PALLIATIVE CARE
CASE OF THE MONTH

"An older woman with progressive decline in function: What are those weird movements?"

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Case: Our service was consulted to see a 78-year-old woman to manage her pain. She had been admitted to the hospital with generalized weakness, malaise, breathlessness and decline in ability to care for herself. She had since been in and out of hospitals and rehabilitation centers after a fall and a hip fracture.

PMH included coronary artery disease, with revascularization, atrial fibrillation, valvular heart disease and pulmonary hypertension.

She reported reduced sensation in her feet and hands and described "jumping and shaking" from shooting and lancinating pain in her hands and feet as well as a deep ache in the proximal muscles of her arms and legs. Symptoms were worse at night and were associated with cramping sensations. She and her spouse noted frequent movement of her arms and legs at night. Walking around improved her symptoms.

The patient was on gabapentin, 800 mg three times per day and tramadol 100 mg q 4 hours as needed. She had been started on duloxetine in the hospital, but it was stopped when she reported ill effects.

On exam, she appeared depressed. Muscles were tender at multiple sites in arms and legs, more proximally than distally. She had decreased sensation in a stocking glove pattern and Romberg showed poor balance imbalance. Strength was normal except for 4/5 right hip flexion (site of hip fracture).

Lab evaluation showed a HbA1C = 7.5 Ferritin 6 mcg/L Iron /TIBC 20/456= 4% and B12 1160.

Given her deep muscle aching and the frequent movement of arms and legs both at night and during the day we thought she had restless legs syndrome.

She was prescribed ropinirole 0.25 mg at night. We recommended weaning gabapentin and initiating venlafaxine. The following day she reported that she had slept better. Ferrous sulfate was started by the internal medicine service. She was then discharged to a rehabilitation center.

During a follow-up phone call two weeks later, she reported that her pain had largely subsided and she was no longer experiencing the abnormal movements during the day or night. Her sleep had improved markedly and she was preparing to leave the rehab center for home.

Discussion: Restless legs syndrome (RLS), also known as Willis-Ekbom disease, is a common disorder. Patients have an urge to move their legs, accompanied by uncomfortable sensations. The symptoms occur at rest, are relieved by movement, and are worst in the evening and at night. Involuntary movements may occur at night or during the day. A response to dopaminergic treatment helps confirm the diagnosis.

Patients often have difficulty describing their discomfort. They often report a deep ache in their muscles and experience a variety of dysesthesias with sensation described as crawling, burning or prickly. Fifty to eighty percent describes the sensation as pain. Symptoms can be bilateral or unilateral. While classically involving the legs, symptoms in the arms occur in many, up to 48% in one study. While symptoms are most common at night, they are often present during the day. The discomfort is relieved at least partially by movement.

Although not required for diagnosis, approximately 80% of patients with RLS have involuntary, repetitive leg movements during sleep. These movements are known as periodic limb movements (PLM) and can occur during sleep and wakefulness. PLM can occur independently of RLS and is seen in other disorders. During sleep, it most commonly presents as dorsiflexion of the ankles or flexion of the knees and hips, but can also present as flexion of muscles in the arms.. During wakefulness, patients often experience more rapid, involuntary twitching of muscles in their legs when sitting or lying, similar to myoclonic jerks.

RLS is common and often not recognized. Hening, et al, administered a screening questionnaire to 23,000 patients of primary care physicians in US and Europe. Of these, 2232 (9.6%) met the diagnostic criteria for RLS. Of these, 551 experienced symptoms that occurred 2 or more times per week and had negative impact on the quality of their life. Only 13.6 % had been diagnosed with RLS. Their symptoms had been ascribed to a variety of conditions included back pain, depression, insomnia/sleep disorder, anxiety, nocturnal cramps, fatigue, neuropathy and radiculopathy. The symptoms may also be ascribed to akathisia from neuroleptics, myoclonus or chronic pain syndromes such as fibromyalgia.

RLS often occurs as a primary syndrome and has a genetic basis in about 50% of patients. However, a number of disorders are associated with the syndrome. Most importantly, iron deficiency is common, with serum ferritin < 75 mcg/l the measure best correlated with RLS. It is very prevalent in uremic patients and commonly persists while on dialysis. It affects 15-25% of pregnant women, usually subsiding after birth. Antihistamines, dopamine antagonists, and antidepressants such as mirtazapine and SSRIs can aggravate symptoms.

(Discussion Continued)

Treatment of RLS includes correction of iron deficiency. Moderate exercise and activities that increase mental alertness during the day may be helpful. Patients with persistent and frequent symptoms should be treated with dopamine agonists (ropinirole, pramipexole, and rotigotine) or alpha2 delta calcium channel ligand (gabapentin, gabapentin enacarbil, and pregablin).

Patients need to be aware that treatment with dopamine agonists may cause augmentation with symptoms becoming more intense, occurring earlier in the day, or spreading to other limbs. Risk factors include higher dose, longer treatment duration and untreated iron deficiency. Augmentation has not been associated with alpha2 delta calcium channel ligands.

Patients on dopamine agonists can also develop impulsive behavior-pathological gambling, impulsive shopping or hyper-sexuality. This has been reported to affect 6-17% of patients, on average 9 months into treatment.

Choice of treatment depends on severity of the RLS age. In general, while dopamine agonists are often rapidly effective and initially well tolerated, the risks of augmentation and impulse control disorder make alternative treatments attractive.

Patients who do not respond to maximum recommended doses of the above agents may yet respond to combination therapy. Opioids can also be effective. A mean daily dose of about 20 mg oxycodone was effective in one trial. Methadone at dose of 10 mg per day was effective in another.

The RLS/WED Foundation updated detailed recommendations for treatment in 2013. These can be found at: http://dx.doi.org/10.1016/j.mayocp.2013.06.016.

The Foundation's website (http://www.rls.org/) has a variety of resources for patients and clinicians.

References:

1. Kerr, S, et al," Descriptors of Restless Legs Syndrome Sensations" Sleep Medicine 13: 409-413, 2012.
2. Hening, W, et al, "Impact, diagnosis, and treatment of restless leg syndrome in a primary care population: The REST primary care study" Sleep Medicine 5: 237-246, 2004.
3. Silber, WH., et al "The Willis-Ekbom Disease Foundation Revised Consensus Statement on Treatment of Restless Legs Syndrome" Mayo Clinic Proc. 88: 977-986, 2013.
4. Karroum, E.G., et al, "Sensations in Restless Legs Syndrome" Sleep Medicine 13:402-408, 2012.
5. Trenkwalder, C, et al, "Restless Legs Syndrome", Lancet Neurol. 4:465-475, 2005