNE}: Uridine Diphospho-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase
MYH2, AD

Biopsy at age 9 months

Biopsy at age 38 yrs

Darin et al, Ann Neurol 1998
D'Amico et al, Neuromuscul Disord 2013
Tajsharghi et al, Acta Neuropathol 2013
Limb-Girdle Muscular Dystrophy 1D

DNAJB6

One of the genes that can cause hIBM features on muscle biopsy is classified as gene responsible of a specific form of limb girdle muscular dystrophy
hIBM

hIBM: Many genes – same muscle biopsy

• If the gene defect is identified, it is preferable to refer to the disease as myopathy (= muscle disease) secondary to the specific defective gene.

• For example, if a patient has a mutation in the gene \( VCP \), it is preferable to say that patient has VCP-myopathy or VCP-IBM
What can be done in hIBM?

• PT, submaximal exercise
• AFO
• Dietary modifications in case of swallowing difficulty
• Monitoring of the breathing to be sure nocturnal oxygen doesn’t drop
Thank you