



Electron Microscopy and Myopathology

Karra Jones, MD, PhD

Case-Based Questions (please see page 3 for answers)

1.	When reviewing a skeletal muscle biopsy from a 35-year-old with ptosis and proximal muscle weakness you identify ragged red fibers on the Gomori trichrome stain. What is the ultrastructural correlate?
a.	Autophagic vacuoles
b.	Excess free subsarcolemmal glycogen
c.	Sarcomeric disruption
d.	Subsarcolemmal mitochondrial pooling
e.	Tubuloreticular inclusions

2.	While reviewing a skeletal muscle biopsy from a patient with suspected dermatomyositis, you perform electron microscopy to look for characteristic tubuloreticular inclusions. Within what structure will you find the inclusions?
a.	Endothelial cells
b.	Lysosomes
c.	Mitochondria
d.	Myofiber nuclei
e.	T-tubules

3.	A skeletal muscle biopsy is performed on a patient with systemic lupus erythematosus treated with hydroxychloroquine and recent onset proximal muscle weakness. The rheumatologist is concerned for toxicity from her medication. The frozen sections are somewhat unremarkable, but you know electron microscopy can be helpful. What ultrastructural finding is most diagnostic of hydroxychloroquine myotoxicity?
a.	Concentric laminated bodies
b.	Curvilinear bodies
c.	Cytoplasmic bodies
d.	Filamentous bodies
e.	Zebra bodies

Scroll to Page 3 for answers

Correct Answers and Rationales

Question 1 Correct Answer and Rationale: D. Subsarcolemmal mitochondrial pooling

Rationale: Ragged red fibers are characteristic of mitochondrial myopathies. Their appearance on frozen sections stained with Gomori trichrome is due to the presence of abnormal aggregates of mitochondria in the subsarcolemmal space of skeletal muscle fibers. The mitochondria also often show other abnormalities such as enlargement, irregular branching, irregular cristae, and inclusions (including paracrystalline inclusions). But the presence of a ragged red fiber itself is directly related to the pooling of mitochondria, not their subtle ultrastructural abnormalities.

Question 2 Correct Answer and Rationale: A. Endothelial cells

Rationale: Tubuloreticular inclusions are a marker of a type I interferon response, classically seen within the cytoplasm of endothelial cells in dermatomyositis or active lupus myositis. They can also be found within inflammatory cells, particularly lymphocytes, and rarely fibroblasts. These inclusions are specifically associated with the endoplasmic reticulum, not lysosomes or mitochondria. Furthermore, they are absent from myofiber nuclei, in contrast to tubulofilamentous or filamentous inclusions in inclusion body myositis or antisynthetase syndrome-associated myositis.

Question 3 Correct Answer and Rationale: B. Curvilinear bodies

Rationale: Hydroxychloroquine (HCQ) myotoxicity is a vacuolar myopathy, but some mild cases only show ultrastructural findings to include autophagic vacuoles/myeloid bodies combined with curvilinear bodies. Zebra bodies can also be seen but are more characteristic of Fabry disease rather than HCQ-toxicity. Concentric laminated bodies, cytoplasmic bodies, and filamentous bodies are all nonspecific myopathic alterations seen variably in skeletal muscle diseases.