MARCH 1999 volume IV, issue 3

CARDIOLOGY Rounds™

As presented in the rounds of the Division of Cardiology, St. Michael's Hospital, University of Toronto

Be still my beating heart: Panic disorder and the cardiologist

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Panic disorder is a common condition with symptoms that can masquerade as a primary cardiovascular disorder. In addition, many patients with cardiovascular disease also have panic disorder. However, many patients go undiagnosed and incur large costs to the healthcare system as a result. Panic disorder is a treatable condition, and cardiologists can easily identify affected patients and initiate appropriate therapy.

All cardiologists have encountered patients with cardiovascular symptoms but no evidence of significant organic disease, or with symptoms that are not consistent with the pre-existing disease. In such patients, the possibility that these symptoms may represent a particular treatable psychosomatic illness – panic disorder (PD) – is frequently not entertained.

Panic disorder is diagnosed by history and is characterized by recurrent, unexpected panic attacks, concern over these recurrent attacks, worry about their meaning or consequences, and a change in behavior related to the panic attacks. Panic attacks are defined as discrete periods of intense fear or discomfort in which greater than 4 out of 13 cardinal symptoms (of which only 4 are cardiac in nature) develop abruptly and reach a peak within 10 minutes (Table 1).

Epidemiology and diagnosis

PD is an anxiety disorder more likely to occur in women between the ages of 25–44. There is, however, a wide age range of presentation, perhaps related to actual somatic symptomatology. For example, in one cohort study, patients with normal coronary arteries on angiography, chest pain, and panic disorder had a mean age of onset of PD at 62 years. Other independent predictors of panic disorder include atypical chest pain, no evidence of structural heart disease, and use of descriptors such as "racing" and "pounding."

The lifetime prevalence of panic disorder in the general population is between 1% and 5%. Atypical chest pain is often experienced, with a prevalence of 25–57%. Of all patients who present to the emergency room with chest pain, 16%–25% have PD, and it has been estimated that 25% of all patients seen in cardiology practices have panic disorder. The prevalence of PD in patients with palpitations is 15%–20%.

Panic disorder is also seen with increased prevalence in patients with coronary artery disease (CAD). Thirty per cent of patients with PD presenting to the emergency room with noncardiac chest

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Table 1: DSM IV symptoms of panic attack

Cardiovascular symptoms

- Palpitations, pounding heart or accelerated heart rate
- Sensations of shortness of breath or smothering
- Chest pain or discomfort
- Feeling dizzy, unsteady, light-headed or faint

Symptoms related to neurohumoral activation

- Sweating
- Trembling or shaking
- Feeling of choking
- Paresthesias (numbness or tingling sensation)
- Chills or hot flashes

Gastrointestinal

- Nausea or abdominal distress

Psychological

- Derealization (feeling of unreality or depersonalization), being detached from oneself
- Fear of losing control or going crazy
- Fear of dying

Note: 4/13 symptoms represent a DSM IV panic attack

pain, have a documented history of CAD, and 6.5% of patients with chest pain who have positive coronary angiograms also have panic disorder.

It is common for patients with significant cardiovascular symptoms not to have evidence of significant organic disease. For example, 10%–20% of all coronary angiograms done on patients with angina-like chest pain are normal , and up to 80% of all patients with chest pain and negative coronary angiograms have panic disorder, depression, or both, with 30%–60% meeting DSM-IV criteria for PD.

It is false to assume that providing reassurance with an angiogram that shows normal coronary artery anatomy will alleviate symptoms. Studies have shown that 75% of patients remain symptomatic and on cardiac medications, 50% of patients continue to visit the emergency department or doctor, and 50% remain unemployed or disabled.

About one-third of patients with panic disorder who present to the cardiologist may have a sub-type called "non-fearful PD;" these patients report most of the same symptoms as other patients with PD, but they do not report fear during their episodes. Such "forme-fruste" panic disorder could be especially germane to a clinical cardiologist, because the prevalence of this disorder might actually be increasing.

