NEUROMUSCULAR UNUSUAL CASE SYLLABUS

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CASE #1

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50-year-old man with ophthalmoparesis, ataxia and spastic paraparesis

A 50-year-old man presented to the neuromuscular clinic with a ten year history of issues with balance and coordination. He first noticed difficulties with jumping and maintaining balance while playing basketball with friends. By the time of his evaluation he had experienced a few falls. He also reported lower extremity cramping and stiffness. A prior cervical spine MRI showed canal stenosis and he had undergone anterior discectomy and fusion with no improvement in his symptoms. His gait instability continued to worsen, he started falling frequently and required a cane for safety. He denied any focal weakness, sensory symptoms, dysphagia, dyspnea or diplopia. There was no significant past medical or family history.

On neurological examination he had significant ptosis, more prominent on the left, and markedly diminished eye movements in all directions of gaze. Saccades were slow. Direction changing nystagmus was noted in vertical and horizontal gaze. Facial sensation and strength were normal. His tongue movements were slow. His speech was clear. Tone was normal in the upper extremities and increased in the lower extremities with a spastic catch. His strength was normal. Vibration was markedly reduced up to the knees with preserved joint position sense but a Romberg was present. He had hyperreflexia at the knees with normal reflexes elsewhere, and a Babinski sign on the right. Coordination testing showed a mild intention tremor, dysdiadochokinesia and dysmetria that were more prominent on the left. He had truncal ataxia with a wide based gait.

An extensive workup was performed. MRI of the brain showed mild cerebellar and extraocular muscle atrophy. EMG/NCS showed reduced activation consistent with central disease but was otherwise unremarkable. Spinal fluid studies were unremarkable. A muscle biopsy of the left vastus lateralis showed type 2 atrophy with no mitochondrial pathology. Mitochondrial enzyme activities were normal. A PEO panel that included TWINKLE, OPA1, POLG, POLG2, RRM2B and ANT1 was performed and was negative. An ataxia genetic panel was negative also, this panel included DRPLA, SCA1-3, SCA5-8, SCA10, SCA 12, SCA12-14, SCA17, SCA28.

An additional test was performed.

CASE #2

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A 34-year old woman with life long weakness and and difficulty walking

A 34-year-old female reported a longstanding history of leg weakness and walking difficulty. Her birth history was unremarkable. In childhood, she walked independently but was unable to run fast or jump. She received a total of 24 foot surgeries. She went to college then graduate school with strong academic performance.

She started to lose ambulation during pregnancy at the age of 24 years. She also complained arm weakness then. There was a suspicion for CMT with possibly superimposed CIDP. She was treated with corticosteroid and IVIG which was complicated with aseptic meningitis. Notes indicated that she may have improved temporarily.

For the last 10 years, her condition has been stable. At presentation she could walk for 40 feet with a walker. Her handgrip was slightly weak. There was a lack of sensation in legs more than her hands.

Past medical, social and family histories were non-contributory. Mother died of ovarian cancer. Father, brother, sister and daughter demonstrated no signs of neuromuscular illness.

Physical examination revealed distal hand and foot atrophy, prominent distal weakness (LE>UE), diffuse areflexia and reduced sensation of pinprick and vibration in distal limbs. Mild ataxia is noted on finger-to-nose with eye closing.

Tests for TSH, B12, folate, vitamin E, immunofixation, HIV, and amino acid profile were normal. Genetic analyses for PMP22, connexin 32, MPZ, EGR2, NF-L, PRX and GDAP were negative. EMG at the age of 24 years revealed a severe mixed axonal and demyelinating neuropathy. Distal motor latencies were as follows: 15.9 ms for median, 21.2 ms for ulnar, 15.5 ms for axillary and 26.3 ms for facial nerves. She remembered that nerve conduction studies performed in childhood showed conduction velocities in the range of 4-10 meters/second but these earlier records could not be found.

A diagnostic procedure was performed.

CASE #3

Christopher Kurahashi
Northwestern Memorial Hospital
Chicago, IL

A 30-year-old man with weakness from the age of two years.

