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Clinical Reasoning: Adult Patient Presenting With Spine Pain Following a Motor Vehicle Accident

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Abstract

A 52-year-old female with a complex past medical history, including history of consanguinity, developed refractory, uncontrollable spine pain following a motor vehicle accident two years prior to presentation. There were no well-defined findings on clinical examination. She was found to have mildly elevated serum CPK levels and spine imaging revealed fatty replacement and atrophy affecting predominantly lumbar paraspinal muscles. Initial EMG sampling of multiple limb muscles was normal. However, follow up concentric needle examination sampling paraspinal and trunk muscles showed abundant myotonic discharges, fibrillations and positive sharp waves, and myopathic motor unit action potential changes. This pattern of neurophysiological abnormalities prompted the search for a myopathic disorder, which was ultimately confirmed with additional studies. This case highlights the critical role of

neurophysiological evaluation of paraspinal and other trunk muscles in the disambiguation of clinical and imaging data, helping to establish the diagnosis of a rare but treatable myopathy at early disease stages.

Section 1

A 52-year-old female with depression, anxiety, non-insulin dependent diabetes, obesity, asthma, obstructive sleep apnea, gastroesophageal reflux, left ventricular hypertrophy, and right sciatica, as well as past medical history of carcinoma in situ of breast, was referred for evaluation of unexplained and refractory spine pain since a motor vehicle accident two years earlier. She reported constant, severe, non-radiating lumbar spine pain, exacerbated with standing and walking, and had been unable to take walks or go hiking, as she did before. She denied limb weakness but endorsed shortness of breath with moderate exertion and occasional choking on food, and episodic tingling and numbness of right leg and of both hands, all of which had an insidious onset around the time of the accident. She was independent for all basic ADLs. Her family history was significant for being the offspring of consanguineous parents. On physical examination she had intact function of all cranial nerves. Body habitus precluded inspection of the proximal and trunk muscles, but distal limb muscles showed normal mass. Manual muscle testing showed hip flexors 4+/5 with fluctuating effort, and otherwise normal muscle strength throughout. Reflexes were 1+ diffusely without post-exercise facilitation. There was no abnormal response to muscle percussion or action myotonia. She had mildly decreased perception of pinprick and light touch sensation in right sided limbs, without a defined anatomical pattern. Finger-to-nose and heel-to-shin tests were normal. The get up and go test was passed with minimal difficulty. Gait was slow, antalgic, with mild hyperlordosis of the lumbar spine.

Her serum creatinephosphokinase (CPK) level was mildly elevated (526 units/L) but an electromyographic (EMG) study was normal (Table). Non-contrast MRI studies of the cervical and thoracic spines showed multilevel degenerative changes without cord or root compression. Non-contrast MRI studies of the lumbosacral spine showed a small disc protrusion at left L3-L4 space, severe narrowing of the right L3-L4 foramen, and atrophy and severe fat replacement of paraspinal musculature, also present with less severity at mid thoracic level (Figure). Reporting was conducted according to local IRB guidelines, the declaration of Helsinki, and the patient provided informed consent.

Questions for consideration:

1. *What are the red flags in this presentation?*
2. *What is the importance of her imaging findings?*
3. *What is the significance of mildly elevated CPK?*

GO TO SECTION 2

Section 2:

The patient in this vignette presents primarily with back pain. Spinal pain, and more specifically lumbar spinal pain, is highly prevalent and caused predominantly by structural musculoskeletal disorders, but its etiologic spectrum includes potentially harmful causes.¹ Neurological causes of spine pain include pathologies affecting the spinal roots or paraspinal muscles. With spine pain of short duration, or in the absence of red flags, imaging studies are usually unnecessary.² In this case a red flag in favor of imaging is her protracted history of refractory spine pain. Spine imaging may reveal atrophy (decreased cross-sectional area) and/or fatty replacement of paraspinal muscles, both of which can be a manifestation of normal, age-related loss in muscular mass and function (sarcopenia).³ Imaging changes related to sarcopenia are notorious in the spine

muscles, affect all spine levels, and correlate with common structural pathologies.⁵ Fatty muscle replacement represents up to 20-30% of muscle volume in older age groups.⁴ However, these changes may also be a manifestation of muscular disease.⁶ The imaging boundaries between age-related changes and pathological conditions are insufficiently established and distinction is highly based on the clinical context. In this case, the relatively young age of the patient is inconsistent with sarcopenia as cause of the extensive fatty replacement found on imaging studies.

CPK is a muscular enzyme central in the anaerobic production of ATP and is considered a useful marker of muscle disease. Mild serum CPK elevations are, however, non-specific and may be due to non-myopathic etiologies such as motor neuron disorders, cardiac causes, physical activity, or trauma. HyperCKemia is defined as a CPK level above 1.5 times the upper limit of normal according to ethnicity and gender.⁷ Women and people of non-black ethnicity tend to have lower CPK levels. In this case the combination of high CPK serum level, extensive fatty replacement of paraspinal muscles, and lumbar hyperlordosis suggested a potential neuromuscular cause.

