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A 55-Year Old Woman from Turkey With Fever of Unknown Origin

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Clinical Presentation

History

A 55-year-old woman of Turkish provenance presents to a hospital in Germany with intermittent fever up to 39.5°C (103.1°F), night sweats, chest pain and fatigue. The patient had visited her relatives in Turkey several weeks before. There is a history of rheumatic fever in her childhood and mechanical mitral and aortic valve replacement at the age of 37 and 53 years, respectively (St Jude Medical prostheses).

Clinical Findings

The patient's blood pressure and heart rate are within normal limits. There are unremarkable prosthetic heart sounds and a systolic grade 1 murmur over the aortic area without radiation. Liver and spleen are not enlarged. No lymph nodes are palpable. No haemorrhages or petechiae are detectable.

Laboratory Results

There is slight anaemia (Hb 11.5 g/dL [reference >12 g/dL]). White blood cell count, lymphocyte–neutrophil ratio and platelet count are within normal limits. The C-reactive protein is 15 mg/dL (reference <0.5 mg/dL). Serum creatinine and transaminases are not elevated. Blood cultures are negative. Urinary cultures yield Enterobacteriaceae.

Additional Investigations

Chest radiography shows no infiltrates. Transthoracic echocardiography demonstrates competent prosthetic valves.

The patient is diagnosed with a urinary tract infection and treated with co-trimoxazole. Her fever settles and the patient's condition improves, but she complains of increasing dyspnoea and eventually slips into congestive heart failure.

Questions

1. What are differential diagnoses in this patient after deterioration?
2. What are the most promising next diagnostic steps?

Discussion

A 55-year old Turkish woman presents with fever of unknown origin. She has travelled to Turkey shortly before and has a history of double heart valve replacement. Treatment with co-trimoxazole results in some improvement, but then the patient develops signs of congestive heart failure.

Answer to Question 1

What Are Differential Diagnoses in This Patient After Deterioration?

Urosepsis could have been the underlying cause of the deterioration in this patient. However, urinary tract infection is usually easily managed with a short course of early antibiotic treatment. The patient's preceding stay in Turkey should raise the suspicion of another infection not detected so far, such as brucellosis, tuberculosis or Q-fever.

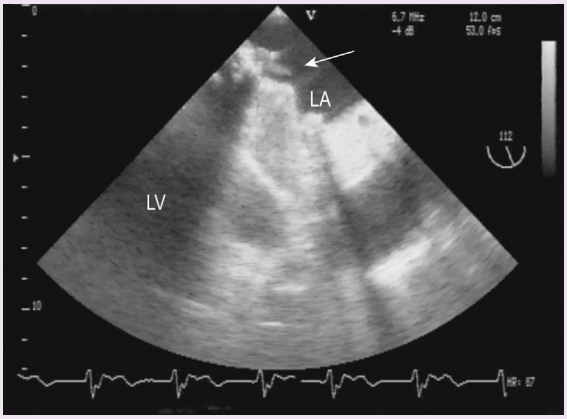
Answer to Question 2

What Are the Most Promising Next Diagnostic Steps?

With two prosthetic heart valves, our patient has an increased risk of infective endocarditis. Transoesophageal echocardiography is indicated to rule out cardiac involvement. Cultivation of blood cultures should be extended to up to 6 weeks in culture-negative endocarditis to reveal *Brucella* or *Coxiella* species.

The Case Continued…

After 4 weeks, the blood cultures taken initially grew *Brucella melitensis biovar 2.* Transoesophageal echocardiography revealed a large vegetation attached to the prosthetic mitral valve (Fig. 76.1). These findings led to the diagnosis of active *Brucella* endocarditis. Treatment with rifampicin, doxycycline and gentamicin was initiated. The patient improved rapidly. C-reactive protein returned to normal after 6 weeks of triple therapy. Two months later, however, an annular



• **Fig. 76.1** Transoesophageal echocardiography showing a two-cornered vegetation (arrow) measuring about 18 mm × 7 mm attached to the posterolateral left atrial side of a St Jude Medical prosthesis in mitral position (LV, left ventricle; LA, left atrium).

abscess cavity around the aortic prosthesis was demonstrated on echocardiography; the patient at that time was on oral rifampicin and doxycycline. Finally, she gave her consent to a third thoracotomy, for prostheses exchange. After surgery she made a complete and sustained recovery.

SUMMARY BOX

Brucellosis

Brucellosis is one of the most common zoonotic infections worldwide. Its true incidence is unknown, because it typically affects rural communities and it is difficult to diagnose. Hot spots of the disease are Eastern Europe, the Middle East, Central and South Asia, Central and South America and Africa.

The disease is caused by intracellular bacteria of the genus *Brucella.* The *Brucella* species most importantly involved in human disease are *B. melitensis* (goats, sheep, camels), *B. abortus* (cattle), *B. suis* (pigs) and *B. canis* (dogs).

Brucellosis is most commonly acquired by eating raw or undercooked meat and offal or untreated dairy products. Also, close contact with infected livestock poses a risk. It is an important occupational hazard among herdsmen, dairy farmers, abattoir workers and laboratory technicians.

Symptoms are non-specific, with fever, sweating, fatigue, weight loss, headache and joint pain persisting for weeks or even months. Its presentation as a non-specific febrile illness poses a differential diagnostic challenge in geographical regions where malaria and tuberculosis are highly prevalent and diagnostic resources are scarce, such as in sub-Saharan Africa. In the latter context, brucellosis is frequently missed as a major aetiology of fever, as has been shown from Tanzania.

Brucellosis may involve nearly every organ of the body. Although endocarditis is a less common manifestation of the disease, cardiac valve involvement was the most frequent cause of death from brucellosis in the past.

Definitive diagnosis requires the isolation of the bacteria from the blood, body fluids or tissues. This can be challenging as culture may take several weeks. In endemic settings, serological tests are often the only available diagnostic test and their interpretation may be challenging.

Treatment of brucellosis requires combination antibiotic therapy of several weeks' to several months' duration to prevent relapses.

The choice of the regimen and treatment duration depend upon clinical course and organ manifestation. Drugs most commonly used are doxycycline, gentamicin, rifampicin and co-trimoxazole.

In the case of cardiac valve involvement, spondylitis or neurobrucellosis, extended parenteral antimicrobial therapy is recommended. Patients with *Brucella* endocarditis will frequently require valve replacement in addition to antibiotic therapy.

Further Reading

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