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American Medical Association Journal of Ethics
October 2010, Volume 12, Number 10: 796-799.

CLINICAL PEARL

Diagnosing and Treating Acute Infective Endocarditis

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Infective endocarditis (IE) is broadly defined as a microbial infection involving the endocardium, or inner chamber lining, of the heart. The process is termed “acute” if it progresses over days to weeks or “sub-acute” if it has a more protracted course. The incidence of infective endocarditis in population studies is estimated to be between 3.6 and 7 cases per 100,000 patient years [1]. Infective endocarditis occurs predominantly in the context of structural heart disease and conditions or procedures that increase the risk of bloodstream infections, such as indwelling intravenous catheters, hemodialysis, prolonged hospitalization, pacemaker or ICD placement, and intravenous drug abuse. Despite advances in modern medicine, infective endocarditis remains a major cause of death from an infectious process, with an overall mortality approaching 20 percent.

Infective endocarditis occurs when platelet-fibrin deposition takes place in an area of endothelial injury caused by a high-velocity jet from a dysfunctional valve. This process results in small sterile vegetations. During episodes of bacteremia, these deposits can become secondarily infected; if untreated, the infection can progress to valve destruction and distal embolization. The most common organisms causing bacterial endocarditis are staphylococci, streptococci, and enterococci species.

Diagnosis

Fever is by far the most common sign or symptom of acute infective endocarditis. Other constitutional symptoms include chills, sweats, loss of appetite, and malaise [2]. Although a new or changed regurgitant murmur is the most common cardiac finding on physical examination, this may be absent in right-sided endocarditis. Classic peripheral manifestations of infective endocarditis include petechiae, splinter hemorrhages, Osler nodes, Janeway lesions, and Roth spots. These are immunologic or embolic phenomena.

Echocardiography is central to the diagnosis of endocarditis. Transthoracic echocardiogram (TTE) should be the initial study of choice in most cases, though transesophageal echocardiogram (TEE) has a higher sensitivity for detecting vegetations. This makes TEE useful for patients with suboptimal images on TTE, a high likelihood of IE, or prosthetic valves.

The Modified Duke Criteria [3] is a well-validated set of clinical, microbiological, and echocardiographic criteria for diagnosing infective endocarditis. The major criteria are two positive blood cultures with a typical microorganism for infective

endocarditis and evidence of endocardial involvement on echocardiogram. The minor criteria include fever, a predisposing condition for IE (such as intravenous drug use), vascular phenomena, immunologic phenomena, and microbiological evidence not included in the major criteria. A classification of definite IE requires the presence of 2 major criteria, or 1 major and 3 minor criteria, or 5 minor criteria. The presence of 1 major criterion and 1 minor criterion, or 3 minor criteria, indicates a possible case of IE.

Treatment

It is of the utmost importance to have blood cultures drawn before initiating therapy. Physicians often infer the diagnosis from symptoms and begin treatment before the causative organism and its sensitivities have been determined. However, if the patient's clinical condition is stable, antibiotics can wait until microbiological confirmation is obtained. If treatment is started before then, it should be aimed at the common pathogens; a combination of nafcillin (or vancomycin, if the patient is allergic to penicillin or in an area with high prevalence of methicillin-resistant *Staphylococcus aureus* [MRSA]) and gentamicin is an acceptable combination. Further tailoring of the antibiotic regimen should occur once the organism is identified. Most patients with uncomplicated IE become afebrile in 3 to 5 days with appropriate antibiotic treatment. Surveillance cultures should be obtained 48 to 72 hours after treatment begins to ensure eradication of the organism.

The most common treatment regimens for specific organisms are as follows [4]:

- Methicillin-sensitive *Staphylococcus aureus* (MSSA): nafcillin or oxacillin for 6 weeks, plus optional gentamicin for 3-5 days;
- Methicillin-resistant *Staphylococcus aureus* (MRSA): vancomycin for 6 weeks
- *Staphylococcus* with prosthetic valve: nafcillin or oxacillin plus rifampin for at least 6 weeks, with gentamicin given for 2 weeks; for methicillin-resistant strains, use vancomycin in place of nafcillin or oxacillin;
- Penicillin-susceptible *Streptococcus*: penicillin G or ceftriaxone for 4 weeks; vancomycin for 4 weeks if penicillin allergy is present;
- Penicillin-resistant *Streptococcus*: ceftriaxone for 4 weeks plus gentamicin for 2 weeks, or vancomycin for 4 weeks;
- Enterococci: penicillin G or ampicillin plus gentamicin for 4-6 weeks, or vancomycin plus gentamicin for 6 weeks;
- HACEK microorganisms: ceftriaxone for 4 weeks, ampicillin-sulbactam for 4 weeks, or ciprofloxacin for 4 weeks.

Indications for surgery

In one-third of patients with IE, antibiotic therapy alone is not sufficient, and surgical intervention is necessary to debride the infected source and restore valve competence. Repair of the valve is preferable, if feasible. A good understanding of the indications for surgery allows for early risk stratification of patients who will benefit from it. Patients who require surgical intervention during the acute phase of

endocarditis are usually ill, and although mortality is high in this setting, survival is still significantly better than with medical therapy alone.

Some of the most common indications for surgery are as follows [5]:

Clear indications

- Acute severe valvular dysfunction or valvular dysfunction resulting in heart failure;
- Persistent infection despite 7-10 days of antibiotic treatment;
- Structural complications such as valve abscess or fistula formation;
- Endocarditis caused by fungi or other resistant organisms.

Relative indications

- Recurrent embolic events despite antibiotic therapy; native or prosthetic valve;
- Mobile vegetation larger than 10 mm;
- IE due to virulent organisms such as *Staphylococcus aureus*, making valve repair preferable to delayed valve replacement.

IE in IV Drug Users

There is a higher incidence of IE among intravenous drug users (IVDUs) than in the general population. The majority of right-sided IE occurs in IVDUs, with septic pulmonary emboli present in 75 percent of such patients. *Staphylococcus aureus* is the most frequent pathogen. As for non-IVDUs, antibiotic therapy is guided by culture results. The prognosis for drug-using patients with right-sided IE is generally good with medical therapy, but problems often arise when these patients have recurrent bouts of IE in the setting of continued IV drug abuse. While indications for surgery are similar whether the patient is an intravenous drug user or not, ethical considerations regarding the indications, timing, and choice of valve are paramount.

Final Points

Treatment of infective endocarditis requires a multidisciplinary approach. It is generally advisable to involve a cardiologist, an infectious disease specialist, and a cardiac surgeon early on in the course of the disease. Prompt antibiotic therapy geared toward the causative organism and careful timing of surgical intervention, if indicated, are essential to ensuring a good outcome.

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