There are several screening tools to help physicians identify patients with panic disorder. A brief screening question can be easily posed: "Have you experienced brief periods—for seconds or minutes—of an overwhelming panic or terror that was accompanied by racing heart, shortness of breath, or dizziness?" This screening question can identify the presence of panic attacks (PA). It has been found that PAs predict the onset of panic disorder within the next year in just over two-thirds of patients, and it is felt that the presence of panic attacks is just as important clinically as the presence of PD.

A variety of panicogenic substances, such as intramuscular and intravenous sodium lactate, intravenous cholecystokinin, and 35% inhaled carbon dioxide, can be used to diagnose panic disorder and to provoke panic attacks. For the moment, however, these provocative tests are mainly used as research tools.

Pathophysiology

No definitive pathophysiologic mechanism for panic disorder has been found to date. The symptoms of panic attacks would suggest a possible disturbance within the autonomic neuroaxis (ANS); however, no consistent abnormality has yet been uncovered, even though initial investigations focused on abnormalities of ANS output. It is possible that amplification of peripheral ANS output is mediated via central processing of afferent input at the level of the midbrain, the same area where afferent nocioreceptive signal processing occurs. Abnormal metabolic activity in the limbic structures has been found by positron emission tomography (PET) studies in patients during a panic attack and in panic disorder.

There has been little study of the hemodynamic changes that occur during a panic attack. PAs are known to be associated with sinus tachycardia, arrhythmia, hypertension, and hyperventilation. Hyperventilation has been shown to cause coronary artery spasm.

Morbidity and mortality

The course of panic disorder is usually chronic but it may wax and wane. Untreated panic disorder has effects on quality of life and is a risk factor for the development of depression and suicide. Patients who present with chest pain to the emergency department and have PD also have higher incidence of panic-agoraphobia, anxiety, depression, and suicidal ideations, and they have higher pain scores than patients without PD.

Untreated panic disorder in patients with CAD might increase morbidity and mortality, perhaps because panic disorder can worsen labile factors. For example, patients with PD are more likely to have elevated blood pressure, higher submaximal exercise treadmill heart rates, and higher serum cholesterol.

Panic disorder presentations

Syndrome X

Syndrome X is a term used for the condition in which patients have typical angina and angiographically-normal coronary (i.e., luminal) anatomy. Initially, the focus of research in syndrome X was to demonstrate subtle degrees of myocardial ischemia in these patients. This led to concepts of microvascular angina and, more recently, disorders of endothelial function.

However, the concept that pain in syndrome X is due to cardiac ischemia has largely been unsupported by physiologic data. As a result, focus has shifted from the heart to a primary disorder of cardiac nocioreception. In patients with syndrome X, pain can be provoked by low-intensity right ventricular pacing, contrast media injection, or adenosine infusion.

Another theory takes into account that syndrome X is associated with rigorously-defined panic disorder in up to 60% of patients, and it is perhaps related to a non-specific nocioreceptive disorder.

Concomitant CAD

Although panic disorder is common among patients with chest pain and normal coronary artery anatomy, PD also occurs in patients with coronary artery disease. The chest pain in this group of patients can have different etiologies. For example, a study of patients with known CAD, recurring chest pain despite medical therapy, and no scintigraphic evidence of active ischemia found that 50% had panic disorder as the cause of their symptoms. Among patients with proven ischemia, 19% also had concurrent PD related to their chest pain.

Palpitations

Patients with palpitations and panic disorder tend to be younger and more disabled, to have somatized more, to have more emergency-room visits, and to have more hypochondriacal concerns about their health compared with patients with palpitations and no psychiatric disorder. There is little symptom-rhythm correlation in this population, and up to 48% of normal people without panic disorder have a similar degree of ectopy when compared with patients with a history of palpitations. Follow-up of patients with PD and palpitations has found that these patients continue to have symptoms, to use medical resources, and to remain functionally impaired.

Other cardiac comorbidities

There is evidence that patients with panic disorder can have other comorbidities. These patients tend to have more mitral valve prolapse and cardiomyopathy. Other patients who might be suffering from PD include those with pacemaker syndrome, syncope, and supraventricular tachycardia.

