QUESTION 18 Movement disorder

A 68-year-old woman is prescribed haloperidol 2 mg nocte for treatment of delirium while hospitalised for treatment of advanced metastatic breast cancer. Two weeks after admission she becomes increasingly agitated and is noted to be constantly pacing around her bed. She complains of difficulty relaxing and feels she cannot keep herself still.

What is the most likely explanation of these symptoms?
A. Dystonic reaction.
B. Akathisia.
C. Anxiety/panic disorder.
D. Major depression.
E. Restless legs syndrome

**Dystonia**

Repetitive, patterned, twisting and sustained movements that may be either slow or rapid

Adverse extrapyrimidal effects that occur shortly after initiation of neuroleptic drug therapy

**Pathophysiology**
- Drug-induced alteration of dopaminergic-cholinergic balance in nigrostriatum
- Most drugs produce dystonic reactions by nigrostriatal dopamine D2 receptor blockade - leads to an excess of striatal cholinergic output.

**Clinical manifestations**
- Occur shortly after initiation of drug treatment
- 50% occur within 48 hrs
- 90% occur within 5 days of initiation of treatment
- Risk factors: Fhx of dystonia, recent hx of alcohol/cocaine use, treatment with potent dopamine D2 receptor antagonist (eg. Haloperidol)

**Signs**
- Oculogyric crisis (deviation of eyes in all directions)
- Buccolingual crisis
- Protrusion of tongue
- Trismus (tonic contraction of muscles of mastication)
- Forced jaw opening
- Difficulty in speaking
- Torticollis
- Altered mental state

**Akathisia**

Extremely unpleasant subjective sensation of “inner” restlessness that manifests itself with an inability to sit still or remain motionless

Common cause: neuroleptic antipsychotics – phenothiazines, haloperidol, rarely antidepressants

**Restless leg syndrome**

Symptoms of spontaneous, continuous leg movements associated with unpleasant paresthesias

Occur at rest and relieved by movement

Sleep disturbances

**Pathogenesis**

Primary idiopathic disorder

Associated with variety of underlying medical disorders

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1 Emedicine – Toxicity, Medication-Induced Dystonic reactions
2 Wikipedia - Akathisia
3 Up to date - restless legs syndrome
Year 2005 Paper two: Questions supplied by Ilynn

Primary:
FHx: consistent with dominant inheritance (40% of pts with idiopathic RLS)

Hypothesis
RLS arises from dysfunction of hypothalamic dopaminergic cells that are the source of spinal cord dopamine

Evidence that support hypothesis:
Increased incidence of RLS in Parkinson’s disease
Data from Spect, and PET are conflicting

Secondary:
1. Iron deficiency – studies not conclusive, but warrant measurement of serum ferritin levels and a trial of oral iron therapy when ferritin levels are low
2. Uremia – incidence of 6 – 60% in dialysis pt
3. Diabetes Mellitus
4. Parkinson’ disease
5. Rheumatic disease – relationship bet RLS and Rheumatic disease is unclear. One study showered RLS present in 25% of pts with RA compared with 4% controls with OA or seronegative arthropathy
6. Venous insufficiency –

Diagnosis

Minimal criteria:
- Desire to move extremities – often associated with paresthesias or dysensthesias
- Motor restlessness
- Worsening of Sx at rest with at least partial and temporary relief during activity
- Worsening of Sx in the evening or at night

Important to exclude:
- Fe deficiency
- Renal failure
- Peripheral neuropathy, lumbosacral radiculopathy and ordinary leg cramps should be considered

RLS should be differentiated from akathisia
- Akathisia is a more constant, generalized feeling of motor restlessness unassociated with subjective discomfort localizing to the legs
- RLS has a circadian rhythm (worse at night when pt is sitting or in bed)

Treatment – devised by Restless legs syndrome foundation

| Intermittent RLS | Levodopa                      |
|                 | Dopamine agonists            |
|                 | Low potency opioids          |
|                 | Benzodiazepines              |
| Daily RLS       | Daily RLS                    |
|                 | Dopamine agonists            |
|                 | Gabapentin                   |
|                 | Low potency opioids          |
| Refractory RLS  | Change to gabapentin         |
| (Daily RLS treated with dopamine agonist but with poor response) | Change to different dopamine agonist |
|                 | Add second agent – gabapentin, benzodiazepine or opioid |
|                 | Change to high potency opioid or tramadol |

Evidence for treatment
1. Levodopa
   Small randomised trials showed good response compared to placebo
   Problems
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a. Worsening of RLS symptoms earlier in day after evening dose of medication - 70%
b. Recurrence of RLS early in the morning
c. Recurrence of symptoms in 2nd half of the night

2. Dopamine agonist (pramipexole & ropinerole)
   Directly stimulate dopamine receptors and have longer half life (4-6hrs) than levodopa
   Superior to levodopa for treatment of daily RLS
   Adverse effects: nausea, lightheadedness and fatigue

3. Benzodiazepines
   Useful in mild cases of RLS
   No controlled trials
   Short acting – triazolam, zolpem, zaleplon (for sleep onset insomnia)
   Intermediate acting – temazepam (for RLS that awakens the pt later at night)
   Longer duration – clonazepam

4. Opiods
   Shown to reduce no. of sleep arousals, PLMS frequency and increase sleep efficiency
   Tramadol, oxycodone, methadone, codeine

5. Gabapentin
   Effective in open label study
   Safe among dialysis patients
   Start from 100-300mg – tendency for drug to cause somnolence and gait unsteadiness

Anxiety/panic disorder

Anxiety is diagnosed by a GAD7 questionnaire and 'being so restless that it is hard to sit still' is indeed one of the symptoms but there are many other symptoms that need to be fulfilled before a diagnosis of anxiety/panic disorder.

Unlikely answer.

Depression

Again, this diagnosis is made by a constellation of symptoms that are present for everyday for a minimum of 2 weeks. At least 5 out of the 9 symptoms:

- Depressed mood
- Loss of interests/pleasure
- Change in sleep
- Change in appetite or weight
- Change in psychomotor activity
- Loss of energy
- Trouble concentrating
- Thoughts of worthlessness or guilt
- Thoughts about death or suicide

The most likely answer is B Akathisia