Box 8—Costs of an MRSA outbreak

- Cost to patients: pain and discomfort, loss of time and earnings, inconvenience, excess morbidity, and mortality
- Cost to the hospital: delayed discharge and attendant costs, drugs and antiseptics, containment measures, infection control procedures, litigation, contracts imperilled, exclusion of affected staff

resistant *S aureus* is about seven times that of treating a bacteraemia with methicillin sensitive *S aureus*.³⁰ Containment measures use increasingly scarce resources. A 1987 study in the North East Thames region put the recurrent annual financial cost then of containing outbreaks at around £250 000 in the worst affected hospitals. In addition, there were capital costs associated with the establishment of an isolation ward. Another cost that must not be neglected is that of litigation by infected patients, a growing hazard of outbreaks in hospitals. Hospitals then need to show that well documented and effective control measures are in place. Furthermore, infection control now features as one of the main quality indicators in contracts between purchaser and provider agencies.

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Tuberculous pericarditis with rapid progression to constriction

Prompt diagnosis and treatment are needed

Pericarditis is the main diagnosis in 1 in 1000 patients admitted to hospital, and 4% of cases are caused by tuberculosis.¹ Tuberculosis is responsible for up to 7% of cases of pericardial tamponade and a similar percentage of cases of tamponade in which the patient requires pericardiectomy because pericardial constriction develops.² We report a case of tuberculous pericarditis in which pericardial constriction developed rapidly despite anti-tuberculous drugs.

Case history

A 28 year old Sri Lankan man was transferred to our hospital for investigation and treatment. He had been admitted to another hospital three days previously with a four week history of malaise, loss of appetite, weight loss (5 kg), reduced exercise tolerance, and rigors. He had recently arrived in England from Sri Lanka and had no significant medical history. He was heterosexual. On examination he had a temperature of 39°C, his pulse was 100 beats/min with a palpable paradox, and his blood pressure was 120/70 mm Hg with 20 mm Hg of paradox. The jugular venous pressure was raised by 7 cm and Kussmaul's sign was

present. A third heart sound was heard together with bibasal crepitations. He had hepatosplenomegaly but no ascites or peripheral oedema.

His haemoglobin concentration was 123 g/l, white blood cell count $12.4 \times 10^9/l$, platelet count $370 \times 10^9/l$, and the erythrocyte sedimentation rate 48 mm in the first hour. His biochemical profile was normal but his C reactive protein concentration was 200 mg/l. Three early morning urine samples yielded no growth. An electrocardiogram showed a sinus tachycardia, with a rate of 119 beats/minute, with T wave inversion in the inferolateral leads. Chest radiography showed cardiomegaly (fig 1). He had good biventricular function, normal valvular structure and function, but a large pericardial effusion (fig 2). Pericardiocentesis yielded 1.5 litres of uniformly blood stained fluid. The fluid contained an exudate with a protein concentration of 540 g/l, glucose concentration of 1.9 mmol/l (serum glucose 5 mmol/l), and numerous lymphocytes. A Mantoux test was performed and gave positive results at a dilution of 1 in 10 000. Computed tomography showed evidence of para-aortic and paracolic lymphadenopathy. On the basis of fever, lymphadenopathy, and the large pericardial effusion he was started on

FIG 1—Chest radiograph showing an enlarged cardiothoracic ratio and clear lung fields

FIG 2—Apical four chamber echocardiogram showing left ventricle (LV), right ventricle (RV), and large pericardial effusion (PE). The right ventricle is collapsing implying tamponade.

rifampicin, isoniazid, pyrazinamide, and ethambutol. He was discharged two weeks later with no fever and a C reactive protein concentration of 59 mg/l. He was readmitted 10 days later with fever, shortness of breath, and right subcostal pain. His temperature was 37.6°C, pulse 120 beats/min, and blood pressure 120/70 mm Hg. The jugular venous pressure was raised by 5 cm with a prominent y descent and a pericardial knock. His C reactive protein concentration was 51 mg/l and white blood cell count $8.5 \times 10^9/l$. His heart was normal size on chest radiography but repeat echocardiography showed evidence of pericardial constriction. This was confirmed by magnetic resonance imaging (fig 3).

The visceral and parietal pericardium were removed four days later and both layers were found to be greatly thickened and adherent, with a complete absence of pericardial fluid. Histology showed necrotising granulomatous infiltration of the pericardium (fig 4). Stains for acid fast bacilli and fungi gave negative results. Sputum, early morning urine, pericardial fluid, and the pericardium did not yield any bacterial growth. He recovered rapidly and has had no evidence of recurrence of his tuberculosis.