He had normal birth at 41.5 weeks by C-section and normal early development. His symptoms were first appreciated by parents at the age of 2, he was described as having difficulty standing from the ground and having a waddling gait. His weakness progressed slowly through his childhood, and at the age of 9 he began to have frequent falls and was put in a wheelchair at school. During his teenage years he began to develop more prominent arm weakness, with difficulty reaching above his head and lifting heavy objects. At the age of 18 he began to have non-restorative sleep and morning headaches. He was put on CPAP at night.

He has had multiple workups since early childhood which included numerous CK levels, genetic tests and three muscle biopsies. His CK levels had been normal, and other tests came back negative per patient and family report. He and has family were told that he has limb-girdle muscular dystrophy.

His present symptoms include weakness of his proximal arms and legs. He is unable to lift heavy objects and unable to stand or ambulate. He has difficulty typing due to weakness of his fingers, he is able to write though he tires quickly. His wife has noticed some drooping of his eyelids recently and mild slurring of his speech that seem worse in the evenings. He has no double vision, no difficulties with swallowing, no sensory symptoms and no cognitive symptoms.

His exam is notable for mild symmetric ptosis, mild bifacial weakness. His motor exam demonstrated mild diffuse atrophy and diffuse weakness that was severe proximally and relatively worse in finger extension. His sensation and reflexes were normal.

Electromyography and nerve conduction study demonstrated normal sensory and motor studies. Repetitive nerve stimulation demonstrated a 20% decrement at baseline. At 1 minute post-exercise this decrement improved to 13%, then worsened by 3 minutes post exercise to 24%. EMG was normal, with no membrane irritability and normal motor unit morphology.

Laboratory evaluation included CK level which was 58 and Anti-MuSK and AChR antibodies which were negative. A diagnostic test was sent.

CASE # 4

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Venice, Italy

A case of lgmd with delayed diagnosis

Case history
This man has complained since adolescence of back pain, difficulty in lifting arms overhead, running, and hopping. At age 36, CK was 1400 U/L. EMG was myogenic. At age 41 years he had waddling gait, marked weakness of biceps, deltoid, pectoral muscles, and mild weakness in iliopsoas muscles and had scapular winging. He had difficulty in rising from the floor, had atrophy of hip girdle muscles. A biceps brachi muscle biopsy showed a nonspecific chronic myopathy. The diagnosis of LGMD was suggested, but proteins involved in LGMD (dysferlin, alpha-sarcoglycan, caveolin-3, emerin, merosin, alpha-dystroglycan) were normal, except calpain-3 which was mildly reduced. The patient developed progressive muscle weakness with difficulty walking and arising from a chair, and respiratory insufficiency, hypoxemia, hypercapnia. At age 44 he became dependent on nocturnal ventilation. At age 52 years, spirometry showed a forced vital capacity (FVC) of 40% of predicted value. He started using a wheelchair at age 66, but he was still able to walk 30 meters with support.

Laboratory tests
At 73 years he was on a ventilator for 22 hours daily; FVC was 22% of predicted value and peak inspiratory force was 25% of predicted value. Echocardiography showed mild mitral insufficiency.

CASE # 5

Reem Alhammad
Peripheral Nerve Fellow, Mayo Clinic Rochester

67 year old woman with pain, numbness and weakness in her right leg and foot for 2.5 years.

67 year old right handed woman presented with Pain, numbness and weakness in her right leg and foot for 2-1/2 years. She notes that 2 -1/2 years prior, she developed sudden onset numbness in bilateral posterior thighs with shooting, electric like pain into the gluteal regions. She did not have associated back pain. Symptoms were intermittent, lasting for few seconds and recurring multiple times per day. Approximately 3 weeks later , symptoms in her left lower extremity improved, while pain and numbness persisted in the right lower extremity. She also had Contact allodynia right foot .She then developed a Painless blister in right foot. One year and a half following onset of symptoms, she developed Gradual Right foot drop, requiring ankle foot orthosis. During the same time, she noticed Genital and perianal numbness and pain. She denied weakness, focal sensory loss, pain in the upper extremities. She denied weakness in the left lower extremity.

She also denied double vision, facial numbness or weakness, lightheadedness, change in sweating pattern, weight loss, night sweats. Past medical and surgical history was significant for Irritable bowel syndrome, hysterectomy, breast reduction, microdiskectomy. There was no Family history of neuropathies. She gave a 15 pack year smoking history, she quit at age 35. She denied recreational drugs.

