Nighttime anxieties

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Treating Mr. J's obstructive sleep apnea controlled his panic attacks for 4 years. After a recent move, his anxiety has re-emerged. How would you treat him?

CASE Stress and chest pain

A primary care physician refers Mr. J, age 40, to our mental health clinic for evaluation of anxiety symptoms. Almost a decade ago Mr. J presented to his primary care physician with anxiety and panic attacks that included chest pain and shortness of breath. Various pharmacologic treatments, including paroxetine, were only moderately successful until 4 years ago, when Mr. J began nighttime continuous positive airway pressure (CPAP) therapy and pramipexole, 0.25 to 0.5 mg/d, for obstructive sleep apnea (OSA), at which point his anxiety completely resolved.

Mr. J reported no anxiety for many years, but when shortness of breath, palpitations, and chest pain re-emerge, he consults his primary care physician. After a negative workup for myocardial infarction, Mr. J is started on short-term beta-blocker therapy and restarted on paroxetine, 20 mg/d. A sleep medicine specialist repeats polysomnography and makes slight adjustments to Mr. J's CPAP therapy. Mr. J relocates to our city and his new primary care physician refers Mr. J to our mental health clinic.

In addition to OSA, Mr. J has mild anemia, hyperlipidemia, and vitamin D deficiency. Mr. J was adopted and has no knowledge of his family psychiatric or medical history. His mental status is normal. Mr. J is not obese, exercises regularly, and has slight micrognathia. His current medications include paroxetine, 20 mg/d, modafinil, 200 mg/d, and ergocalciferol, 50,000 units/week for vitamin D deficiency.

Mr. J says he experienced a single panic attack 7 months ago, but none since then. However, he complains of chronic chest pressure and mild intermittent anxiety associated with the stress of his new job and recent relocation.

The authors' observations

Mr. J's anxiety resolved fully only after receiving treatment for OSA, which is characterized by episodes of blocked breathing during sleep ***(Table 1)***.[1] Multiple studies show a significant association between OSA and panic attacks.[2-5] In a survey of 301 sleep apnea patients, Edlund et al[6] demonstrated that OSA may cause nocturnal panic attacks. Untreated OSA can worsen anxiety symptoms. In a study of 242 OSA patients, those who were not compliant with CPAP therapy had significantly higher anxiety scores as measured on the Hospital Anxiety and Depression Scale.[7]

OSA treatment options include CPAP, oral appliance, and surgery; weight loss

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Table 1

Obstructive sleep apnea risk factors, symptoms, and features

Established risk factors	Obesity, craniofacial abnormalities, upper airway soft tissue abnormalities, male sex
Potential risk factors	Heredity, smoking, nasal congestion, diabetes
Symptoms	Daytime sleepiness; nonrestorative sleep; witnessed apneas by bed partner; awakening with choking; nocturnal restlessness; insomnia with frequent awakenings; impaired concentration; cognitive deficits; mood changes; morning headaches; vivid, strange, or threatening dreams; gastroesophageal reflux
Common features in patients with obstructive sleep apnea	Obesity, large neck circumference, systemic hypertension, hypercapnia, cardiovascular or cerebrovascular disease, cardiac dysrhythmias, narrow or 'crowded' airway, pulmonary hypertension, cor pulmonale, polycythemia

Source: Reference 1

Clinical Point

OSA treatment options include CPAP, oral appliance, and surgery; weight loss and positional therapy may help

and positional therapy may help. Thyroid function, B12, folate, ferritin, and iron studies, and complete blood count can rule out secondary causes of OSA.

HISTORY A succession of diagnoses

Approximately 9 years ago, Mr. J experienced several episodes of waking in the middle of the night from a bad dream with severe shortness of breath and chest pain. He also reported increasing fatigue, anxiety, and stress regarding work, graduate school, and his wife's recent miscarriage. After negative cardiac workups, his primary care physician diagnosed panic attacks. He referred Mr. J to stress management classes and prescribed clonazepam, 1.5 mg/d, which was discontinued after 2 months.

One week after discontinuing clonazepam, Mr. J experienced chest pain, shortness of breath, and anxiety while awake. A cardiologist ruled out cardiac pathology. Mr. J's primary care physician prescribed sertraline, 25 mg/d, and propranolol, 60 mg/d and 10 mg as needed, for anxiety.

