INCLUSION BODY MYOPATHIES

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DISCLOSURE

Relevant Financial Relationship

None

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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)

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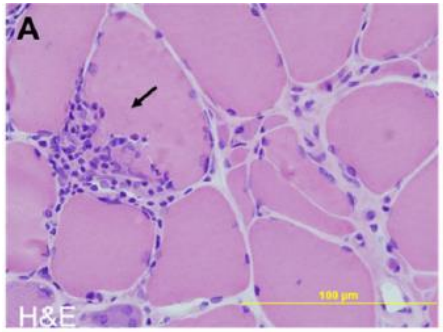
Muscle biopsy

sIBM

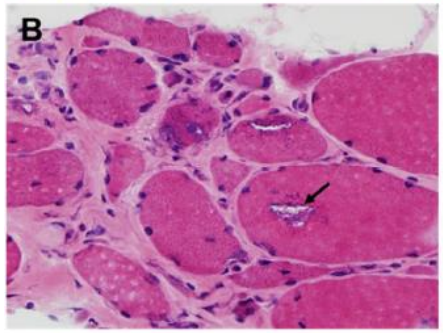
hIBM

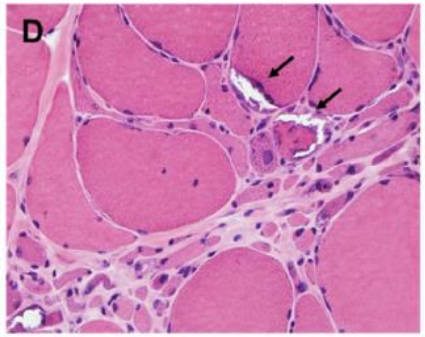
Arrow: Inflammation attacking a healthy muscle fiber



No inflammation in hIBM

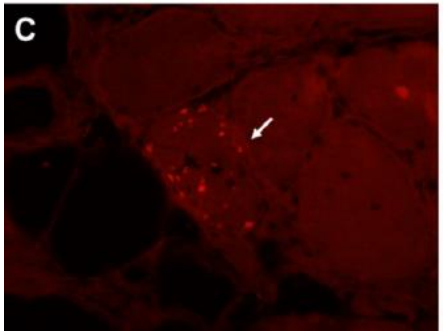
Arrows: Rimmed vacuoles

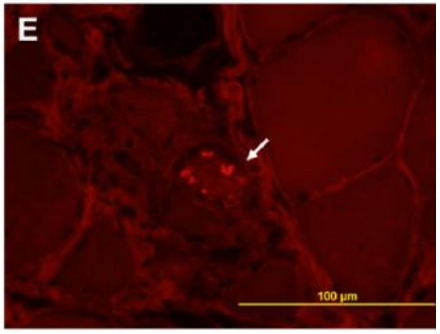




Arrows: Rimmed vacuoles

Arrows: Inclusions (= abnormal accumulation of proteins)





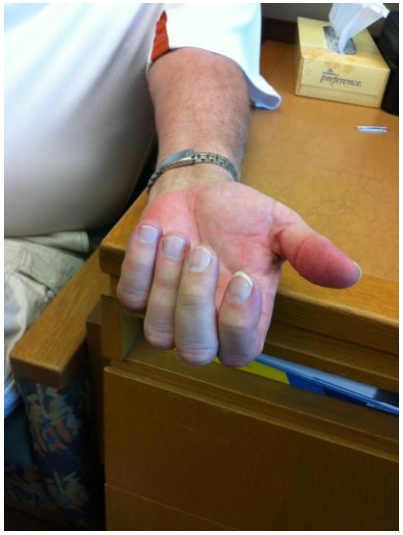
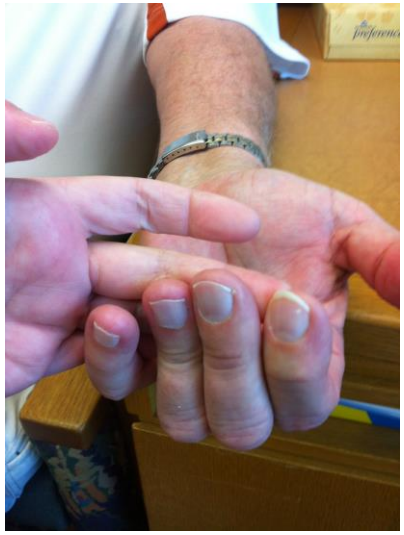
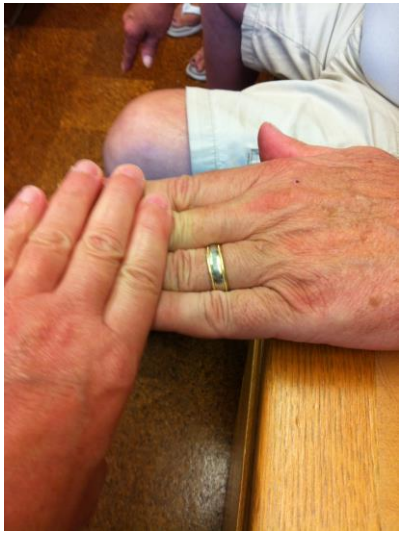
Arrows: Inclusions (= abnormal accumulation of proteins)

