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'I just don't feel right'

Background

Much undifferentiated illness is seen in general practice. Patients with vague feelings of general unwellness may have multiple unrelated problems, serious underlying pathology, definite but indefinable pathology, no definable pathology, and/or illness of psychological origin.

Objective

This article looks at an approach to a patient who complains of feeling 'not quite right'.

Discussion

Assessment of undifferentiated illness is a complex process and may require more time than a 15 minute consultation. Considering the patient's age and gender helps guide history, examination and investigation. Red flags for serious disorders must be sought.

Case study

Sally, 23 years of age, presents saying she 'just doesn't feel quite right'. She has been feeling generally unwell for at least 6 months with tiredness and multiple aches and pains. She says that she sleeps too much but still wakes up feeling tired. She describes a 'brain fog' and finds that this is affecting her work as an articled clerk. Her arms and hands often feel swollen and tingling, she suffers frequent typical migraine headaches and her periods are very painful. She has no relevant past medical history and is not taking any regular medications.

■ **Sally presents with a 6 month history of feeling 'not quite right' with associated tiredness and aches and pains. It is useful to reflect on a preliminary differential diagnosis to guide further history taking. Thinking about what is more common in a young adult female can narrow the list down. Differential diagnoses to consider at this point include:**

- Organic disorders
 - autoimmune disorders
 - multiple sclerosis
 - migraines
 - iron deficiency
 - fibromyalgia
- Nonorganic disorders
 - depression/anxiety
 - intimate partner abuse – up to a quarter of women may have been affected by violence in the preceding 12 months, and may present with chronic pain and depression as a result¹
- Lifestyle issues
 - overwork/stress
 - substance abuse
 - poor diet.

Less common organic disorders are important to consider and include:

- chronic infections (eg. Ross River virus, Lyme disease)
- mercury toxicity
- postviral fatigue
- chronic fatigue syndrome
- lymphoma
- seronegative spondyloarthropathies (more common in males, but should be considered in a young person with chronic pain)
- myofascial pain syndrome.

Further history

History of Sally's complaint

Details of the onset of Sally's symptoms are important, ie. 'what was happening at the time?' Did she have symptoms of a viral infection and was there a history of recent travel? Did a major life event or stressor coincide with the onset? Also important is the pattern of symptoms, triggers, relievers and associated symptoms. Is there a cyclical component to her symptoms? What are her periods like?



Psychosocial and family history

A psychosocial and family history will help guide management, whether or not an organic cause is found. It is important to find out about Sally's work and home life and any major stressors. Is she suffering from depression or anxiety? A dietary and drug and alcohol history is also important.

Case study continued

On further questioning, Sally tells you that her symptoms began insidiously several months after she graduated as a law student and started her clerkship. They did not appear to start after a virus. She works long hours in a busy job and feels she is under some degree of pressure, but she feels that this does not explain her symptoms. She wakes up most mornings feeling stiff all over, and has aches and pains which feel 'burning' over her upper and lower back, neck, knees and wrists. She also has headaches. She feels tired all the time, and has had to stop her regular gym sessions because of the fatigue. Despite getting 10 hours sleep each night, she wakes feeling tired. The pain and fatigue have been constant, and seem to be worsening. Recently she has started to miss work and her boss is starting to ask questions. She is starting to feel depressed and frustrated about her pain and fatigue, but denies feeling depressed when her symptoms started. She complains of 'brain fog' and inability to concentrate. She is not enjoying doing things she used to enjoy, such as socialising with friends, because she is often too tired. She has tried Nurofen for the pain with little relief, and a chiropractor has not been able to help.