Examination revealed right lower extremity weakness : -4 weakness(MRC grade 0) of foot and toe extensors, eversion ,foot plantar-flexion ,-3 weakness(MRC grade 4-) of toe flexion, inversion,hamstrings. There was sensory loss to all modalities in the distribution of the right common peroneal nerve.

Nerve conduction and EMG showed right electrophysiologically severe sciatic neuropathy with minimal evidence of reinnervation. There was also evidence bilateral L5-S1 radiculopathies, more severe on the right with ongoing denervation and incomplete reinnervation. MRI of the lumbosacral plexus showed Nerves of bilateral (right more than left) lumbosacral plexus, were enlarged and extended into the right sciatic nerve.

The findings were suggestive of inflammatory demyelinating neuropathies or infiltrative neuropathies. MRI of the lumbar spine showed Multilevel degenerative changes most marked at L4-5 and L5-S1 .Mild to moderate narrowing of neural foramina. No enhancement of the visualized lower thoracic spinal cord, conus medullaris, or cauda equina roots. Metastatic bone survey was negative for metastasis or myeloma. Fat aspirate was negative for amyloid. Autonomic reflex screen showed normal cardiovagal testing, mild cardiovascular adrenergic impairment, and focal postganglionic sympathetic impairment related to right sciatic nerve distribution. Thermoregulatory sweat test showed anhidrosis of the entire right foot, right lateral leg, and left medial and lateral leg. Quantitative sensation testing showed reduced Touch, vibration, cooling in the right foot, and Hyperalgesia to heat pain in the right foot. Blood tests including CBC,ESR,TSH, Rheumatoid factor, SPEP with immunofixation, HbA1c, ACE,CTD cascade, creatinine, B12, HIV screen, Hepatitis screen, were unremarkable or normal. UPEP with IF was normal. CSF analysis showed 1 nucleated cell, protein of 71, glucose of 60, and negative CSF cytology.

What is the differential diagnosis and what would you do next?

CASE #6

Safiullah Shareef, MD
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Rapidly progressive proximal arm weakness and gait changes in a toddler

Case Presentation:
EG is a previously healthy girl with progressive gait changes and arm weakness. Her first steps were at 12 months of age. Around 15 months old she fell off a bench and suffered no fractures. Her gait became progressively unsteady. Her proximal arm usage deteriorated - described as limp appearing. MRI of the brain and C-Spine were normal. Her weakness did no fluctuate through the day and was not affected by exercise. By 20 months of age, she lost the ability to use utensils for feeding. She would often stumble backwards and would be unable to brace herself with her arms upon falling. Her language development was normal. There was no bulbar or respiratory weakness.

Previous History: EG was born full-term via C-section due to breech presentation. She had normal development until the age of 12 months.

Family History: There is no family history of similar symptoms.

Physical Examination:
A playful, non-dysmorphic, easily agitated toddler girl. Her proximal arm muscles felt soft to palpation. She had decreased truncal tone and bilateral arm tone. There was very minimal movement of her upper extremities. There was no dysmetria in reaching – however limited by her shoulder weakness. She had a wide based gait with minimal arm swing and tendency to fall backwards. She would bend at the waist to pick up objects. Her reflexes were absent in the arms and normal in the legs.

EMG/NCS:
Upper extremity motor and sensory responses were diminished. Lower extremity sensory responses were diminished. Lower extremity motor responses were normal with normal F-wave latencies. Needle EMG showed large and broad motor units in the TA and deltoid without evidence of active denervation. Activation in the hand was absent. These findings indicated electrophysiological evidence of a severe chronic sensorimotor axonal polyneuropathy worse at the arms compared with the legs.

Laboratory Testing:
Thyroid Tests, Vitamin B12, Homocysteine, Thiamine, Methylmalonic acid, Mycoplasma IgG/M, West nile virus PCR, IgG index, Heavy metal screen, and CSF studies all normal.

Disease Progression:
By age 21 months, she lost the ability to bring her hands to her mouth. Despite 2 courses of IVIG and Plasma Exchange transfusion (PLEX), by age 2 years, she lost finger grip strength and lost the ability to ambulate independently.

What would you do next?