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

sIBM

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

  or

  - Two mutations are necessary to cause disease

- The lack of muscle disease in other family members does not exclude hIBM

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hIBM

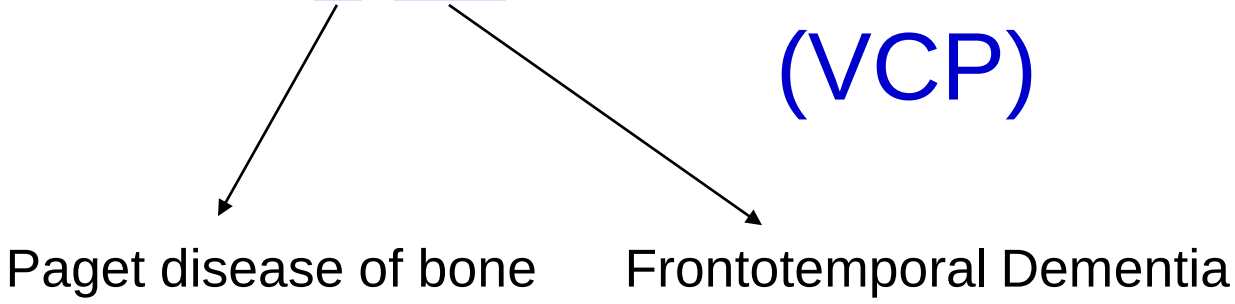
hIBM: same gene can cause other diseases

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

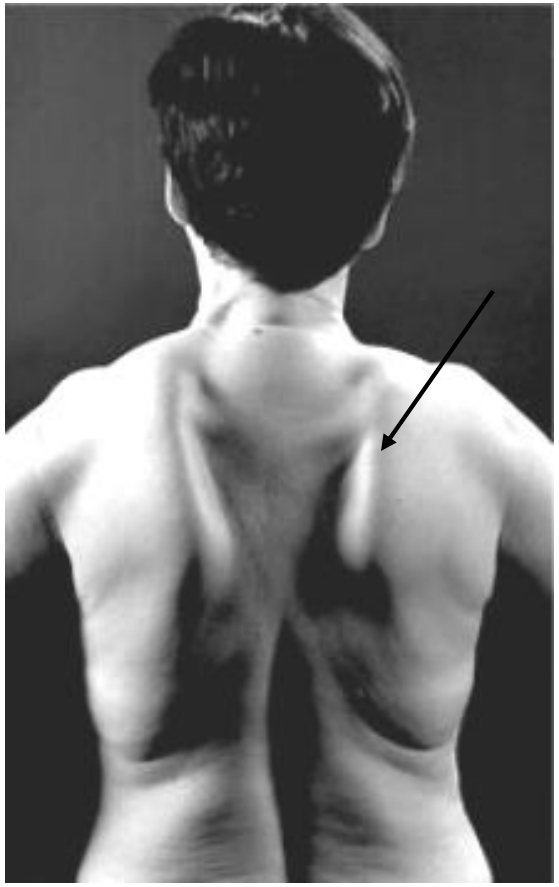
- Measurement of a bone enzyme, called alkaline phosphatase, may suggest co-existence of Paget disease of bone, if elevated

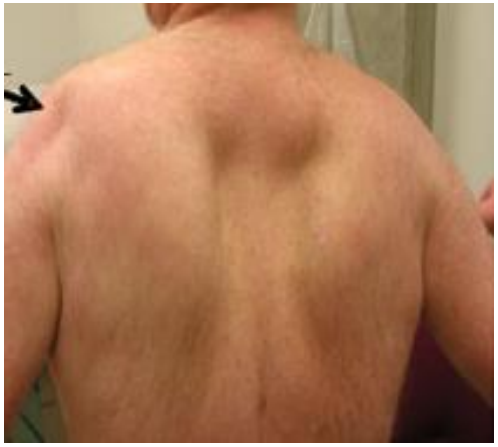
- Family history is important: muscle weakness? Other diseases possibly caused by the same gene?

