

When is it infective endocarditis?



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A 62-year-old man with ongoing flu-like illness presents with frequent episodes of palpitations (suggestive of arrhythmia), night sweats and overwhelming fatigue. At what stage should he be investigated or referred on for consideration of a diagnosis of infective endocarditis?

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CASE SCENARIO

Peter is a 62-year-old accountant who presented after two and a half weeks of an ongoing flu-like illness. He reported headaches, arthralgia and general malaise initially, but over the most recent week, he had been experiencing frequent episodes of palpitations (suggestive of arrhythmia), night sweats and overwhelming fatigue. There was no history of travel or insect bites or extramarital sexual activity. He reported that he had a long-term heart murmur that had followed an attack of rheumatic fever as an adolescent.

Physical examination revealed only a loud systolic ejection murmur in the aortic area. Blood tests were not helpful, with the only abnormality reported being elevated levels of C-reactive protein (CRP; 70 mg/L) and erythrocyte sedimentation rate. Blood cultures were negative.

At what stage should Peter be investigated or referred on for consideration of a diagnosis of infective endocarditis?

COMMENTARY

Occasional episodes of flu-like illness are a near universal human experience, and it is the role of the clinician to decide when further investigation is justified. In this case, we are told that Peter has been unwell for two weeks with systemic symptoms of headache, arthralgia and progressive fatigue. In the second week

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of his illness he reported night sweats and palpitations. These symptoms combined with a moderately raised CRP level in the setting of rheumatic heart disease raise the diagnostic question of endocarditis. Further investigation of Peter's illness is justified on the basis of duration and severity of symptoms.

History is key

Acquiring a thorough history is the key to intelligently investigating the plethora of potential causes of Peter's illness. Establishing the presence of fever would be an important first step and it may be helpful for Peter to document the pattern of fever at home. Considering some of the more common and important causes of a persistent systemic syndrome with fever can help direct specific questions (see the box on this page).

Identification of localising symptoms is the most important historical factor, particularly as it helps target investigations. Some febrile illnesses that occasionally may perplex physicians with an absence of localising symptoms include tuberculosis, pyogenic liver abscess and endocarditis. Relevant historical factors sometimes overlooked include complementary and prescribed medications and specific exposures from travel (including local travel) as well as occupational and recreational activities.

Directly enquiring about injecting drug use is indicated in all cases of suspected endocarditis as it has a strong association, particularly in patients with underlying cardiac lesions. Peter has had no new sexual encounters, which reduces the likelihood of several viral illnesses that would be sufficient explanations for his presentation, including infection with HIV, cytomegalovirus or Epstein-Barr virus.

Preceding transient bacteraemia associated with dental work or infected skin lesions would increase the clinical suspicion of endocarditis in this case. Peter would not have qualified under current

Australian guidelines for prophylaxis for invasive procedures, although he will in future if endocarditis is confirmed.¹

Infective endocarditis: an important differential

The clinical presentation of endocarditis is usually acute, but occasionally may be subacute, especially when less virulent bacteria, such as viridans (streptococci) are the cause of endocarditis. Subacute presentations of infective endocarditis may occur in individuals with underlying cardiac lesions, with symptoms evolving over weeks to months. These patients will often first present to a GP.

Fever is the most common symptom and sign of infective endocarditis but in rare cases it may be absent, with night sweats and lethargy being the dominant symptoms. Cardiac murmurs are usually pre-existing in patients with subacute presentations of infective endocarditis. The subtle peripheral embolic and vasculitic signs of endocarditis, when present, strongly support the diagnosis. Fundoscopy is also recommended.

Cases of endocarditis complicating rheumatic heart disease lesions are now a rare presentation that likely reflects the falling prevalence of rheumatic heart disease. Less than 5% of hospital admissions with endocarditis are associated with underlying rheumatic heart disease lesions.²

Investigating infective endocarditis

The most important investigation to diagnose endocarditis is blood culture. Collecting two sets of blood cultures may miss 10 to 20% of bacteraemia episodes, but if three sets are collected the false-negative rate falls to 2 to 4%.³ Antibiotic use within the past week is an important cause of false-negative blood cultures.

It is important that the laboratory performing the analysis is notified of the possibility of endocarditis because many laboratories have protocols in place for

COMMON AND IMPORTANT CAUSES OF PROLONGED FEVER

Infection

- Viral – e.g. Epstein-Barr virus, cytomegalovirus, HIV, Ross River virus
- Bacterial – e.g. tuberculosis, endocarditis, deep abscess (including liver), Q-fever
- Returned travellers – e.g. dengue fever, enteric fever, malaria

Noninfectious inflammatory conditions

- Systemic lupus erythematosus
- Giant cell arteritis
- Polymyalgia rheumatica
- Antineutrophil cytoplasmic antibody-associated vasculitis
- Adult-onset Still's disease
- Granulomatous disease – e.g. sarcoidosis
- Reactive arthritis/arthritis

Neoplasm

- Lymphomas
- Leukaemia
- Solid tumours

Others

- Drug fever
- Thromboembolic disease
- Thyroiditis
- Factitious fever

extending cultures and additional laboratory measures, such as supplementary media, may be employed to identify fastidious organisms. Performing serology for *Coxiella burnetii* (Q-fever), *Bartonella* and *Brucella* species may be appropriate in the setting of negative blood cultures, even when a prior history of relevant exposure is not provided.

Echocardiography has an increasingly important role in clinical assessment and should be strongly considered in the evaluation of difficult-to-diagnose patients

with fever, as well as for high-risk patients with underlying valvular heart disease, such as the current case.

Echocardiography is all the more useful if the nature of the cardiac murmur has changed recently.

Transthoracic echocardiography can be a valuable noninvasive screening test, although frequently transoesophageal echocardiography is needed to confirm the presence of valvular vegetations. In some instances, CT scans of the abdomen and chest will demonstrate suggestive embolic lesions (such as within the spleen or psoas) when other superficial lesions are not evident.

Palpitations are not a discriminative symptom in patients with endocarditis, but arrhythmias may complicate endo-

carditis. Peter requires an electrocardiogram in the first instance.

CONCLUSION

Although there are many potential causes that would be sufficient to explain Peter's presentation, his history of rheumatic heart disease requires the treating clinician to consider infective endocarditis early in the course of his illness. It is particularly important to consider the diagnosis because untreated infective endocarditis is invariably fatal. Further blood cultures are indicated in Peter's case. In relation to the other potential causes of Peter's systemic symptoms, using a predetermined pathway for investigation would not be good practice. A thorough history focusing on localising symptoms with

directed investigations is most likely to reward the clinician and patient with a diagnosis. **MT**

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