Comment

Pericardial tamponade can result from any illness which causes pericarditis, but constriction is only common when the aetiology is infective, neoplastic, autoimmune, or toxic. The source of the mycobacteria

in tuberculous pericarditis remains uncertain, with less than half of patients having evidence of pulmonary tuberculosis.¹ Retrograde spread from mediastinal lymph nodes may often be responsible. Once tuberculous pericarditis has become established virtually all patients will develop constriction unless they receive tuberculous drugs, and even with treatment 30-50% of patients will progress within two to four months.¹⁻⁴ Tuberculous pericarditis, however, is often difficult to diagnose and long delays may occur between admission to hospital and diagnosis (mean time of 5.2 weeks)¹ because of the slow growth of the organism in culture. Culture of the sputum and gastric aspirates will allow diagnosis in about half of cases, even when the chest radiograph appears normal.¹ This yield is further increased by histological examination of lymph nodes or pleural biopsy if these are clinically indicated. Pericardiocentesis will detect 30-75% of cases, especially if performed early in the course of the disease when the concentration of bacteria in the fluid is highest.^{5,6} Culture and histological examination of a pericardial biopsy specimen will detect virtually all cases of tuberculous pericarditis, but it is difficult to justify this procedure unless it is clinically indicated because of recurrent tamponade or persistent pericardial effusion.

Once tuberculous pericarditis has been diagnosed the treatment consists of conventional anti-tuberculous drugs.^{2,7} Corticosteroids remain controversial. Non-randomised studies have suggested that although steroids may have a role during the effusive stage,⁷⁻⁹ they do not reduce the risk of constriction or its

FIG 3—Magnetic resonance image in coronal plane showing severely thickened pericardium (arrow) encasing the heart

FIG 4—Histological specimen showing numerous epithelioid granulomas including a Langhans-type giant cell

progression. Nevertheless, a randomised controlled trial of high dose prednisolone (up to 60 mg per day according to age and weight) in 143 patients with active constrictive pericarditis in South Africa suggested that patients treated with steroids have a greater resolution of their symptoms (exercise capacity) and signs (pulse rate and height of jugular venous pulse) during treatment.¹⁰ This effect was not completely sustained once the treatment was stopped. In addition fewer patients progressed to pericardectomy (21% v 30%) or death (4% v 11%) in the steroid treated group. One fifth of patients will require pericardectomy once they constrict regardless of the treatment they receive.

Pericardectomy is now a safe procedure with a 97% survival rate if performed early in a patient with good left ventricular function.¹¹ It is generally recommended that the pericardium is removed from the anterolateral and diaphragmatic aspects of the left ventricle extending to the atrioventricular sulci and subsequently removed from the anterior and inferior surfaces of the right ventricle, especially around the inflow tracts.

Discussion

GJD: Tuberculous pericarditis remains an uncommon disease in the United Kingdom and normally presents late in the effusive stage. The striking feature of this case is the rapidity with which classic tamponade progressed to classic constriction. The South African study included only patients who had already developed constrictive physiology, and there is no evidence that steroids prevent the development of constriction. Once constriction has developed early pericardectomy has a better prognosis than delaying the operation and therefore giving steroids at this stage is probably not beneficial.

ss: The usefulness of adjunctive steroid therapy in tuberculous infection has been shown for only pericardial effusion and meningitis. This patient did not receive steroids. Tuberculosis is commonly associated with HIV infection, especially in patients from sub-Saharan Africa.

js: This case highlights the current lack of understanding of mechanisms by which acute inflammation may become persistent and lead to scarring with loss or serious derangement of organ function. Apparently successful treatment, with a fall in markers of acute inflammation, failed to prevent postinflammatory scarring. This is commonly seen in inflammatory disease of other organs, including the kidney, where

despite high efficacy in suppressing acute inflammation no clear evidence has emerged that steroids prevent scarring. New approaches to this problem are required.

JSC: Was it possible to make a diagnosis in this case from the pericardial fluid?

CPC: No; neither the Ziehl-Neelsen staining nor the subsequent culture of the fluid showed any evidence of tuberculosis.

JSC: What is the differential diagnosis based on the histology?

JBS: The two main differential diagnoses are lymphoma and sarcoidosis. Granulomas may be seen in both these conditions, but in lymphoma an infiltrate of atypical lymphoid cells is present and the granulomas are not necrotising. In sarcoidosis caseation is not usually seen. Mycobacteria are often difficult to identify in tissue sections and the most likely diagnosis remains tuberculosis.

JSC: What is the role of the polymerase chain reaction in diagnosing tuberculosis when bacteriology has been unhelpful?

CPC: It has been shown to be helpful in diagnosing tuberculosis in clinical specimens when conventional bacteriological tests are not diagnostic.¹² The increased sensitivity of this technique would be useful in establishing the diagnosis of tuberculous pericarditis in difficult cases, but it has not been widely applied in clinical practice.

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Correction

Guidelines for the management of asthma:
A summary

Several authors' errors occurred in chart 6 of the British Thoracic Society and others' guidelines for the management of asthma (20 March, pp 776-82). In the pathway for moderate asthma the >50-75% values should read 50-75% throughout. Further amendments are shown as dotted arrows (or a dotted line in the box to the left) in the figure below, which is a detail of the chart showing the management of moderate and mild categories of asthma.