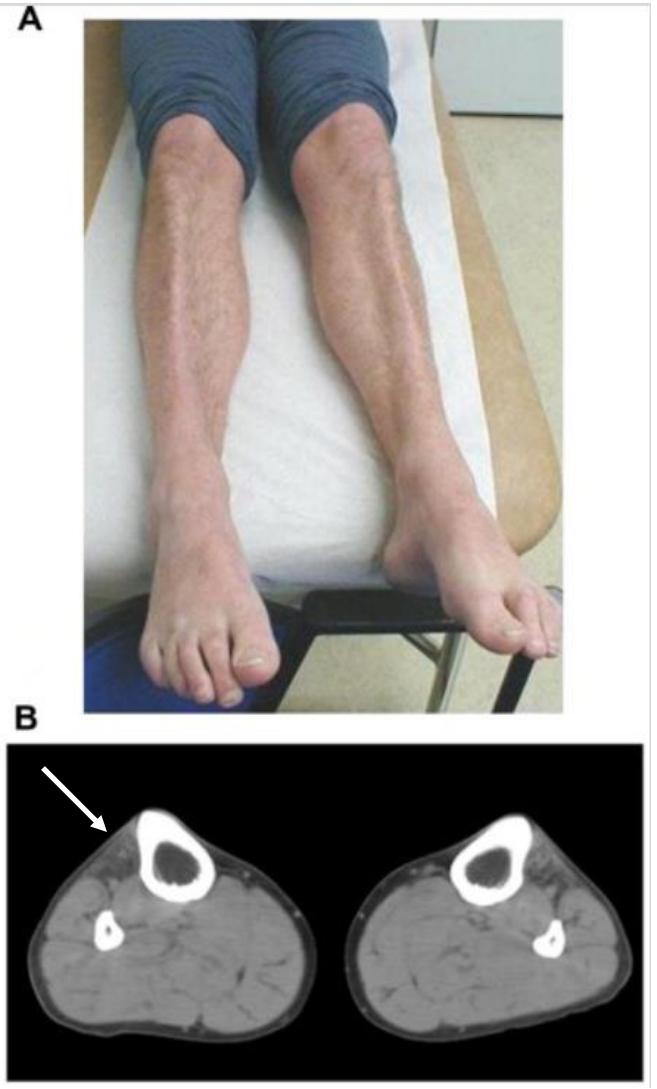
IBMPFD: Valosin-containing protein (VCP)