CASE #7

Vera Prisacari
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University of Missouri, Columbia

45 year old with recurrent urticaria with heat

A 45 year old male presented with recurrent episodes of heat exertion followed by generalized hives since his 20s on mild physical exertion. He had an unremarkable childhood, participated in sports and was able to keep up with his peers. There were no similar symptoms among his siblings or parents. He had a history of tonsillectomy when he was 10 years old which was unremarkable.

Since last 5 years he had noticed progressive weakness and fatigue. He had noted weakness when he was getting up from the floor after playing with his children. He had also noticed shortness of breath on climbing three flight of stairs. He continued to have episodes of heat exertion and hives especially in summer when he did yard work and was diagnosed with cholinergic urticaria.

Neurological exam showed symmetric (4/5) weakness with hip flexion and knee extension. Rest of the exam was normal. Creatinine Kinase levels was 400 U/L (52-336 U/L, Mayo Clinic). Nerve conduction and needle electromyography was normal.

Vastus Lateralis biopsy with H & E stain showed mild fiber type variation with internal nuclei and mild endomysial fibrosis. NADH stain showed central cores with predominance of type 1 fibers.

What is the differential diagnosis and what test would you suggest?

CASE # 8

Amy Chen, MD, PhD
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A 23 year old man with one year of left foot pain and numbness

A 23-year-old man presents with one-year history of left foot pain and numbness. The symptom started acutely under his toes and rapidly progressed to involve the entire left sole over 2 weeks of time. Within 6 months of symptom, he noted difficulty with plantar flexion of the left ankle and abduction of the left toes. He wore a foot boot to alleviate the pain at his left sole. There was no history of trauma. Family history was negative for neuromuscular diseases.

Examination was notable for an asymmetrically enlarged left calf muscle with focal tenderness. Muscle tone was normal. Strength was 4/5 MRC in the left toe flexors, with concurrent pain. He has allodynia at the left sole with tactile stimulation. Vibratory sensation was early diminished at the left great toe compared to the right. Deep tendon reflexes were normal and symmetric throughout, except for the left ankle which could not be tested due to focal pain.

NCS/EMG done at 8 months of symptom showed reduced sural response (4 uV). Tibial nerve showed prolonged distal motor latency, DML (6.6 ms), reduced response (0.9 mV), normal conduction velocity, CV (56 m/s). The left peroneal nerve was normal. EMG report indicated increased insertional activity, 2+ fibrillation potentials and 'myotonic discharges' in the gastrocnemius medialis. EMG of left tibialis anterior, gastrocnemius lateralis, vastas lateralis, gluteus maximus, and lumbar paraspinal muscle was normal. Another NCS/EMG done at 10 months of symptom showed an interval progression of the left tibial neuropathy, with prolonged DML (8 ms), reduced response (0.4 mV), and normal CV. The left sural nerve showed normal SNAP response (7 uV), but mildly prolonged peak latency (4.9 ms). EMG findings in the left gastrocnemius were unchanged.

X-ray of the foot and MRI of lumbar spine were unremarkable. MRI of the left lower extremity showed 'mild edema in medial soleus muscle, that is non-specific and could be related to muscle strain or potentially denervation'.

A repeat NCS/EMG was done at one year of symptom onset, when he was referred for further evaluation of left tibial neuropathy of uncertain etiology. The left tibial nerve showed prolonged distal motor latency (9.01 ms), reduced amplitude (0.6 mV) with distal stimulation, and no responses with proximal stimulation at the popliteal fossa. EMG of the left gastrocnemius muscle showed myokymia and neuromyotonia (~40-70Hz). Bilateral medial and lateral plantar cutaneous nerves were not recordable. The left sural SNAP response was approximately 50% of the right, with normal peak latency. EMG of the left VL, biceps femoris, right gastroc, and left L5/S1 paraspinal muscles were normal.

Lab work for CBC, BMP, TSH, HgbA1C, B12, SPEP/IFE, ESR, CRP, ANA, Lyme, ACE, tTG IgA, gliadin ab, and paraneoplastic panel was normal or negative.

MRI neuropathy showed: "T2 hyperintensity in tibial nerve beginning near the level of the soleus muscle and extending inferiorly for appoximately 2.5cm. There is mild edema within the adjacent soleus muscle. No discrete soft tissue mass, fluid collection, or intramuscular hematoma.

Diagnosis?

CASE # 9

Ahmed Bamaga, MD
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Washington University School of Medicine in Saint Louis

A 17 year-old girl with life long hypotonia and weakness.

