Sleeprelated movements disorders and REM sleep behavior disorder are the hallmarks of RBD, followed by cognitive, behavioral, and psychiatric disorders such as depression, anxiety, and substance abuse, which may occur in up to 70% of patients. Cognitive impairment and depression can be seen in up to 90%. Depression has a 10-15% prevalence in the general population. In RBD, 75% of patients have depression, and 60% have anxiety. 

### Pearls & Oy-sters

**PEARLS**
- RBD has an estimated prevalence of 0.02-0.12% in the general population.
- It may be underdiagnosed and undertreated.
- Sleep-related movements disorders and REM sleep behavior disorder are the hallmarks of RBD, followed by cognitive, behavioral, and psychiatric disorders such as depression, anxiety, and substance abuse.
- Cognitive impairment and depression can be seen in up to 90% of patients. Depression has a 10-15% prevalence in the general population. In RBD, 75% of patients have depression, and 60% have anxiety.

**OY-STERS**
- Patients presenting with nocturnal symptoms should be screened for RBD.
- The presence of a family history of RBD is a strongly positive predictor of RBD.
- Patients with REM sleep behavior disorder should be screened for REM sleep-related injuries.

### Patient 1

A 58-year-old woman began to have symptoms at age 44 of slowly progressive proximal muscle weakness predominantly affecting the lower limbs. She had difficulty climbing stairs and standing from a seated position. She had undergone evaluation of asymptomatic CK elevation, noted a year before, and was diagnosed as mononucleosis. His complaints of muscle weakness were not examined as it was determined this would not add to the diagnosis. GAA activity was 1.3 (normal 10–49 pmol/punch/h) and he was found to have 2 heterozygous mutations at c.-32-13T>G and c.1841C>A in the GAA gene.

### Patient 2

A 71-year-old man began to have slowly progressive proximal lower limb muscle weakness at age 51. His symptoms began with difficulty climbing stairs. He was diagnosed at age 52 with SMA type III following an EMG reporting neurogenic changes and a muscle biopsy from a hamstring muscle that demonstrated denervation atrophy. Staining for PAS and acid phosphatase was normal. Genetic testing for SMA was not performed. Serum CK was 208 U/L (normal range 70–185). There was no family history of muscle disease. On examination, there was normal strength in the upper extremities with moderate weakness of hip flexion at 3/5, hip abduction 3–4/5, hip adduction 3–4/5, and hamstrings 4/5. He was referred to our EMG laboratory at age 71 for evaluation of a right lower limb radiculopathy. EMG showed myotonic discharges in the anterior tibialis, medial gastrocnemius, ilioptos, tensor fasciae latae, and biceps brachii muscles. The paraspinal muscles were not examined as it was determined this would not add to the diagnosis. GAA activity was 0.6 (normal range 10–49 pmol/punch/h) and he was found to have 2 heterozygous mutations at c.-32-13T>G and c.1841C>A in the GAA gene.
γ-glutamyl transpeptidase. Liver ultrasound and biopsy at an outside facility were normal. Serum CK was elevated at 1,373 U/L (normal range 70–185). There was no family history of muscle disease. His examination demonstrated a muscular man with mild weakness (4/5) of iliopsoas muscles. EMG performed at our institution demonstrated prominent myotonic discharges isolated to the lumbar paraspinal muscles. Iliopsoas, tensor fascia latae, and cervical and thoracic paraspinal muscles demonstrated myopathic changes without spontaneous activity or myotonic discharges. GAA level was 1.4 (normal range 10–49 pmol/punch/h) and he was found to have 2 heterozygous mutations, c.-32-13T>G and c.877G>A, in the GAA gene.

