11-Year-Old Boy with Fatigue, Stiffness, Back Pain, and Difficulty Opening Jars
Rachel Bass, D.O. and Michael A. Lopez, M.D., Ph.D.
Division of Pediatric Neurology, Department of Pediatrics,
University of Alabama at Birmingham | Children’s of Alabama

Case Presentation

11-year-old boy with speech delay and colitis presented with:
- 3 years of worsening fatigue, back pain, and hand weakness
- Pain in his shoulder, low back, and neck that worsened with physical activity
- 1 year of difficulty opening jars and significant fatigue with prolonged physical activity

Pertinent history:
- Paternal grandfather with cardiac-related death at 44 years of age (long-standing)
- Mother with joint stiffness, pernicious anemia, and Hashimoto’s disease
- Motor milestones achieved normally, but history of speech delay (first words at 18 mos)

Exam Findings

- Pectus excavatum
- Levo-dextro thoracic scoliosis
- Restricted range in neck rotation, hip flexion, finger extension, and ankles
- Mild distal weakness (4+/5) with atrophy in hands and feet
- Normal facial strength, reflexes, sensation, and coordination

NCS/EMG Results

Differential Diagnosis

Findings consistent with EDMD2:
- Autosomal dominant
- Pattern of distal weakness
- Prominent neck and back contractures
- Onset of symptoms
- No facial weakness

Non-LMNA findings:
- Colitis not seen with LMNA mutations
- LMNA VUS maternally inherited and unclear if mother affected

Next steps:
- Patient’s mother referred for neuromuscular and cardiac evaluation
- Patient referred to multi-disciplinary clinic for management of stiffness and weakness
- Rheumatology considering treatment of sacroiliitis

Prior Evaluation

- Evaluated by Rheumatology and Undiagnosed Disease Program
- Whole exome sequencing performed
- Labs: Creatine kinase levels between 346 – 1,300 IU/L, ESR 6, and CRP <0.5
- Normal EKG and echocardiogram
- GI endoscopy with focal areas of mild colitis, treated with sulfasalazine (completed therapy)
- MRI pelvis showed evidence of sacroiliitis

Genetic Results

Whole exome sequencing (GeneDx)
Two maternally inherited heterozygous variants of unknown significance in clinically related genes:

- LMNA (Lamin A/C) - c.1004G>A, p.Arg335Gln. Missense variant located in exon 6 in the Coil-2 domain. Many previously reported mutations, ex. R336Q, 16 total reported in Coil-2.


Laminopathies

LMNA-associated myopathies:
- Limb-girdle muscular dystrophy (LGMD-1B)
- Emery-Dreifuss muscular dystrophy 2 (EDMD2)
- Congenital muscular dystrophy (LMNA-CMD)

Other laminopathies include:
- Progeria
- Lipodystrophies
- Dilated cardiomyopathy

Summary

- Electrodiagnostics: distal, non-irritative myopathy
- Exam: prominent neck and back contractures + distal extremity weakness
- Genetics: maternally inherited variant of unknown significance in the LMNA gene, presumably pathogenic
- Diagnosis: LMNA-associated myopathy

References