Shortly after, Mr. J moved to a different city. His new primary care physician discontinued sertraline and propranolol and started paroxetine, titrated to 20 mg/d. A psychiatrist diagnosed Mr. J with panic disorder without agoraphobia, continued paroxetine, and added alprazolam, 1 mg/d as needed. Mr. J's anxiety symptoms were moderately controlled for several years.

After his son was diagnosed with attention-deficit/hyperactivity disorder (ADHD), Mr. J also was evaluated and found to have ADHD and major depressive disorder, single episode. Mr. J received methylphenidate, 54 mg/d, and paroxetine was titrated to 40 mg/d, with moderate results.

Approximately 6 years before presenting to our clinic, Mr. J reported worsening daytime fatigue, which was treated with modafinil, 200 mg/d. He experienced significant improvement. The next year methylphenidate was switched to amphetamine/dextroamphetamine, then discontinued because of side effects. His physician started Mr. J on atomoxetine, which also was discontinued because of side effects.

Two years later, Mr. J complained of gradual worsening daytime sleepiness. Polysomnography revealed that Mr. J had severe OSA and periodic limb movement disorder. After he began nighttime CPAP and pramipexole, 0.25 to 0.5 mg/d, and continued modafinil, 200 mg/d, his anxiety symptoms completely resolved. Several months later Mr. J's physician discontinued paroxetine because Mr. J reported it caused mildly decreased concentration.

continued

Clinical Point

There may be etiologic relationships among daytime panic attacks, nighttime panic attacks, and OSA

Table 2

Diagnostic criteria for panic disorder without agoraphobia

A. Both 1 and 2:

1. Recurrent unexpected panic attacks
2. At least one of the attacks has been followed by 1 month (or more) of 1 (or more) of the following:
   a. Persistent concern about having additional attacks
   b. Worry about the implications of the attack or its consequences (eg, losing control, having a heart attack, 'going crazy')
   c. A significant change in behavior related to the attacks

B. Absence of agoraphobia

C. The panic attacks are not due to the direct physiologic effects of a substance (eg, a drug of abuse, a medication) or a general medical condition (eg, hyperthyroidism).

D. The panic attacks are not better accounted for by another mental disorder, such as social phobia (eg, occurring on exposure to feared social situations), specific phobia (eg, on exposure to a specific phobic situation), obsessive-compulsive disorder (eg, on exposure to dirt in someone with an obsession about contamination), posttraumatic stress disorder (eg, in response to stimuli associated with a severe stressor), or separation anxiety disorder (eg, in response to being away from home or close relatives).

Source: Diagnostic and statistical manual of mental disorders, 4th ed, text rev. Washington, DC: American Psychiatric Association; 2000

Which disorder most likely accounts for Mr. J's presentation?

a) panic disorder
b) generalized anxiety disorder
c) substance-induced anxiety disorder
d) anxiety disorder due to a general medical condition
e) anxiety disorder not otherwise specified

The authors' observations

The etiology of Mr. J's anxiety is unclear; however, he does not meet criteria for:

- panic disorder, because he denies persistent concern about having more attacks or the implications or consequences of panic attacks, or significant change in behavior related to panic attacks ***(Table 2)***[8]
- generalized anxiety disorder, because between panic attacks Mr. J's baseline anxiety related to "real-world" stressors is mild, intermittent, and easily controllable[8]
- substance-induced anxiety disorder, because Mr. J denies using caffeine, tobacco, alcohol, or illicit drugs. Also, for many years he worked for a company that performed random drug screening.

Although it is difficult to draw a conclusion from a single case, Mr. J's dramatic improvement with CPAP warrants speculation about possible etiologic relationships among daytime panic attacks, nighttime panic attacks, and OSA.

According to DSM-IV-TR, a panic attack has a distinct period of intense fear or discomfort (***Table 3, page 62***).[8] Recurrent panic attacks can lead to anticipatory anxiety, which is an intense fear and/or dread of having another panic attack.[9] According to Steven Reiss' expectancy theory, anxiety sensitivity—ie, the fear of anxiety or fear of fear—may be a risk factor for panic disorder.[10] Therefore, past panic attacks may increase the likelihood of future panic attacks.

Mr. J's panic symptoms may be caused by multiple OSA-induced nocturnal panic attacks. These nighttime panic attacks may predispose him to daytime attacks. It is possible that Mr. J had subclinical panic disorder before developing OSA. In this scenario, his OSA-induced nocturnal panic attacks may have worsened his panic disorder. Unfortunately, we do not know

precisely how long Mr. J has had OSA—only that he was diagnosed with the condition 4 years before presenting to our clinic.

