Case 7: Generalised Anxiety Disorder

Why do I keep worrying?

Jamie is a 40-year-old female who comes in for insomnia. She is currently a teacher with two children of school-going age. For the past eight months, she has had difficulty falling asleep and is waking up earlier than planned. She sleeps only four hours a day. In addition, she experiences stiff shoulders and headaches and feels fatigued most of the day. She feels on edge throughout the day, with her mind constantly worrying about everyday events, from her children to work to finances, etc. She worries whether they will get to school safely and cope well. She has difficulties controlling her worries, which occur throughout the day. Her concentration at work has been affected, and her superiors recently gave her a warning letter.

- **Question 1: What is the most likely diagnosis? Which differential diagnoses would you consider?**

- **Question 2: What investigations would you order to confirm your diagnosis and guide management?**

You diagnosed Jamie with generalised anxiety disorder.

- **Question 3: What are the risk factors for generalised anxiety disorder?**

- **Question 4: What other psychiatric co-morbidities would you screen for?**

- **Question 5: Jamie is keen for treatment, how would you manage her generalised anxiety disorder?**

Jamie was started on a trial of sertraline. However, despite an adequate trial of sertraline over four weeks her symptoms failed to remit.

- **Question 6: When first-line treatment has failed, what other pharmacological treatments can be considered?**

Answers to Case 7

Question 1

What is the most likely diagnosis? Which differential diagnoses would you consider?

Answer

Generalised anxiety disorder is the most likely diagnosis. Other differential diagnoses to rule out include hyperthyroidism, phaeochromocytoma and other anxiety spectrum disorders including panic disorder, etc.

Explanation

Diagnosis of generalised anxiety disorder

Marked symptoms of anxiety are required for diagnosis, manifested in either [1]:

1. General apprehensiveness that is not restricted to any particular environmental circumstance (i.e., 'free-floating anxiety'); or
2. Excessive worry (apprehensive expectation) about negative events occurring in several different aspects of everyday life (e.g., work, finances, health, family)

Anxiety and general apprehensiveness or worry are accompanied by additional:

- Muscle tension or motor restlessness
- Sympathetic autonomic overactivity as evidenced by frequent gastrointestinal symptoms such as nausea and/or abdominal distress, heart palpitations, sweating, trembling, shaking and/or dry mouth
- Nervousness, restlessness or being 'on edge'
- Difficulty concentrating
- Irritability
- Sleep disturbances

Anxiety spectrum disorders are a good masquerade of one another. Some of the defining features include:

Condition	Defining feature(s)
Panic disorder	Anticipatory anxiety of the next panic attack
Agoraphobia	The individual fears or avoids certain situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms
Social phobia	Specific to social situations where the individual might come under the scrutiny of others
Post-traumatic stress disorder (PTSD)	Follows a traumatic event (actual or threatened death, serious injury or sexual violence). The main features are hyperarousal, avoidance, intrusion symptoms and dissociation

Generalised anxiety disorder tends to present with free-floating anxiety while the other anxiety spectrum disorders have a waxing and waning anxiety pattern.

Exam Essentials

- Symptoms of generalised anxiety disorder – **MR TICS**
  - **M**uscle tension
  - **R**estlessness
  - **T**ired
  - **I**rritability
  - **C**oncentration
  - **S**leep difficulties

Clinical Pearls

- Rating scales such as the clinician-administered Hamilton Anxiety (HAM-A) rating scale and, more specifically, self-administered GAD-7, may help with the assessment and monitoring of symptoms
- Consider caffeine use as a contributor to anxiety

Question 2
What investigations would you order to confirm your diagnosis and guide management?

Answer

Category	Investigations
Point-of-care test	ECG Blood pressure reading
Biochemistry	Full blood count Renal panel Liver function test Thyroid function test Urine 24-hour catecholamines Urine drug screen (for suspected cases or unusual presentation – e.g., sudden onset)
Imaging	MRI adrenals (only if history and if biochemical tests are suggestive of phaeochromocytoma)

Explanation
We need to have high levels of suspicion for organic causes if Jamie presents with high blood pressure, tachycardia, diarrhoea, weight loss, extreme diaphoresis and throbbing headache, which do not go away with symptomatic treatment. Imaging such as MRI adrenals should only be ordered if biochemical tests are suggestive of phaeochromocytoma.

Other prescribed medications can cause anxiety symptoms as well (refer to the Diving Deep section).