Sally is single and lives by herself. Her parents are close by. She has not been overseas in the past 12 months but she did visit family in rural far north Queensland for 1 week, 1 year ago. Her mother takes thyroxine, but there is no other significant family history. She usually goes to the gym three times per week and walks once or twice a week but has only been able to walk occasionally in the past 4 weeks. If she pushes herself at the gym she 'crashes' the following day and has to miss work. She does not smoke, drink or take any illicit substances. She sometimes skips breakfast, usually eats out at lunch (a sandwich or a salad) and will have pasta or 'stir fry' for dinner. She has fish once every fortnight. She admits she probably doesn't eat enough vegetables, and often reaches for sweet foods to try to boost her energy levels. She now has 3–4 cups of coffee per day to keep awake.

Sally's periods are regular, painful and heavy for 2 days. She does not have a rash or any joint swelling. She sometimes feels dizzy but has not had any vertigo, ocular pain or bladder problems. She has not noticed a change in weight or any lymphadenopathy. Her bowel habits and appetite are normal.

Examination

A thorough physical examination of Sally would include: mental state; vital signs; and abdominal, cardiovascular, respiratory, joint, trigger point and pelvic examination.

Case study continued

A general examination of Sally reveals a tired looking young woman, with stable vital signs and body mass index of 22. There is no postural hypotension. Abdominal, cardiovascular and respiratory examination is unremarkable. There is no lymphadenopathy or oedema. Her sclerae are not yellowed, there is no obvious pallor. Neurological examination is normal apart from some subjective tingling in the forearms. There is no joint swelling or limitation of movement. She has generalised hyperalgesia and pain on palpation of the trapezius muscles, cervical spine region, gluteal region, medial knee fat pads, and lateral epicondyles bilaterally. Pelvic examination is unremarkable.

Investigation

The list of possible causes is extensive. Complete exclusion of all of these conditions would require an enormous number of tests. Judicious use of investigations strives for a balance between overinvestigation and the need to exclude serious organic causes. Reasonable initial investigations include:

- full blood count (FBE)
- erythrocyte sedimentation rate (ESR), c-reactive protein (CRP)
- antinuclear antibody (ANA), rheumatoid factor (RF)
- thyroid stimulating hormone (TSH)
- glucose
- liver function tests (LFTs)
- urea and electrolytes (U&E)
- urinalysis for glucose, protein, blood
- transglutaminase antibodies (for coeliac disease)
- iron studies
- Ross River virus serology (Sally's trip to rural far north Queensland may have put her at a slightly increased risk).

Lyme disease serology is more controversial and probably not indicated in this case. Sally has not travelled to a Lyme disease endemic area (mainly in the northern hemisphere) and does not have a rash. In addition, Lyme disease serology can be misleading as IgG may not form for months or years.²

If inflammatory markers are raised, radiology of the sacroiliac joint may help with diagnosing ankylosing spondylitis; HLA B27 is only useful if negative.

Case study continued

Investigations are all within normal limits apart from a borderline raised TSH. Further testing reveals a normal T3 and T4 but her antithyroid antibodies are raised, suggesting Hashimoto disease.



Management

- Thyroid – you start Sally on 25 µg of thyroxine but are not satisfied that this explains all her symptoms
- Mood – on further questioning, Sally's mood issues appear to be a result of her illness and not the cause, although you suspect they may hamper her recovery. You advise a regular balanced diet including an adequate protein intake, five serves of vegetables per day, and avoidance of sugar or stimulants. She declines an offer to speak to her boss on her behalf about her absence from work. You recommend cognitive behavioural therapy (CBT) and she agrees to try this
- Fibromyalgia – you refer Sally to a rheumatologist and she returns with a diagnosis of fibromyalgia. The rheumatologist also arranged a neurology review and multiple sclerosis was excluded after a normal clinical examination and magnetic resonance imaging (MRI) brain result. The rheumatologist has started her on low dose amitriptyline
- You spend some time with Sally explaining the diagnosis to her and provide information sheets from your state arthritis foundation (see Resource). You organise to perform a chronic disease management plan and suggest a gentle and gradual return to aerobic exercise combined with strength training, to be supervised by an exercise physiologist. You consider other evidence based management strategies for fibromyalgia
- Other – you suggest a 2 week trial of a low amine diet to see if the migraine headaches improve and a trial of vitamin E,³ magnesium and B6 for presumed primary dysmenorrhoea⁴

- Review – you ask to see her monthly to monitor her exercise tolerance, pain and moods.