History:
Perinatal history showed that she had decrease fetal movement and polyhydramnios. She was born at 30 weeks EGA by C-section due to breech presentation. She had significant respiratory distress at the time of delivery requiring intubation followed by tracheostomy tube placed at age of 16 days. She was also noted to have significant arthrogryposis in all limbs. Her breathing has subsequently improved and by 4 months of age she was only on trace collar. Developmentally she continues to have difficulties. She is currently using wheelchair for transportation. She is not able to stand or crawl. She is able to sit with support. She is able play on her IPAD and to drive the wheelchair without difficulties. Hearing, Vision, Cognitive and social development are up to her age.

Examination:

At 2 year of age:
She was alert and able to fixe and follow. General examination showed distal more than proximal arthrogryposis, hip flexor contractures and mild equine varus deformity of both ankles. Neurologically, she had bifacial weakness, high arch palate, diffuse axial and appendicular hypotonia. She was able to flex her arms and extend her leg against gravity. Sensory exam to light touch was intact. Muscle stretch reflexes were 1+ at the biceps and absent elsewhere.

At 17 years of age:
She continued to have bifacial weakness (orbicularis oris > orbicularis oculi), mild dysathric speech. No tongue fasciculation or atrophy were noted. Motor examination revealed proximal more than distal weakness in upper limb. In lower limb she has very week tibialis anterior and quadriceps. The other muscles were at 4-/5 range. Muscle stretches reflexes were 2+ all over except at the ankles which could be due to the sever contractures.

Investigations:
Blood test: CK has always been normal or slightly elevated (200-500).
Muscle biopsy
10 days old: increase fiber size variability, dystrophy related stains were normal.
1 year old: increase fiber size variability, prominent fibrosis in several regions, no internal nuclei and no abnormal storage material.
Electrodiagnostic studies:
2002: chronic denervation (large broad fast firing MUPs) in three muscles (left triceps, Ta and Hamstring)
Genetic test: 2002: SMA genetic testing: negative

CASE # 10

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UC Irvine Neuromuscular Center
Orange, CA

29-year-old woman with progressive weakness

CASE PRESENTATION:
A 29-year-old Afghan woman with no family history of muscle disease who developed proximal limb-girdle weakness in her early 20s that slowly progressed to prominent distal weakness with bilateral foot drops.

Neurologic exam:
She had atrophy of the forearm flexor and anterior leg compartments and hypertrophy of bilateral (L>R) calves. No facial weakness, oculobulbar involvement, or scapular winging. Weakness was asymmetric, affecting proximal and distal muscles in lower > upper extremities. MRC strength was as follows (R/L): neck flexors 4/5, neck extensors 4+/5, deltoid 4+/4-, biceps 5/5, triceps 4+/4-, wrist extensors 4/3, wrist flexors 4/4, finger extensors 3/3, finger flexors 4+/4, first dorsal interosseous 4/4, hip flexors 2/2, hip extensors 4+/4, hip adductors 4/4, hip abductors 4+/4+, knee flexors 4/4, knee extensors 4/4, dorsiflexors 2/2, plantar flexors 4+/4+. She had a waddling and steppage gait with bilateral foot drops.

Laboratory data:

Pulmonary function tests:
Maximum Inspiratory Pressure (MIP): -25 cm of water
Sniff Nasal Inspiratory Pressure (SNIP): -36 cm of water
Forced Vital Capacity (FVC), sitting: 0.85L, Predicted: 29%

Prior cardiac workup including ECG and echocardiogram was reportedly normal.

CK level was mildly elevated at 318 U/L.
Dried blood spot GAA assay: Acid 17.6 (control >= 10), Neutral 58.8 pmol/punch/hour (control 23.8-132.6)

Electrodiagnostic study showed evidence of a generalized myopathy with irritability.

MRI of the lower extremities revealed significant fatty infiltration of the vastus muscles and anterior leg compartment muscles, relatively sparing the hamstrings and the posterior calf muscles.