DISCUSSION Pompe disease (glycogen storage disease type II) is a deficiency of acid-α-glucosidase, an enzyme that degrades lysosomal glycogen. A deficiency of the enzyme leads to deposition of glycogen in the heart, skeletal, and respiratory muscles. In the infantile-onset form of the disease, symptoms present in the first month or year of life with hypotonia, macroglossia, generalized muscle weakness or delayed motor milestones, liver failure, feeding difficulties, failure to thrive, and respiratory distress, with or without cardiomegaly. There is progressive proximal muscle weakness and respiratory insufficiency without cardiac involvement in late-onset (i.e., childhood, juvenile, and adult-onset) Pompe disease. The muscle weakness predominantly affects the lower limbs and can be specific to the iliopsoas muscles. Presentation is usually in the second to the seventh decade of life.

Our patients demonstrate key diagnostic features that should lead the clinician to consider adult-onset Pompe disease early in the workup of a myopathy. This is important as enzyme replacement therapy is available. These key features include 1) predominant involvement of hip flexion weakness at the onset of the disease; 2) EMG findings of myotonic discharges predominating in the lower extremities; and 3) isolated myotonic discharges to one or more paraspinal levels when EMG of the limb is unrevealing. Although myotonic discharges are non-specific and can be seen in many disorders, including myotonic dystrophy, inflammatory myopathies, and some inherited myopathies, the presence of myotonic discharges (figure 1) in a specific distribution with the characteristic clinical features is highly suggestive of acid maltase deficiency. None of our patients presented with exercise-dependent weakness.

The clinical presentation of late-onset Pompe disease has been previously described as variable in presentation, laboratory values, and EMG patterns of abnormality. There are no reports regarding the electrophysiologic specificity of myotonic discharges isolated to the lower limbs despite the well-known involvement of lower extremity weakness. In an earlier case report of 4 patients with Pompe disease, extensive testing of muscles demonstrated that 3 of the 4 patients had myotonic discharges predominantly in the torso and proximal limb muscles. Examination of our patients demonstrated the predilection of the disease to affect the lower extremities, particularly early in the course of the illness, and their EMG findings of myotonic discharges correlated well with the examination findings of predominantly lower extremity weakness.

Predominant findings of myotonic discharges in the paraspinal muscles in Pompe disease have been reported. However, we further recommend that all 3 paraspinal levels be sampled as one particular level may not be affected. Our third case demonstrates the importance of multilevel evaluation of the paraspinal muscles, especially when the EMG is otherwise unrevealing. A recent study that reviewed the clinical and neurophysiologic spectrum of 38 patients reported that 9% of the patients had a normal EMG. The study did not include paraspinal muscle evaluation of patients whose EMG was normal and therefore it is unknown whether myotonic discharges may have been present in the paraspinal muscles of these patients. There is a case report of a patient who presented with respiratory failure whose EMG was abnormal in only the thoracic paraspinal muscles and the patient was later found to have Pompe disease on muscle biopsy.

It should also be noted that in our patients respiratory complaints were not part of their presentation and all had a normal forced vital capacity; therefore, the lack of respiratory muscle involvement should not guide the clinician away from this diagnosis. The association of respiratory insufficiency and degree of weakness or muscle involvement has been previously noted to have poor direct correlation. Muscle biopsy can be nonspecific in these patients,
as illustrated in our first and second cases, where the biopsy demonstrated denervation atrophy. The first 2 cases presented were misdiagnosed as SMA, for which there is no treatment.

All of our patients were ambulatory at the time of their diagnosis; one used a walker and the other used a cane. Diagnosis at an early presentation may prove to be important with the advent of enzyme replacement. An algorithm (figure 2) is proposed to facilitate the diagnosis. There should be a high index of suspicion for late-onset Pompe disease when predominant lower extremity weakness and myotonic discharges are noted on EMG examination as enzyme replacement is available for these patients and enzyme testing is readily available and relatively inexpensive.

**AUTHOR CONTRIBUTIONS**

Tania Beatriz Beltran Papsdorf: drafting/revising the manuscript, accepts responsibility for conduct of research and final approval. James Francis Howard Jr.: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval, acquisition of data. Nizar Chahin: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval, study supervision.

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