RLS
Restless Legs Syndrome

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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 opiods, 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

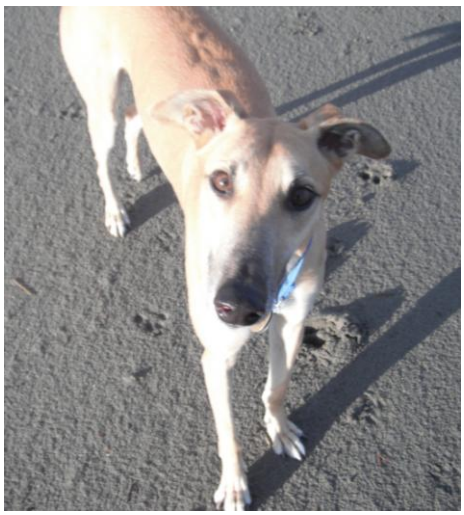
Carbamazepine

- 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.

Allen RP, Picchietti D, W.A. Hening WA. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med, 2003; 4:101–119.

Kohnen R, Allen RP, Benes H. Assessment of Restless Legs Syndrome—Methodological Approaches for Use in Practice and Clinical Trials. Movement Disorders 2007; (Suppl 18): 485–S494.

Trenkwalder C, Hening WA, Montagna P, et al. Treatment of Restless Legs Syndrome: An Evidence-Based Review and Implications for Clinical Practice. Movement Disorders 2008; 23: 2267–2302.