VCP- IBM: Clinical Features





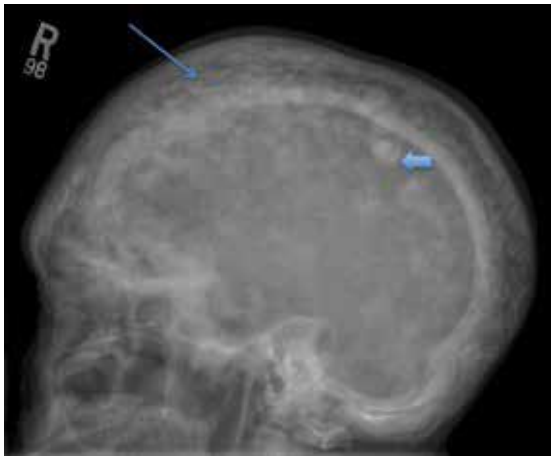


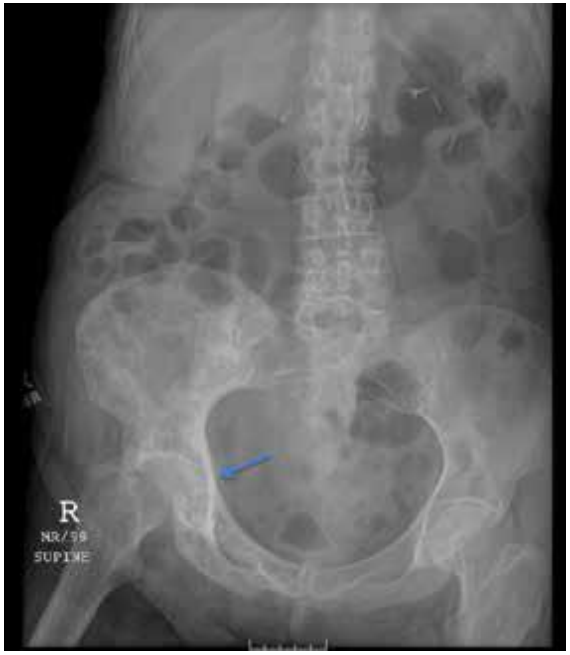
Nalbandian et al, J Mol Neurosci 2011

Palmio et al, Neuromuscular Disord 2011

VCP- IBM with Paget Disease of Bone

- Bone radiographs:





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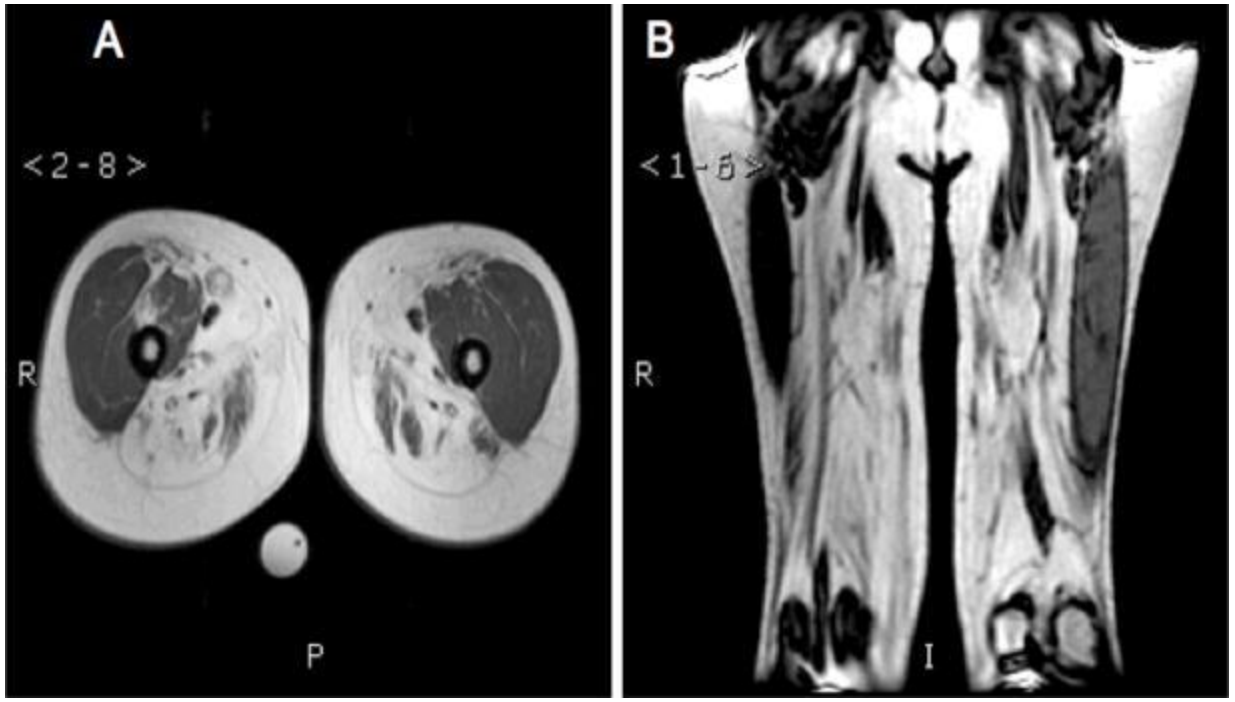
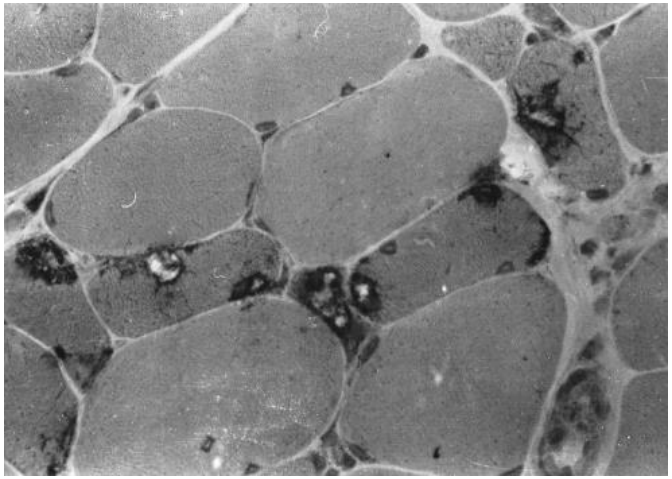
GNE-hIBM: Muscle MRI