Muscle biopsy (of left biceps) showed myofibrillar changes and necklace cytoplasmic bodies.
What would you do next? What is the differential diagnosis

CASE # 11

Cory Kogelschatz
Reem Alhammad
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Mayo Clinic
Rochester, Minnesota

64 year old female presented with Right lower extremity weakness, numbness. In November 2015, she noticed sudden onset numbness of top and bottom of right foot with right foot "flopping". Approximately 2-3 months later, she developed Pins and needles on medial aspect and top of right foot associated with shock-like sensations, zingers. Later she noticed Numbness on her right lateral leg. In January 2016, she started to have difficulty bending toes of her right foot with continued progression of her right foot drop. She denied gait imbalance, bowel or bladder dysfunction, bulbar or ocular symptoms, or autonomic symptoms. She denied weight loss, fevers, night sweats. She had a 15 pack year history of smoking and consumes 4-5 alcoholic beverages/day. Family history was significant for colon cancer in patient's mother. Her neurological exam showed -3 (MRC grade 4-) of the right tibialis anterior and -3.5 weakness (MRC grade -2) of right extensor hallucis longus. Muscle strength was normal elsewhere. Her right gastrocnemius reflex was absent. She had sensory loss to multiple modalities in the right common peroneal nerve distribution. She had significant impairment of standing on her right heel. CBC, AST, ALT, Creatinine, SPEP, UPEP, CK, CTD cascade, Paraneoplastic panel, Cryoglobulins, HIV screen, ACE level were negative or unremarkable. CSF analysis showed Protein 60, glucose 71, 5 WBC, 0 RBC, negative cytology, no OCB, Normal IgG index. NCS/EMG showed chronic right lumbosacral plexopathy with most severe changes in distal peroneal innervated muscles. MRI of the lumbosacral plexus showed Heterogeneous increased T2 signal and enhancement in the right sciatic nerve, predominantly involving the peroneal division. There was also Increased T2 signal and enhancement of the right peroneal nerve and its branches, as well as a few fascicles of the tibial nerve. QST shows reduced cooling in the right foot that normalized in the leg, Hyperalgesia in the right foot and leg, Normal touch pressure and vibration in the right foot.

What is your differential diagnosis? Next steps

CASE # 12

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University of Pittsburgh

A 9 month old with hepatomegaly, anemia and arrest of motor development

This boy presented at about 9 months of age, when he developed a viral infection and was noted on physical exam to have hepatomegaly. A complete blood count revealed anemia, with a hemoglobin of 4 mg/dL and transaminases were elevated. He went on to have progressive liver failure with portal hypertension and ascites. He concomitantly developed arrest of developmental skills, low muscle tone, and cachexia. An echocardiogram at about 13 months of life demonstrated moderate left ventricular dilation, left atrial dilation, and borderline right atrial and ventricular dilation.

He was born after an uncomplicated pregnancy and delivered at term. His initial development was normal; he sat independently at six months and pulled to stand at 8 months, but never ambulated, and family noticed progressive cachexia from around the time of onset of his liver disease. There was no history of liver, muscle, or other genetic disorder in his family, and he had two healthy full siblings and one half-sibling. He began to receive physical and occupational therapies shortly after his diagnosis. On examination at 15 months of age he had jaundice and

icterus, ascites, upper extremity telangiectasias, hepatomegaly and splenomegaly, low muscle bulk and diffuse severe hypotonia with at least antigravity strength in all extremities and otherwise normal neurologic examination. A creatine kinase level was not available.

Cardiac and liver biopsies were positive for PAS positive inclusions that were diastase resistant. Subsequent skeletal muscle biopsy showed abnormal fiber size variation with internalized nuclei. Many fibers had a granular appearance on Gomori trichrome stain, and these fibers showed increased granular PAS positive staining that was incompletely digested with diastase.

What is your differential diagnosis and what would you do next?

CASE # 13

Shruti M Raja, MD
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A 67 year old woman with "myasthenia gravis" presenting for management

A 67 year old woman was referred for management of myasthenia gravis 6 months after developing subacute finger extensor weakness, dysarthria, and oropharyngeal dysphagia necessitating gastrostomy tube placement. No neck or limb pain was present, though she endorsed some paresthesias and numbness of the right arm and leg. She had no respiratory complaints. Acetylcholine receptor binding antibodies were positive, however, five plasma exchanges and intravenous immunoglobulin infusion at 2 gm/kg did not substantially improve her symptoms. Five months of high dose prednisone resulted in some improvement in dysarthria but continued dependence on gastrostomy for nutrition. Response to pyridostigmine was equivocal. Her past medical history was remarkable for congenital right trochlear neuropathy, tic disorder, Meige syndrome treated with facial botulinum toxin injections and cervical spondylosis with myelomalacia.

