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

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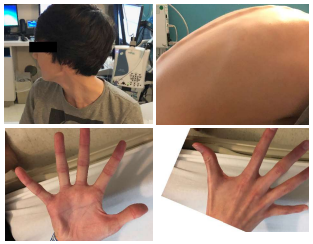
Case Presentation

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 acheived 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

Sensory Nerves	Rec. Site	Onset Lat	Peak Lat	NP Amp	Segments	Distance	Vel. Pk
		ms	ms	uV		cm	m/s
R Median - Digit II (Antidromic)							
Wrist	Dig II	2.60	3.44	46.4	Wrist - Dig II	14	54
R Ulnar - Digit V (Antidromic)							
Wrist	Dig V	2.50	3.44	34.9	Wrist - Dig V	14	56
R Sural - Ankle (Calf)							
Calf	Ankle	2.71	3.28	13.7	Calf - Ankle	14	42

Motor Nerves	Muscle	Latency	Amplitude	Segments	Distance	Lat Diff	Velocity	Temp.
		ms	mV		cm	ms	m/s	°C
R Median - APB								
Wrist	APB	3.28	12.1	Wrist - APB	8			31.6
Elbow	APB	7.24	11.9	Elbow - Wrist	24.5	3.96	62	31.5
Upper arm	APB	8.85	11.7	Upper arm - Elbow	10	1.61	62	31.5
R Ulnar - ADM								
Wrist	ADM	3.07	12.9	Wrist - ADM	8			30.8
B.Elbow	ADM	6.67	12.8	B.Elbow - Wrist	21.5	3.59	60	30.8
A.Elbow	ADM	8.44	11.9	A.Elbow - B.Elbow	10	1.77	56	30.6
R Peroneal - EDB								
Ankle	EDB	3.70	4.8	Ankle - EDB	8			33.9
Fib head	EDB	8.74	4.7	Fib head - Ankle	32	6.04	53	34
Pop fossa	EDB	11.67	5.0	Pop fossa - Fib head	10	1.93	52	34

Muscle	Nerve	Roots	IA	Fib	PSW	Fasc	H.F.	Amp	Dur.	PPP	Pattern
R. Deltoid	Axillary	C5-C6	N	None	None	None	None	1-	1-	2+	Early
R. Pronator teres	Median	C6-C7	N	None	None	None	None	1-	1-	2+	Early
R. Rectus femoris	Femoral	L2-L4	N	None	None	None	None	1-	1-	1+	Early
R. Tibialis anterior	Deep peroneal	L4-L5	N	None	None	None	None	2-	1-	2+	Early

Differential Diagnosis

Findings consistent with EDMD2:
- Autosomal dominant
- Pattern of distal weakness
- Neck extensor 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 refered to multi-disciplinary clinic for management of stiffness and weakness
- Rheumatology considering treatment of sacroilitis

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 sacroilitis

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.Arg-335Gln. Missense variant located in exon 6 in the Coil-2 domain. Many previously reported mutations, ex. R336Q, 16 total reported in Coil-2.

- *TMEM* - c.200C>T, p.Gly67Val

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, presumbably pathogenic
- Diagnosis: *LMNA*-associated myopathy

References

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3. Benedetti S, Menditto I, Degano M, et al. 2007. Phenotypic clustering of lamin A/C mutations in neuromuscular patients. Neurology. 69: 1285-