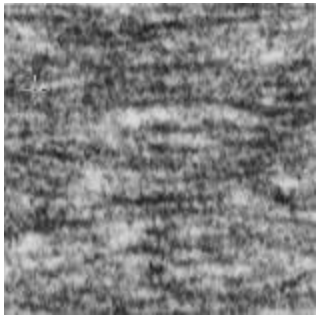


T1 weighted MRI

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
- *GNE* gene delivery

GNE: Uridine Diphosho-N-acetylglucosamine 2-epimerase/N- acetylmannosamine kinase

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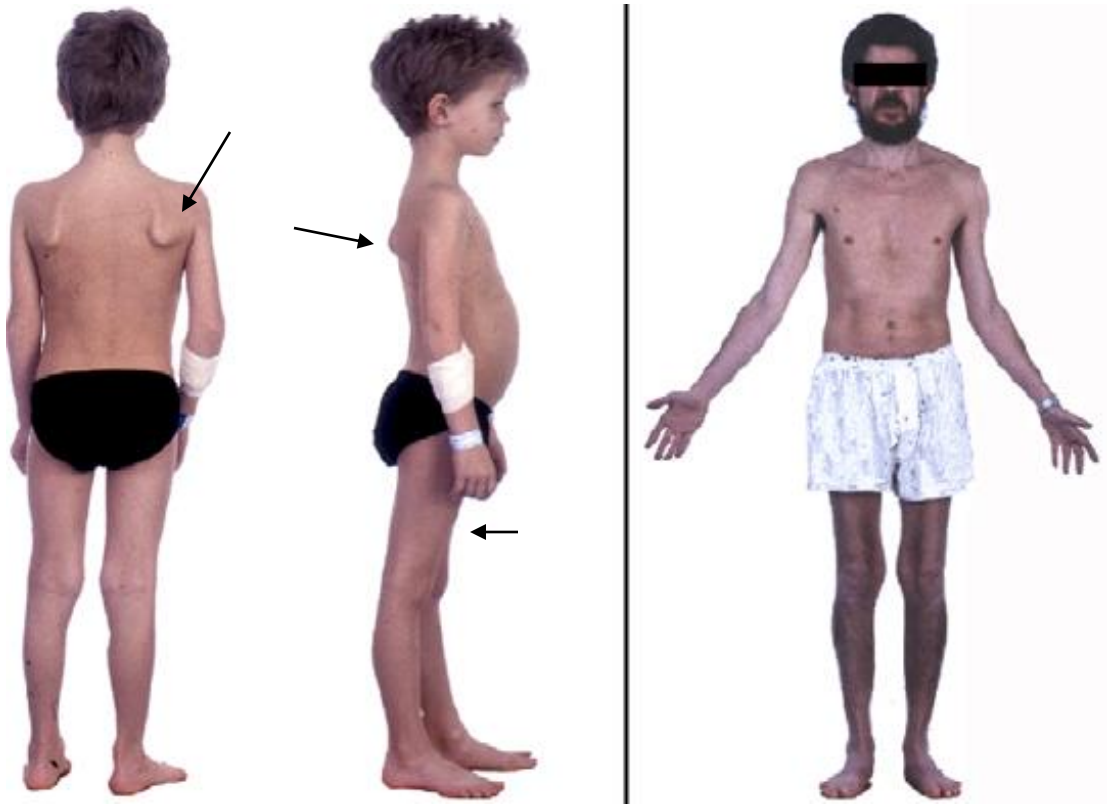
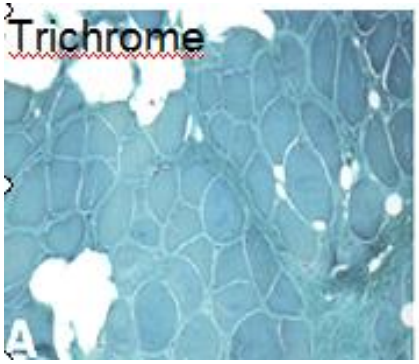
MYH2-hIBM