Case study continued

At her first monthly review she reports a gradual improvement in her exercise tolerance, pain tolerance, and moods. Her migraines disappear if she avoids amines, and her periods are less painful now she is taking supplements. She is attending work regularly and able to socialise more frequently.

About fibromyalgia

Fibromyalgia is a common condition characterised by widespread pain, fatigue and sleep disturbance. Common associated features are anxiety/depression, migraines/headaches, cognitive difficulties and paresthesia. Comorbidities include irritable bowel syndrome, dysmenorrhoea, premenstrual syndrome, restless leg syndrome, and irritable bladder.⁵

The cause of fibromyalgia remains unknown but pathophysiology is thought to include peripheral and central hyperexcitability,⁶ defects in the serotonergic and adrenergic systems,⁷ and altered sleep patterns.

Diagnosis is made on clinical grounds alone. The American College of Rheumatology classification criteria for fibromyalgia are the most commonly used diagnostic criteria (*Table 1*).⁸

Management of this often disabling condition begins with patient education. Resources are available from arthritis foundations

Table 1. 1990 criteria for the classification of fibromyalgia⁸

History of widespread pain

Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. 'Low back' pain is considered lower segment pain

- Pain in 11 of 18 tender point sites on digital palpation
- Pain, on digital palpation, must be present in at least 11 of the following 18 sites:
 - occiput: bilateral, at the suboccipital muscle insertions
 - low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5–C7
 - trapezius: bilateral, at the midpoint of the upper border
 - supraspinatus: bilateral, at origins, above the scapula spine near the medial border
 - second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces
 - lateral epicondyle: bilateral, 2 cm distal to the epicondyles
 - gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle
 - greater trochanter: bilateral, posterior to the trochanteric prominence
 - knee: bilateral, at the medial fat pad proximal to the joint line
- Digital palpation should be performed with an approximate force of 4 kg
- For a tender point to be considered 'positive' the subject must state that the palpation was painful. 'Tender' is not to be considered 'painful'

For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia



around Australia (see *Resource*). Treatments for which there is some evidence for efficacy include:

- pharmacological
 - amitriptyline and fluoxetine can reduce pain and improve function⁶
 - the new serotonin and norepinephrine reuptake inhibitor duloxetine, has shown encouraging results in preliminary studies⁷
- Nonpharmacological
 - tailored exercise programs
 - cognitive behavioural therapy⁶
- Complementary therapies
 - S-adenosyl-methionine (SaMe) may help improve function.⁹ However, interactions can occur with thyroxine and tricyclics. Regular monitoring is recommended
 - co-enzyme Q10 may help with fatigue.¹⁰ Higher doses may be required on tricyclic antidepressants due to increased hepatic metabolism.

Comorbid conditions may also require treatment.

Fibromyalgia is a complex and heterogeneous condition, and a tailored management plan should be formulated utilising shared decision making. A multidisciplinary approach is recommended,⁸ and patient education is a form of treatment in itself.⁶ Remissions do occur, but a proportion of patients will report an improvement over time.¹¹

Summary of important points

- Assessment of an undifferentiated condition is complex process – don't be pressured into doing this over a 15 minute consultation!
- Considering the patient's age and gender helps guide a good history (which is of paramount importance) and appropriate investigations.
- Red flags for serious disorders must be sought. In this particular case, red flags include:
 - significant weight loss
 - clinically significant lymphadenopathy
 - localising/focal neurological signs
 - signs/symptoms of inflammatory arthritis or connective tissue disease
 - signs/symptoms of cardiorespiratory disease
 - sleep apnoea
 - red flags for back pain.¹²

Resource

www.arthritisaustralia.com.au has links to state and territory websites.

Conflict of interest: none declared.

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