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Poster P16

Whole-Body muscle MRI in Non-5q Spinal Muscular Atrophy: Patterns, Genotype Prediction, and Diagnostic Implications

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Non-5q spinal muscular atrophies (SMA) are genetically heterogeneous hereditary motor neuropathies with progressive motor-predominant weakness and minimal sensory involvement. Over half remain unresolved, and muscle MRI may reveal distinctive fatty replacement patterns that support diagnosis.

We evaluated 25 adults (mean age 42.1 ± 13.5 y) meeting clinical and electrophysiological criteria for SMA, all negative for SMN1 deletions/mutations. Nineteen (76%) carried pathogenic variants in 13 genes, most often VRK1, DYNC1H1, and VWA1 (n=3 each). Whole-body MRI was graded with the Mercuri scale across 42 paired muscles and compared to published gene-specific signatures by counting discordant muscles.

Motor weakness was mainly proximo-distal (80%) with a mean clinical diagnostic delay of 20.4 ± 14.9 y. MRI patterns were highly concordant for DYNC1H1 and BICD2 with only 3.3 ± 1.2 and 4 discordant muscles, respectively. Reproducible patterns of fatty replacement were seen in following genes: VRK1: severe gluteal, thigh, and leg involvement with iliopsoas sparing; DYNC1H1: selective adductor magnus and anterior thigh involvement, long head of biceps femoris affected with short head spared, severe triceps surae with tibialis posterior sparing, and consistent gluteus maximus sparing; VWA1: severe anterior and posterior thigh involvement with gracilis and sartorius sparing. Cohort-wide key patterns" included selective sartorius/gracilis sparing despite quadriceps involvement (n=5), sparing of the long head of biceps femoris (n=4), and tibialis posterior (n=12) or extensor digitorum longus (n=6) sparing in the leg.

WB-MRI in non-5q SMA identifies reproducible gene-associated pattern (DYNC1H1, VWA1 and BICD2) and distinctive patterns improving genotype prediction. WB-MRI may resemble that of dystrophies, as VWA1-mutated patients show typical gracilis and sartorius sparing, suggesting dual pathophysiology, giving rise to motor neuropathies as well as myopathic involvement.