Mr. J responded moderately to paroxetine monotherapy but experienced rapid resolution of his panic attacks with a combination of paroxetine and CPAP. CPAP monotherapy sufficiently prevented panic attacks for 4 years. Finally, when Mr. J experienced a single panic attack several months before presenting to our clinic—at the end of a very stressful year—reintroducing paroxetine prevented subsequent attacks. This supports our hypothesis that OSA may predispose or indirectly cause patients to develop daytime panic attacks. Alternately, this case suggests that OSA may cause subclinical panic disorder to present as an acute condition.

We rule out anxiety disorder secondary to a general medical condition (OSA) and diagnose Mr. J with anxiety disorder not otherwise specified.

How would you treat Mr. J?

a) continue his current pharmacologic regimen and refer him back to his primary care physician
b) continue his current regimen and provide medication management at the mental health clinic
c) taper and discontinue paroxetine
d) cross titrate paroxetine to another selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor

The authors' observations

We continue paroxetine at 20 mg/d because it was working fairly well with

Clinical Point

OSA may cause subclinical panic disorder to present as an acute condition

Table 3

Diagnostic criteria for panic attack*

A discrete period of intense fear or discomfort, in which 4 (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes:

1. Palpitations, pounding heart, or accelerated heart rate
2. Sweating
3. Trembling or shaking
4. Sensations of shortness of breath or smothering
5. Feeling of choking
6. Chest pain or discomfort
7. Nausea or abdominal distress
8. Feeling dizzy, unsteady, lightheaded, or faint
9. Derealization (feelings of unreality) or depersonalization (being detached from oneself)
10. Fear of losing control or going crazy
11. Fear of dying
12. Paresthesias (numbness or tingling sensations)
13. Chills or hot flushes

*Panic attacks occur in the context of several anxiety disorders and cannot be diagnosed as a separate entity

Source: Diagnostic and statistical manual of mental disorders, 4th ed, text rev. Washington, DC: American Psychiatric Association; 2000

Clinical Point

OSA may predispose or indirectly cause patients to develop daytime panic attacks

minimal side effects. The sleep medicine specialist maintained modafinil, 200 mg/d. Laboratory studies—including a comprehensive metabolic panel, complete blood count with differential, and thyroid stimulating hormone—were within normal limits except a fasting blood glucose of 123 mg/dL, for which we referred Mr. J to his primary care physician.

OUTCOME Discontinue paroxetine?

One month later, Mr. J denies panic attacks, other anxiety symptoms, or other psychiatric symptoms and is sleeping well. However, he reports that his mildly decreased concentration persists and he wants to stop paroxetine.

After discussing the risks and benefits, Mr. J and the treatment team decide to continue paroxetine at 20 mg/d. We cite peer-reviewed literature that recommends continuing antidepressants for at least 1 year and possibly indefinitely after symptom resolution to control panic disorder symptoms.[9] In addition, we discuss the lack of studies comparing different lengths of treatment with SSRIs for apparent OSA-induced panic attacks that respond to SSRI/CPAP therapy. Because Mr. J was doing well and experiencing minimal side effects, he feels he would be better served with a longer period of psychopharmacologic treatment.

Six months later, Mr. J says his anxiety symptoms are well controlled and gener-

Bottom Line

Although more research is needed, obstructive sleep apnea (OSA) could cause nocturnal panic attacks that could exacerbate subclinical anxiety or lead to daytime attacks. Consider screening patients who suffer from panic attacks for sleep apnea risk factors or symptoms. If a patient exhibits symptoms of panic attacks and OSA, a sleep study referral may be warranted.

Related Resource

• Saunamäki T, Jehkonen M. Depression and anxiety in obstructive sleep apnea syndrome: a review. Acta Neurol Scand. 2007;116(5):277-288.

Drug Brand Names

Alprazolam • Xanax
Amphetamine/dextroamphetamine • Adderall
Atomoxetine • Strattera
Clonazepam • Klonopin
Ergocalciferol • Calciferol
Modafinil • Provigil
Methylphenidate extended release • Concerta
Paroxetine • Paxil
Pramipexole • Mirapex
Propranolol • Inderal
Sertraline • Zoloft

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

ally unchanged except for an occasional "little flutter" of anxiety every 3 or 4 days that lasts several seconds. For 1 year, he reports no recurrence of panic attacks, compliance with CPAP, and stable OSA.

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