Unusual cases of endocarditis

Endocarditis is an uncommon disease, with approximately one episode per 1000 admissions. However, patients frequently have a prolonged hospital stay and may need cardiac surgery, sometimes with a difficult postoperative course requiring intensive care. Endocarditis can mimic many other illnesses and sometimes other illnesses can present like endocarditis. Consequently, delayed diagnosis is a major factor in patients who fail treatment. Management of this disease is only likely to be successful if there is close cooperation between physician, surgeon and microbiologist.

This issue of *Hospital Medicine* includes case reports from three centres which illustrate different aspects of diagnosis. The first concerns two patients with *Staphylococcus aureus* endocarditis in whom the organism was possibly seeded from long-standing atopic eczema (p. 356). The second describes a patient with tricuspid valve endocarditis caused by *Enterococcus faecalis* (p. 358), and the third endocarditis associated with acute rheumatic fever (p. 360).

The mitral and aortic valves are most often involved, involvement of the tricuspid being uncommon except in intravenous drug abusers. Endocarditis caused by *Staph. aureus* can affect normal heart valves and progresses rapidly resulting in high fever, rigors and malaise. Patients present to hospital with only a few days of illness. Disease caused by β-haemolytic streptococci or enterococci usually develops on already damaged valves and follows a slow course with fever and night sweats, often misinterpreted as a viral illness. Patients may have a history of weeks or months before the diagnosis is made.

Acute rheumatic fever is a delayed complication of a pharyngitis caused by *Streptococcus* group A, usually in the 6–15-year-old age group, with an attack rate around 3%. The similarity between some streptococcal antigens and certain human tissue antigens suggests it is an immunological phenomenon rather than a result of bacterial invasion.

Rheumatic heart disease occurs in approximately half of patients with acute rheumatic fever, and rheumatic endocarditis damages the mitral valve more frequently than the aortic valve. Although rheumatic fever remains common in the Middle East and India, it has become rare in Europe and the USA. As a result rheumatic heart disease as a predisposing factor to infective endocarditis has fallen from 38% in 1967 to 6% in 1984 (Cherubin and Neu, 1971; McKinsey et al, 1987).

RISK FACTORS

Over 70% of patients have pre-existing cardiac lesions, the most common apart from rheumatic heart disease being mitral valve prolapse, degenerative disease of aortic or mitral valves, and congenital heart disease (McKinsey et al, 1987). Mitral valve prolapse is present in 5% of the population but only a minority have an audible murmur (Savage et al, 1983).

The risk of endocarditis is increased 14-fold in patients with a mitral valve prolapse and a systolic murmur but not at all in those with prolapse and no murmur (Danchin et al, 1989). Two of the cases described later had mitral valve prolapse. Tricuspid valve disease is rare except in drug misusers. Previous infective endocarditis is a common risk factor, especially in a patient with cardiac disease, continued drug abuse or dental decay. The patient described with tricuspid valve disease may have had previous damage related to drug abuse.

PATHOGENESIS

The first stage of endocarditis follows endothelial damage when platelets and fibrin are deposited giving rise to non-bacterial thrombotic endocarditis. If bacteraemia occurs, for example from soft tissue infection, the organisms adhere to and colonize any lesions. Only a small number of organisms are necessary (<10 organisms per ml of blood). Bacteria are then covered by further layers of platelets and fibrin protecting them from the host defence.

In one of the papers in this issue, atopic eczema was the probable source of *Staph. aureus* which could then establish infection by direct invasion of the endocardial surface. In another, enterococcal bacteraemia may have arisen from a genitourinary source (especially if the urine was infected). Organisms within vegetations divide very slowly, reducing the efficacy of some normally bactericidal antibiotics, but can increase to high titres over time.

Dissemination of bacteria from the vegetations cause the wide variety of symptoms and signs of endocarditis. If disrupted, vegetations form emboli to any other organs including, in the case of the tricuspid valve, the lung. Perforation or rupture of the valve leaflet or the chordae tendinae causes regurgitation. The spleen enlarges. Infarction of the heart, spleen or kidneys is common. Cerebral emboli usually pass into the middle cerebral artery causing infarction, abscesses or haemorrhage but can reach other sites including vessels supplying the eye or the optic nerve. Petechiae of the skin develop in a third of patients.