Initial examination at 6 months after symptom onset revealed vitiligo that was most prominent in the lower extremities. There was bilateral ptosis with mild eye closure weakness, right-sided hypertropia, and flaccid nasal dysarthria with tongue weakness and reduced palate elevation. Strength was normal save for mild weakness of elbow flexion, elbow extension, and wrist extension with severe weakness of finger extension and normal strength of deep and superficial finger flexion. Prominent metacarpophalangeal contractures were present bilaterally. Posture was mildly kyphotic. Sensory examination was normal in the face and extremities.

Corticosteroids were gradually tapered over the next 6 months to 20mg daily and by 12 months after onset, dysphagia had improved to permit limited oral intake. Repeat examination at that time was remarkable for evolution of mild weakness of shoulder abduction and atrophy of the antebrachial and intrinsic hand muscles. Prominent metacarpophalangeal contractures persisted.

By 18 months, she developed shoulder girdle weakness with difficulty performing overhead tasks. Examination revealed additional weakness in shoulder girdle muscles (internal and external rotation, shoulder abduction) as well as elbow flexors and extensors.

Several additional diagnostic tests were performed at this time. What is the differential and what would you do next?

CASE #14

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15 year old with progressive weakness

This is a 15-year-old girl, who since the age of 8 years developed slowly progressive weakness, occurring intermittently. She had been always actively involved in sports. However, since age 14, she noted occasional problems walking up stairs, and arising from a sitting position or from the floor. Currently, her lower extremities are affected more than her upper extremities. Her weakness is worse in the morning, and she has some improvement after being up for a short while. Yet, she wears out with activity or towards the end of day. Lately she has had minimal ptosis on the right more so than the left eye. Her voice gets hoarse faster than her peers with excessive use of her voice.

She was the product of a cesarean section for breech presentation, following an uncomplicated pregnancy. She had normal milestones. She walked on her toes until 2-3 years of age. Motor function was essentially normal from ages 4-7 years. However, she was never able to do a cartwheel, as her legs would bend during attempts. She has frequent and impairing sharp headaches, with no other associated symptoms. She also has a tremor in both hands. She is doing well in school and is taking honor courses. She has not had any learning difficulties. Her parents and brother are alive and healthy. There is a history of tremors in her maternal aunt and maternal great aunt.

Examination revealed minimal ptosis bilaterally, slightly more on the right than the left, but without eye opening weakness. Her strength was decreased proximally in upper and lower extremities: 4+/5 in shoulder abductors and elbow flexors; 4-/5 in hip flexors and adductors, 4/5 hip extensors and abductors. Reflexes were trace throughout except in both patellar tendons which were absent. Normal casual gait. Hyperlordotic stance. Able to walk on her toes, but not her heels. Able to ascend stairs 2 steps at a time with alternating legs. Decreased hip excursion when running. Low jump.

CK level, lactate, electrolytes were normal. Normal CBC. Acetylcholine receptor and MuSK antibody titers were negative. Anti-titin and anti-LRP antibodies were negative. MRI of the thoracic and lumbar spine were normal. A diagnostic study was performed.

CASE #15

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36 year-old woman with "CMT"

A 36-year-old female was referred to neuromuscular clinic for Charcot-Marie-Tooth disease.

Her past medical history was significant for Achilles tendon lengthening procedures at age 4 and 8 years and a hip surgery at age 14. Family history was non-contributory.

Pregnancy and birth were unremarkable. She could "cruise" (walk only by holding onto furniture) at 17 months and was never able to ambulate completely independently.

She reports bilateral mild distal hand weakness and severe proximal and distal lower extremity weakness. She holds on to furniture to walk indoors and uses and a motorized scooter to mobilize outside her home. She uses ankle foot orthoses for bilateral foot drop but nevertheless falls frequently. She describes decreased sensation in both legs up to the knees. In addition, for many years now, she has been experiencing binocular horizontal diplopia as well as fluctuating left more than right eyelid ptosis. She reports myalgias, mainly with physical activity, since age 8.

