Ology Medical Education

Practice guide
Diagnosis of SMA in adults

Signs and symptoms of SMA in adults

Typically presents with symmetrical, predominantly proximal, muscle weakness

Common presentations include

- Progressive difficulty with walking, running, and climbing stairs
- Poor balance, with an increased risk of falls
- Difficulty rising from the floor or from a chair
- Postural tremor of fingers
- Loss of patellar reflexes
- Limb contractures and scoliosis

How is SMA diagnosed?

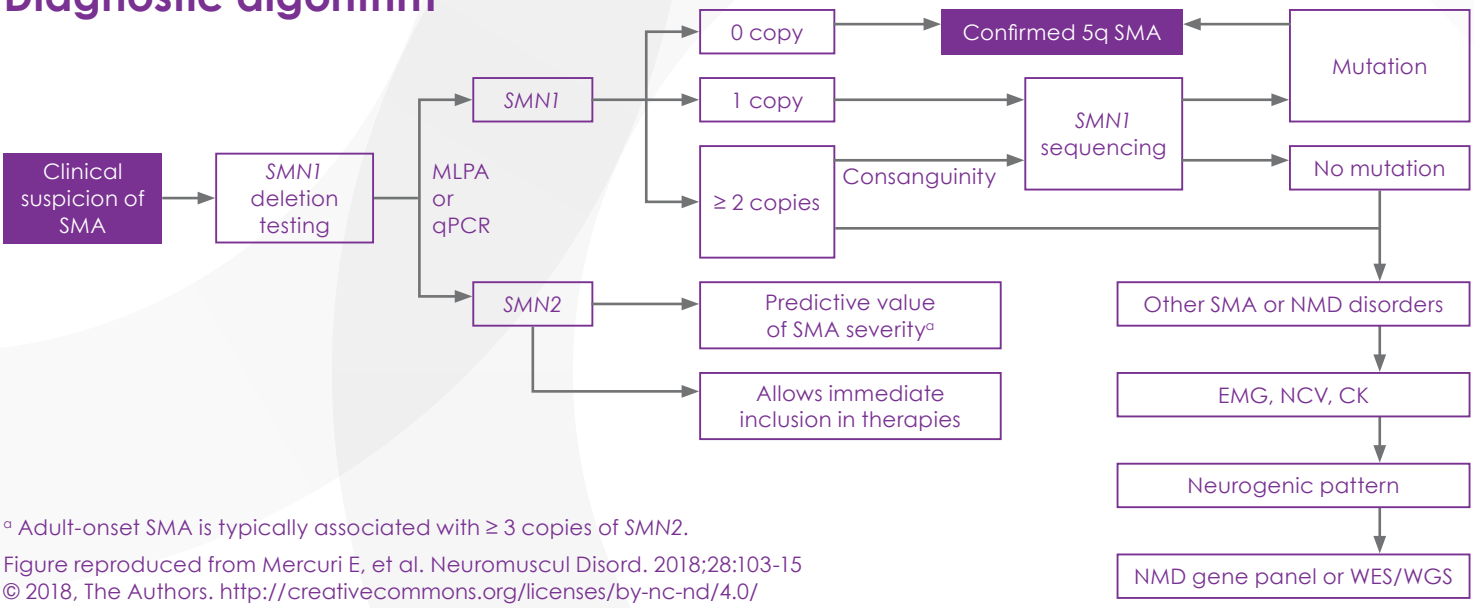
The conclusive diagnosis of SMA is based on highly specific and sensitive genetic testing of the *SMN1* gene

- Homozygous deletion of the *SMN1* gene → confirms a diagnosis of SMA
- One full copy of *SMN1* (plus clinical phenotype consistent with SMA) → sequence *SMN1* to look for other mutations
- The *SMN2* gene copy number correlates with disease severity

Other diagnostic tests typically performed in the diagnostic work-up of adults include

- EMG and NCS: may show signs of motor neuron or motor axonal loss, large MUAPs, low CMAPS, fibrillation potentials
- CK levels: normal to mildly elevated, never highly elevated

Diagnostic algorithm



[a] Adult-onset SMA is typically associated with ≥ 3 copies of *SMN2*.

Figure reproduced from Mercuri E, et al. Neuromuscul Disord. 2018;28:103-15

Developed in collaboration with Emma Ciafaloni, MD, FAAN.

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Differential diagnosis of SMA in adults

Disorders to consider	Potential distinguishing features from SMA
Duchenne/Becker muscular dystrophy	Serum CK concentration > 5–20× ULN
Limb-girdle muscular dystrophy	Elevated CK levels; myopathic changes on EMG
Spinal and bulbar muscular atrophy (Kennedy disease)	Gradually progressive; gynecomastia, testicular atrophy, decreased fertility
Amyotrophic lateral sclerosis	Upper motor neuron signs are present; weakness starts in asymmetric fashion; progression is rapid
Peripheral neuropathy (including autoimmune)	Distal weakness greater than proximal weakness; numbness and tingling
Late-onset Pompe disease	Early respiratory insufficiency
Other hereditary, metabolic, and acquired myopathies	Myopathic changes on EMG

Abbreviations

CK, creatine kinase; CMAP, compound motor action potential; EMG, electromyography; MLPA, multiplex ligation-dependent probe amplification; MUAP, motor action unit potential; NCS, nerve conduction study; NCV, nerve conduction velocity; NMD, neuromuscular disorder; qPCR, quantitative polymerase chain reaction; SMA, spinal muscular atrophy; SMN, survival of motor neuron; ULN, upper limit of normal; WES, whole exome sequencing; WGS, whole genome sequencing.

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Access the CME program "Diagnosis and management of SMA in older adolescents and adults" at **https://ologyeducation.org**

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