The cost to health care

More than 50% of people with panic disorder are undiagnosed. One study found that up to 98% of patients who presented to the emergency department with chest pain and who met criteria for panic disorder were not recognized by cardiologists as suffering from this condition. Among patients who present to their family physicians with chest pain, about 50% will have PD; however, in one study, few cases were recognized.

Patients with chest pain and panic disorder have more follow-up, more referrals, more testing, increased prescribing of medication, and often inappropriate pharmacotherapy. Even though a psychiatric disorder is suspected in some patients with palpitations or chest pain, referral or treatment is often not initiated. Patients identified as high utilizers of primary care had a lifetime prevalence of PD of 30%.

Treatment

The mainstay of therapy is pharmacotherapy (table 2) and cognitive-behavioral therapy. Improvements are noticed with either or both treatments within 6–8 weeks or sooner, and treatment will be successful for 70–90% of patients.

Table 2: Specific pharmacotherapy used for the treatment of panic disorder						
	Selective serotonin reuptake inhibition (SSRI)			Tricyclic antidepressants (TCA)	Benzodiazepines	
	Paroxetine	Fluoxetine	Sertraline	Imipramine	Alprazolam	Clonazepam
Initial dose	10 mg po every other day	5 mg po OD	25 mg po every other day	10 mg po od	0.25 -0.5 mg po TID	0.25-0.5 mg po BID
Onset of action (wk)	4	4	4	8	1	1
Efficacy data in panic disorder	Placebo-controlled	Open-label	Open-label	Placebo-controlled	Placebo-controlled	Placebo-controlled
Efficacy data in depression	Placebo-controlled	Placebo-controlled	Placebo-controlled	Placebo-controlled		
Safe in overdose	YES	YES	YES	NO	YES	YES
Risk of dependence	NO	NO	NO	NO	YES	YES

Psychiatric pharmacotherapy

Multicenter placebo-controlled trials have shown clinical efficacy of benzodiazepines, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs) for the treatment of panic disorder. Imipramine is the only anti-panic agent shown to be effective specifically in patients with syndrome X. However, imipramine has also been shown to increase heart rate and blood pressure in some patients, and it can cause orthostatic hypotension, therefore it might not be the most desirable medication for patients with possible cardiac disease who also have PD.

SSRIs are now the first-line agents for panic disorder. They have been found to be very effective, there is no abuse potential, and treatment can be easily initiated by a cardiologist. Their efficacy has been shown in several placebo-controlled trials, with the greatest benefit on panic symptoms seen with paroxetine. In addition, SSRIs cause no adverse drug reactions when taken with cardioactive medications. However, these drugs do have a slow onset of action compared with the benzodiazepines.

Specific cardiac pharmacotherapy

In patients with palpitations and no arrhythmia, suppressing ectopy with cardiac medications has been suggested as therapy; however, these cases have poor—if any—symptom-rhythm correlation, and there is no proof that cardioactive medications have a role. ß-blockers have also been studied in the treatment of panic disorder. Results have been variable in both the ability of ß-blockers to reduce anxiety symptoms in general and their effects on somatic symptoms in PD.