From the age of 2 to 4 years old, she suffered from 2-3 episodes per year of vomiting and lethargy, associated with falls, weakness and myalgias which recovered over weeks.

Since age of 14, she has experienced three episodes of rhabdomyolysis triggered by hip surgery and swimming. These episodes were associated with respiratory failure requiring ventilation and acute renal failure requiring hemodialysis.

On examination, she demonstrated moderate left more than right ptosis. Extraocular movements were mildly limited for up-gaze and lateral gaze and were associated with horizontal diplopia. Motor exam revealed mild symmetric atrophy of the intrinsic hand muscles and of the anterior and posterior compartments lower leg. In the hands, mild joint contractures were observed at the proximal interphalangeal joints. Scapular winging and myotonia were absent. Segmental power examination demonstrated severe symmetric bilateral weakness of wrist and intrinsic hand muscles: EDC, FDI and APB all 0/5 and FDP and FPL 3/5. Proximal upper extremity power was preserved. Power in the lower extremities was as follows (Right/Left): iliopsoas 3/3, hip abduction 4-/4-, hip adduction 3/3, knee flexion 4/4, quadriceps 5/5, ankle dorsiflexion 0/0, ankle plantar flexion 1/1 and inversion, eversion, EHL, toe flexion and extension all 0/0. Deep tendon reflexes were absent and Babinski sign was not observed. Pes cavus and hammer toes were absent but foot length was reduced. On sensory examination, there was decreased pinprick in a glove and stocking distribution up to the mid-hand and distal one-third of the legs. Vibration was significantly reduced in the feet and mildly reduced in the hands.

Recent CK was 267 U/L. A left biceps muscle biopsy at age 18 demonstrated chronic partial denervation with re-innervation. Recent EMG was remarkable for a severe axonal sensorimotor polyneuropathy involving both the lower and upper extremities.

A diagnostic test was performed.

CASE #16

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31 old woman with painful swelling of the right chest wall

History and examination:
A 31-year-old woman with a past history of T1-T8 thoracic laminectomy for thoracic myelopathy presented with an episode of painful swelling in the right chest wall. Symptoms resolved after 1-2 weeks. A month later she presented with a similar episode of painful swelling in the left chest wall and posterior hemithorax. Symptoms again resolved within 1-2 weeks spontaneously. 3 months later she developed another episode of painful swelling and lumpiness of the right chest wall and posterior hemithorax which resolved without intervention.

During these episodes, there was no upper or lower extremity weakness, bulbar symptoms, or dark urine. Neurological examination during one of these episodes showed a young woman, not in acute distress. She was alert, oriented with normal language and mentation. Cranial nerves were unremarkable, and motor exam showed thoracic kyphosis, and prominence of left shoulder blade swelling. Strength was normal in upper and lower extremities. Deep tendon reflexes were symmetric. Sensations were intact, and gait was normal. Musculoskeletal examination showed hallux valgus deformity of big toes bilaterally. Past history is significant for right total hip arthroplasty followed by two revisional surgeries for excision of heterotopic bone. Family history was unremarkable. There was no prior history of trauma, bleeding diathesis, fever, or other systemic complaints.

Investigations:
Blood count, liver function, creatine kinase, aldolase and blood work for connective tissue disorders were normal. C-reactive protein (CRP) was elevated at 6.4. MRI of the chest wall showed diffuse edema and non-specific enhancement of the chest wall musculature, which were reported as possible myositis. Trapezius, latissimus dorsi and serratus anterior muscles were the most affected chest wall muscles. Nerve conduction study (NCS) and Needle electrode examination (NEE) were normal. Right latissimus dorsi muscle biopsy showed no increase in endomysial connective tissue, no inflammatory infiltrates, good distinction of fiber types, and a normal distribution of fiber types. X-rays of the hip showed heterotopic ossification along the soft tissues. MRI of the thoracic spine revealed postsurgical changes related to T1 through T8 laminectomies. In addition, thoracic spine imaging showed heterogeneous enhancement of the surgical site soft tissues and granulation tissue along the posterior elements. Indeterminate chunky soft tissue calcifications were noted in X-rays of both the knees. X-ray of the left foot showed congenital fusion of the 3rd, 4th, and 5th distal interphalangeal (DIP) joints and the 1st interphalangeal (IP) joint.

What is the differential diagnosis?