Questions for Consideration:

1. *What is the role of EMG?*
2. *What is the significance of her family history?*

GO TO SECTION 3

Section 3:

This patient's previous EMG showed normal nerve conduction studies and concentric needle examination of several limb muscles (Table). However, a follow up concentric needle examination study aiming to include sampling of trunk muscles showed frequent myotonic discharges in those muscles along with profuse fibrillations and positive sharp waves. There

were also myopathic motor unit action potentials without significant abnormalities in the motor unit recruitment pattern in trunk muscles. Importantly, there were no needle EMG abnormalities detected in proximal and distal limb muscles, corroborating the findings of the first EMG study (Table). The right median neuropathy at the wrist was considered an incidental finding. Her family history of consanguinity confers an increased risk to recessively inherited genetic disorders.

Questions for Consideration:

1. *Based on these findings what are the diagnostic considerations*
2. *What are the next steps?*

GO TO SECTION 4

Section 4:

EMG findings indicated the presence of a myopathic disorder with electrical myotonia and, in the context of this patient's family history of consanguinity, recessively inherited myopathies became a strong diagnostic consideration. Electrical myotonia without clinical myotonia, as neurophysiologic manifestation of a non-dystrophic myopathy, points to a limited number of causes, such as necrotizing myopathies (i.e. immune mediated necrotizing myopathies), several muscle channelopathies, and toxic myopathy caused by statins, chloroquine, cyclosporine, colchicine, and other agents. Electrical myotonia may also be seen in myofibrillar and myotubular myopathies, and it is also a typical feature of acid-maltase deficiency (Pompe disease). In the clinical context of this patient's family history of consanguinity, late-onset Pompe disease (LOPD) became a strong diagnostic possibility. Panel genetic testing was sent to include DNA analysis of the *GAA* gene. Results showed one homozygous pathogenic variant (c.-32-13T>G) and one homozygous variant of uncertain significance (VUS) (c.510C>T) in *GAA*, and two additional VUS in different genes. Biochemical assays confirmed reduced activity of

lysosomal acid alpha-glucosidase (GAA) (0.51 $\mu\text{mol/L/hr}$; normal $> 2.10 \mu\text{mol/L/hr}$), confirming the diagnosis of Pompe disease. The patient was then referred for multidisciplinary care including pulmonary, cardiac, ENT evaluation, and genetic counselling, and was recommended to start enzyme replacement therapy (ERT) with avalglucosidase alfa.

Discussion

Pompe disease is an autosomal recessive glycogen storage disease caused by a deficiency in GAA, leading to the inability to break down lysosomal glycogen.^{8,9} The resulting deposition of glycogen in various tissues, such as cardiac, skeletal, and smooth muscle causes cardiomyopathy, muscle weakness, hypotonia, and respiratory failure.¹⁰ Pompe is often thought of as an infantile disease, thus the rarer late onset form (onset after 1 year of age) is frequently overlooked. While the presentation of LOPD is highly varied, the most common presenting symptoms include proximal lower extremity and trunk weakness with early compromise of respiratory muscles.⁹ Other features may include dysarthria, dysphagia, facial muscle involvement, vertebral fractures, scoliosis, sensorineural hearing loss, neuropathies, paresthesias, pain, fatigue, and an increased risk for aneurysms and thromboses.^{8,11} The presence of progressive limb girdle weakness with respiratory impairment and elevated CPK serum level are suggestive of LOPD and warrant further testing. The diagnosis is based on measurement of GAA activity, usually in dried blood spots, with confirmatory genetic testing.¹² While previously a fatal condition, since 2006 ERT has become a disease-modifying treatment of Pompe Disease with beneficial effects on walking, rate of respiratory deterioration, quality of life and survival.

The diagnosis of LOPD is often delayed. A study of 38 LOPD patients showed that the mean delay from onset of symptoms to diagnosis was 10.4 years, despite the fact that the majority of cases presented with hyperCKaemia and limb girdle muscle weakness,¹³ which is the most

common presentation.¹² Other, less typical, phenotypes of LOPD may occur including rigid spine syndrome, scoliosis, low body weight, cardio-cerebrovascular symptoms or even bulbar and cranial nerve symptoms.¹¹ A study of 137 patients with asymptomatic or minimally symptomatic hyperCKemia found 2.2% caused by LOPD, suggesting this diagnosis should be considered in relatively benign scenarios.¹⁴ Some patients may exhibit early imaging findings of fatty replacement in paraspinal and proximal limb muscles,¹² similar to our case. In routine clinical practice, most patients with isolated CPK elevation eventually undergo an EMG to screen for myopathy. Thus, it is crucial to incorporate sampling of paraspinal and other trunk muscles in the electrodiagnostic planning in this context. Indeed, a study of 29 patients with Pompe disease, found 72% of the adult patients had electrical myotonic discharges, which were often isolated to the paraspinal muscles.¹⁵

Our case illustrates that the myopathic burden in LOPD is commonly restricted to trunk as opposed to limb muscles. Evaluation of those muscle groups clinically, radiologically, and neurophysiologically critically increases the diagnostic yield at earlier stages of the disease in which ERT might have optimal efficacy in achieving disease modification.