Circulating immune complexes appear in response to the persistent antigenic stimulus and contribute to the formation of splinter haemorrhages, Osler's nodes, purpura, glomerulonephritis and arthritis. Immune complexes can be demonstrated in blood vessels in purpura (Lowenstein et al, 1977). Immune complexes and complement deposition in the basement membrane of the kidney are responsible for a diffuse glomerulonephritis.

CAUSATIVE ORGANISMS

There are few organisms that have not at some time been reported as causing endocarditis. The most common are the β-haemolytic streptococci, especially *Streptococcus sanguis*, *Strep. bovis*, *Strep. mutans* and *Strep. mitis*. They originate in dental plaque or, in the case of *Strep. bovis*, the large bowel. Enterococci are implicated in 10% of cases of endocarditis, usually in elderly men following genitourinary procedures.

Staphylococci account for one-third of cases: *Staph. aureus* on native and prosthetic valves and *Staph. epidermidis* on prosthetic valves. As in the cases described in this issue, *Staph. aureus* can cause rapid destruction of the valve and give rise to septic emboli to other organs. Mortality is high despite antibiotic and surgical treatment.

TREATMENT

Antibiotics do not penetrate the relatively avascular vegetation well, particularly those with a large molecular size, such as the glycopeptides. The rapidity of onset, severity of illness and development of complications determine the nature of antibiotic or surgical treatment. The minimum inhibitory concentration (MIC) can be used as an aid to selection or dosage of an antibiotic but clinical progress should always be the final arbiter.

A bactericidal and synergistic combination of antibiotics is important to overcome the relatively low antibiotic concentration in the centre of vegetations. Penicillins and glycopeptides (teicoplanin and vancomycin) should be given in a dose sufficient to keep the concentrations in the vegetation above the MIC. Penicillins may require dosing every 4 hours. Vancomycin should be administered at a dose sufficient to achieve 10–15 mg/litre at trough, while teicoplanin may need to be maintained above 20 mg/litre if used as monotherapy for staphylococcal endocarditis. The aminoglycosides require high peaks for bacterial killing but must be monitored every 1–2 days to avoid potentially toxic serum concentrations.

Flucloxacillin or oxacillin (2 g every 4–6 hours intravenously for 4–6 weeks) are effective in endocarditis caused by methicillin-sensitive staphylococci. Although a combination of flucloxacillin and gentamicin is more rapidly bactericidal, trials have failed to demonstrate improvement in duration of fever, mortality or complications (Bayer, 1993). Gentamicin is usually given but for only 3–5 days in the USA compared with 1–2 weeks in the UK (Wilson et al, 1995). In the treatment of enterococcal endocarditis, a combination of penicillin, ampicillin or a glycopeptide with an aminoglycoside is synergistic and bactericidal in most cases. Gentamicin (1 mg/kg every 8 hours) is given for 4 weeks with benzyl penicillin (10.8–18 g/day) or ampicillin (12 g/day). If there is a long delay before treatment, failure is much more likely (Bayer, 1993).

Surgical replacement of the valve is often needed when there is valvular destruction and cardiac failure. Large vegetations are likely to embolize and not be cured by medical treatment alone. Of 140 patients, 32 had to undergo surgery during active infection and of the remainder 47% had surgery within 2 years (Tornos et al, 1992). The aortic valve is the most likely to require replacement and mortality is greatest in staphylococcal infection.

CONCLUSIONS

Although the risk factors for endocarditis have changed over the years, outcome has improved little. The great variety of presentations and the range of causative organisms delay diagnosis and so worsen outcome. Cooperation between physicians and surgeons is essential once the disease is recognized to achieve the best outcome, particularly in the aggressive disease caused by *Staph. aureus*. HM

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KEY POINTS

- Endocarditis is an uncommon disease but presents in various and sometimes misleading ways.
- *Staphylococcus aureus* causes endocarditis on previously undamaged valves and follows an aggressive course.
- Emboli are responsible for many of the peripheral complications and are most common with large rapidly growing vegetations.
- Antibiotics do not penetrate vegetations well and synergistic combinations are usually recommended.

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