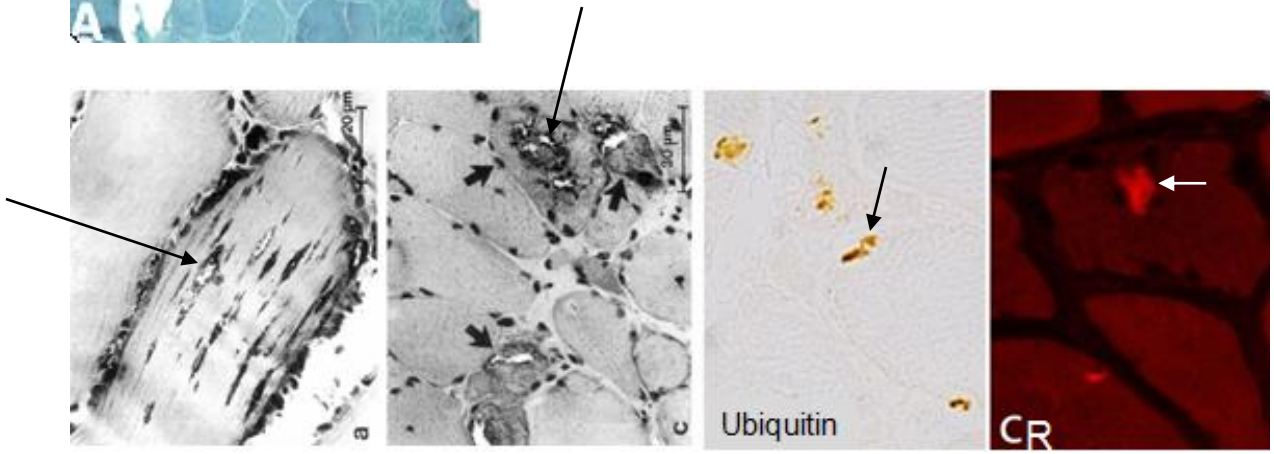


Darin et al, Ann Neurol 1998

MYH2, AD

Biopsy at age 9 months





Biopsy at age 38 yrs

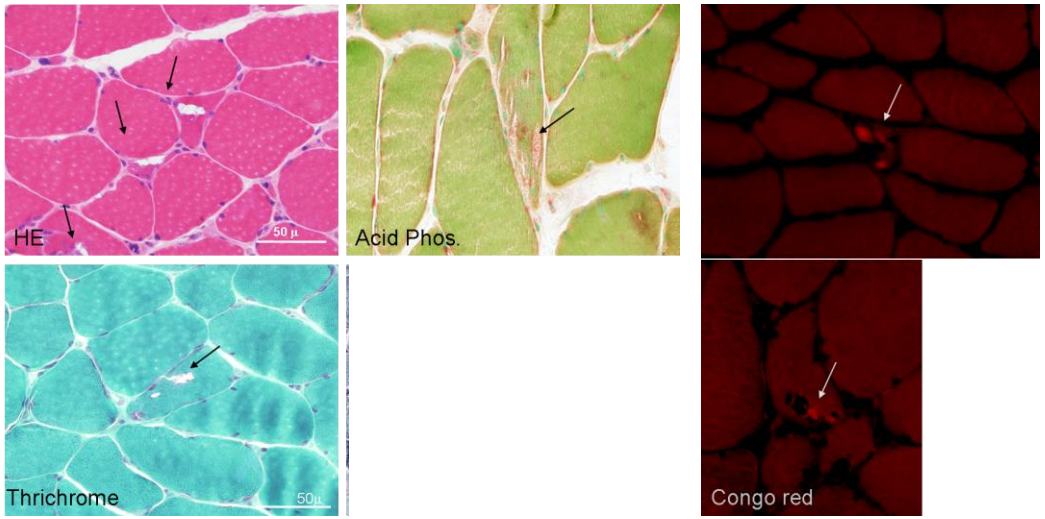
Darin et al, Ann Neurol 1998

Tajsharghi et al, Acta Neuropathol 2013

D'Amico et al, Neuromuscul Disord 2013

Limb-Girdle Muscular Dystrophy 1D *DNAJB6*

Muscle Biopsy



Features of hIBM

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

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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

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hIBM

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