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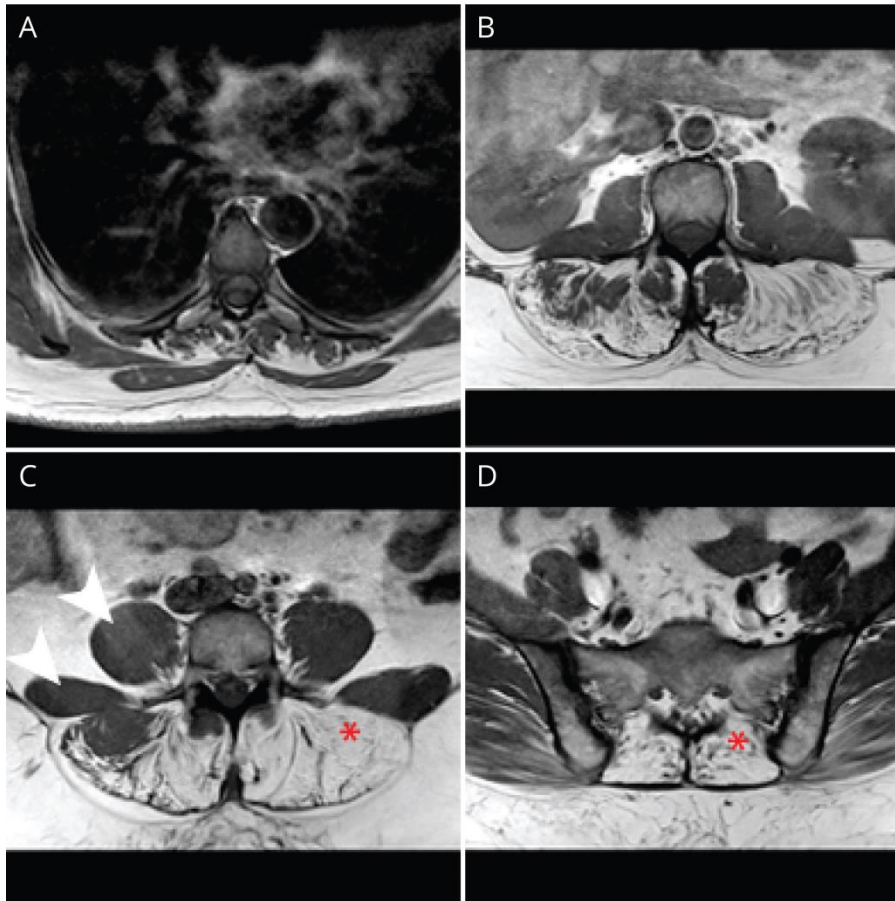
Table: EMG results:

Muscle	Side	January 2021				December 2021			
		SA		MUAP	RP	SA		MUAP	RP
		Fibs/PSW	Other			Fibs/PSW	Other		
Tibialis anterior	R,L	0	0	N	N	-	-	-	-
Medial gastrocnemius	R,L	0	0	N	N	-	-	-	-
Vastus lateralis	R	0	0	N	N	0	0	N	N
Vastus lateralis	L	0	0	N	N	-	-	-	-
Biceps femoris-lh	R,L	0	0	N	N	-	-	-	-
Gluteus medius	R,L	0	0	N	N	-	-	-	-
Deltoid	R	-	-	-	-	0	0	N	N
Trapezius	R	-	-	-	-	1+	Myotonia	MP	N
1st dorsal nterosseous	R	-	-	-	-	0	0	N	N
Tensor fascia lata	R	-	-	-	-	1+	0	MP	N
Iliopsoas	R	-	-	-	-	1+	Myotonia	MP	N
Lumbosacral-PSP	R	-	-	-	-	2+	Myotonia	-	-
Cervical-PSP	R	-	-	-	-	2+	Myotonia	-	-

Abbreviations: R: right; L: left; SA: spontaneous activity; MUAP: motor-unit action potential; RP: recruitment pattern; Fibs/PSW: fibrillations/positive sharp waves; MP: myopathic potential; N: normal. *Muscles:* Biceps femoris-lh: Biceps femoris, long head; Lumbosacral -PSP: Lumbosacral paraspinal; Cervical-PSP: Cervical paraspinal.

Figure legend:

Axial T1 MR images of lower thoracic (A), upper lumbar (B), mid-lumbar (C), and lower lumbar (D) spine. Note the severe atrophy/fatty replacement of the paraspinal musculature (red asterisks), with sparing of quadratus lumborum and psoas (white arrow-heads).



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