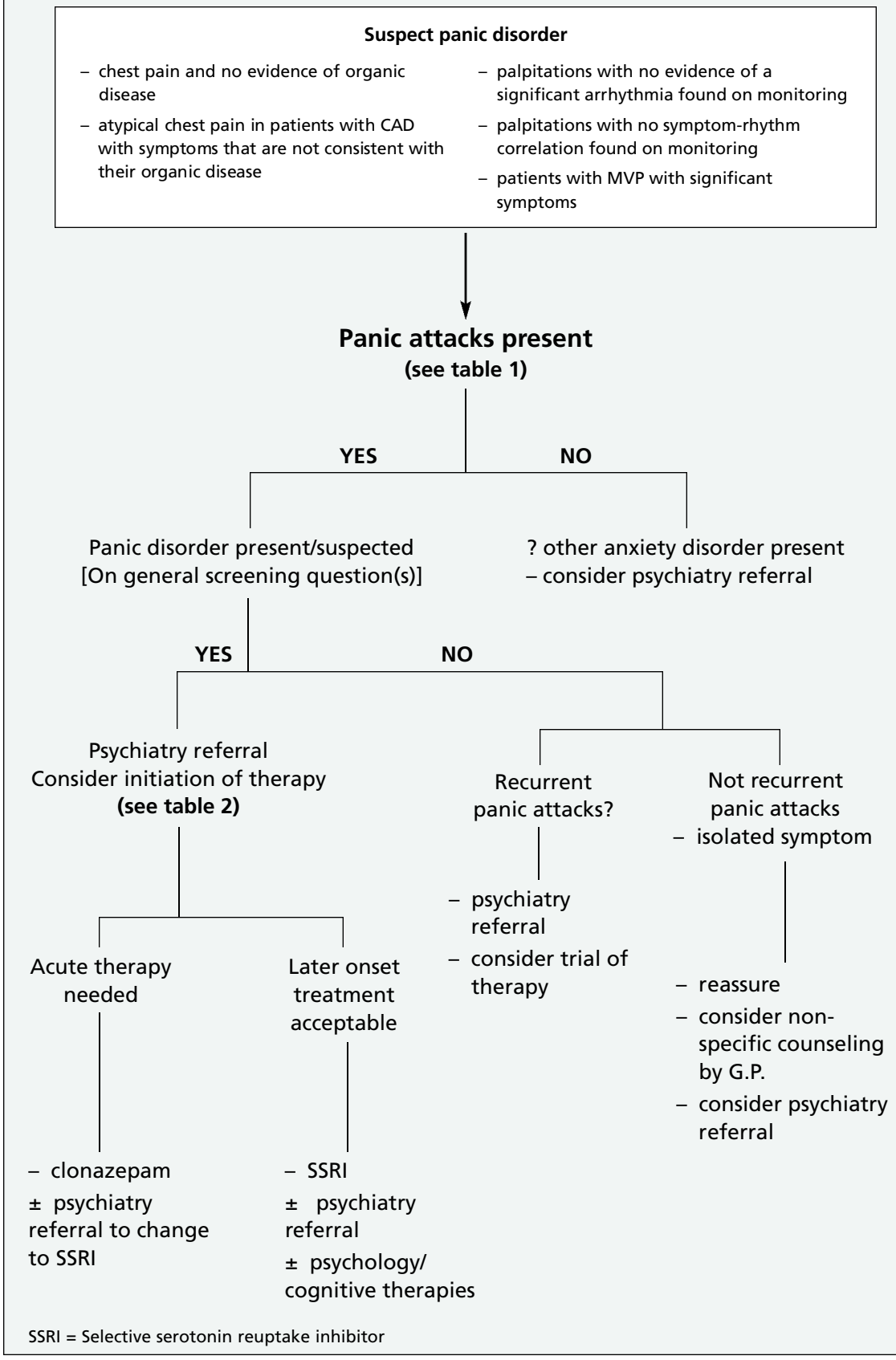
The future

Estrogen was shown in one study to reduce the frequency of chest pain in postmenopausal women with syndrome X. Although this may return the search for the cause of symptoms back to the heart, recent work suggests that estrogen may also have central mood and cognitive effects and that its efficacy in symptom control might reside centrally. Further study in this area is required.

Approach to treatment

Once the diagnosis of panic disorder is suspected, a definitive diagnosis should be sought. The cardiologist can pose a simple screening question. If this is suggestive of PD, the cardiologist should consider a trial of specific anti-panic therapy and refer the patient to a psychiatrist for in-depth assessment and treatment (table 3).

Table 3: A flow chart of panic disorder diagnosis and treatment



SSRI = Selective serotonin reuptake inhibitor

Summary

Panic disorder is common and may be present in patients presenting with somatic manifestations to their cardiologist. As a group, however, cardiologists frequently fail to consider or treat this disorder. Nondiagnosis or inappropriate treatment of panic disorder masquerading as an obscure cardiovascular symptom complex is frustrating to all concerned, and with our present knowledge, unnecessary, particularly since initiation of antipanic therapy is safe and effective.

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