Clinical Pearls

- Always take a history and potentially **screen for illicit substance use**, as anxiety symptoms may be part of the withdrawal or intoxication syndrome

Question 3
What are the risk factors for generalised anxiety disorder?

Answer

Modifiable risk factors: lower economic resources, unemployment, divorced/widowed

Non-modifiable risk factors: age, female gender, family history of psychiatric disorders, history of sexual abuse

Explanation

Age is known to be a risk factor up to the age of 65. Early-onset generalised anxiety disorder is associated with childhood fears and marital or sexual disturbances, while cases with a later onset often occur after a stressful event.

Question 4

What other psychiatric co-morbidities would you screen for?

Answer

The following are common co-morbidities of generalised anxiety disorder [1]:

- Mood disorders: major depressive disorder (62%) [2], bipolar disorder (18%) [3]
- Anxiety spectrum disorders: obsessive–compulsive disorder (OCD) (33.5%) [4], panic disorder (24%) [5]
- Alcohol and other substance use disorders (20–40%) [6]

Explanation

Anxiety disorders are independent risk factors for suicide attempts [7].

Question 5

Jamie is keen for treatment, how would you manage her generalised anxiety disorder?

Answer

Pharmacology: selective serotonin reuptake inhibitors (SSRIs)

Psychotherapy: CBT

Self-help/psychoeducational groups

Explanation

The NICE guidelines [8] suggest a step-based approach. Education and active monitoring are the first steps. The second step requires psychological interventions (CBT, self-help, psychoeducational groups). The third step involves the pharmacological use of an SSRI such as sertraline, or more intensive psychological intervention.

The Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines [9] for the management of anxiety, PTSD and OCD suggest that psychotherapy and pharmacotherapy have equivalent efficacy for the treatment of most anxiety and related disorders. While CBT is traditionally delivered as an individual or group therapy for most anxiety and related disorders, recent studies have shown that self-directed or minimal intervention formats (e.g., bibliotherapy/self-help books, or internet/computer-based programs with or without minimal therapist contact) are effective [10, 11]. There are different areas that CBT focuses on. In exposure, the patient faces their fears in a graded

manner. In safety response inhibition, patients are taught to restrict anxiety-reducing behaviours (e.g., the need for reassurance), which decreases negative reinforcement and breaks the cycle of anxiety. Cognitive strategies include cognitive restructuring and behavioural experiments. Arousal management uses relaxation and breath control techniques. Safety-signal learning refers to the conditioning of distinct stimuli in one's environment to the absence of aversive events. In surrendering safety signals, self-efficacy beliefs are adopted and safety signals relinquished.

Exam Essentials

- Refer to Case 3 for further reading on SSRIs

Clinical Pearls

- Do not offer benzodiazepines except for short-term use in breakthrough anxiety
- Risks of benzodiazepines include:
  - Dependence
  - Cognitive impairment
  - Fall risks
  - Respiratory depression (especially in patients with lung diseases)

Question 5

When first-line treatment has failed, what other pharmacological treatments can be considered?

Answer

Benzodiazepines as an adjunct therapy
Other antidepressants (e.g., imipramine, bupropion extended release (XL), vortioxetine)
Antipsychotics (e.g., quetiapine)
Buspirone

Explanation

Based on the CANMAT guidelines [9], the above medications are second-line treatment options.

While benzodiazepines have level 1 evidence, they are usually only prescribed for short-term use because of their side effects and risk of dependence.

Imipramine has a similar level 1 evidence for generalised anxiety disorder but because of its side effects and potential lethality in overdose, it is used as a second-line treatment. There are fewer data on both bupropion XL and vortioxetine, but they are deemed to be effective treatment options. Quetiapine, while effective, carries side effects of weight gain and sedation with accompanying higher dropout rates. Buspirone has limited clinical effectiveness in practice and is hence considered a second-line treatment option.

Diving Deep …

Generalised anxiety disorder is more common in high-income countries and has a lifetime prevalence of around 5.7% [12].

Medications can also cause anxiety-like symptoms, and these include:

- Cardiovascular: antihypertensives, antiarrhythmics
- Respiratory: bronchodilators, alpha-1- or beta-adrenergic agonists
- Central nervous system: anticonvulsants, withdrawal from a benzodiazepine or alcohol, reaction from disulfiram
- Others: levothyroxine, chemotherapy, non-steroidal anti-inflammatory drugs

Generalised anxiety disorder can be a chronic and disabling disorder, with low remission rates, and up to 68% of patients continue to have residual symptoms even after years of treatment [12].

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