RLS
Restless Legs Syndrome

Elise Anderson MD
Movement Disorders Fellow
Portland VA Medical Center – NW PADRECC
OHSU – Parkinson’s Center of Oregon
Case

45 year old man
CC: “I can’t sleep!”
• Legs feel funny, has to get up and walk around for relief
• “Funny” how?
  • Creepy crawly sensation, hard to describe . . .
  • Eventually falls asleep but awakened several times a night with discomfort
  • Sleepy during the day because of poor sleep, starting to affect his work
Features

Sensory symptoms:
• Creepy, crawly, tingly, painful, burning, achy . . .
• “Unpleasant, difficult to describe sensations”
• Like worms or bugs crawling deep in the muscle or water running under the skin
Usually affects both legs simultaneously
May be unilateral or alternating
Arms may be involved

Primary RLS

Four RLS diagnostic features:
1. an urge to move the legs,
2. that is present at rest,
3. relieved by movement, and
4. demonstrates a circadian pattern with peak symptoms occurring at night or in the evening
Secondary RLS

Medical conditions associated with RLS:
- Iron-deficiency anemia
- Peripheral neuropathy
- End-stage renal disease
- Pregnancy
- Commonly comorbid with Parkinson’s disease

Meds that can worsen RLS

- Medications
  - Tricyclic antidepressants
  - SSRIs
  - Monoamine oxidase inhibitors
  - Lithium
  - Antihistamines
  - Dopamine antagonists
- Other
  - Caffeine, smoking, alcohol
Background

- Prevalence: 5-10%
- The most common movement disorder
- Prevalence increases with age
- Age of onset is often < 30 years old
- Gradually progressive so age at diagnosis is often in mid-life

Quality of life impacts

- Poor sleep
- Daytime sleepiness
- Days of work missed
- Impacts on mood and social interactions
Pathophysiology: dopamine?

- Dopaminergic drugs are effective for RLS
- RLS and akathisia occur with dopamine antagonists
- Dysfunction of hypothalamic dopaminergic cells resulting in decreased CSF dopamine?
- Some imaging studies support central dopamine dysfunction in RLS: PET and SPECT studies conflicting results with increased, decreased, and unchanged receptor binding

Pathophysiology: iron?

- Strong association with iron deficiency
- Low iron studies in CSF
- MRI brain shows low iron in putamen and substantia nigra
Work-up

- History:
  - Four core diagnostic features
  - Often confused with hypnic jerks, peripheral neuropathy, periodic leg movements in sleep (PLMS)
- Neuro exam: normal if idiopathic
- Lab testing if indicated: CBC, serum ferritin, folate, serum chemistries, glucose, glycosylated hemoglobin
- Consider referral for EMG/NCV study
- Consider referral for polysomnography-not needed routinely

Sleep study in RLS

Polysomnography:
- Increased sleep latency
- Frequent nocturnal arousals or awakenings
- Reduced sleep efficiency
- Reduced total sleep time
- Increased number of periodic leg movements in sleep (PLMS)
RLS vs. PLMS

PLMs are involuntary movements measured by surface electromyography from the tibialis anterior muscle.

- PLMs are currently thought to reflect the amount of RLS motor symptoms
- But PLMs can occur in the elderly without causing any sleep disturbance and are a widely observed motor sleep phenomenon

Treatment

- Lifestyle modifications
  - Reduce EtOH, smoking, caffeine
- If possible reduce meds affecting RLS
- Sleep hygiene: reduce evening exercise, standardize bed time, reduce sleep interruptions
- If iron studies are low
  - Further workup
  - Ferrous sulfate 325 mg TID given concurrently with vitamin C (improves absorption)
  - Repeat labs q2-3 months
Dopamine agonists

- First line therapy
- Directly stimulate dopamine receptors
- **Ropinirole**: 1.5 to 4 mg/d-single or divided doses
- **Pramipexole**: 0.375 to 0.75 mg/d- single or divided doses
- Others: bromocriptine, apomorphine, cabergoline, pergolide (cardiac valve disease)

Dopamine agonist side effects

- Sleepiness
  - “Sleep attack”
- Orthostasis
- Nausea
- Augmentation
  - Higher doses:
  - Dyskinesias
  - Compulsive behavior disorder (gambling, shopping, pornography)
    - Rare but potentially devastating
Carbidopa/Levodopa

Combination pill (Sinemet)
- Levodopa – converted to dopamine by brain
- Carbidopa – stops breakdown of levodopa in blood
- Sinemet IR 25/100, half or full tab at bedtime
- Sinemet CR (controlled release) 25/100 at bedtime

BUT . . .
- Augmentation and rebound are common
- Consider using carbidopa as adjunctive or PRN only for intermittent RLS

Augmentation and Rebound

Augmentation
- Earlier onset of symptoms during the day
- Shorter latency to occurrence of symptoms when the patient is at rest
- Spreading of symptoms from the legs to other parts of the body
- Occurs in up to 70%

Rebound: recurrence of symptoms early in the morning
- Occurs in up to 30%
Other options

**Benzodiazepines**
- Best in mild RLS, younger patients
- Clonazepam 1 mg at bedtime

**Propanolol**
- 40-120 mg daily

**Opiods**
Effective for mild RLS, but with dependence and prescribing issues
- Tramadol 50 – 100 mg at bedtime
- Codeine (often in combination with acetaminophen) 30-60 mg at bedtime

Refractory RLS: higher potency opioids, may be required during day
- Oxycodone (5-15 mg), methadone (5-10 mg)
Anticonvulsants

**Gabapentin**
- 800-1800 mg/d
- Effective in hemodialysis patients
- Nausea, dizziness, somnolence

**Carbamazepine**
- 100-300 mg/d
- Nausea, dizziness, somnolence, liver toxicity

**Pregabalin:**
- 150 mg daily

Questions?
References

Adler CH, "Restless Legs Syndrome". Movement Disorder Society teaching files, movementdisorders.org.

