

PATHOLOGY AND PATHOGENESIS OF INFECTIVE ENDOCARDITIS IN NATIVE HEART VALVES

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Definition

Endocarditis is an endovascular microbial infection of intracardiac structures facing the blood including infections of the large intrathoracic vessels and of intracardiac foreign bodies (1). Formerly known as bacterial endocarditis, endocardial infections are currently named infective endocarditis, in order to include both bacterial and fungal microorganisms. As a consequence, sterile thrombotic lesions (thrombotic non-bacterial endocarditis) should be termed non-infective endocarditis (2).

Pathogenesis and predisposition

Sterile thrombotic vegetations are considered the crucial lesions underlying the development of infective endocarditis, since they serve as a suitable milieu for bacterial sticking on valve surfaces (3). Endothelial injury is the most plausible factor leading to platelet deposition. The rarity of endocarditis, despite frequent transient bacteriemia, indicates that the intact endothelium is resistant to infection.

Haemodynamic and mechanical stress seem to play an important role in the development of initial lesions and location of the infection (4). The predilection site of infective endocarditis is the area of valve's line closure, due to the impact of the pressure, a matter which accounts for the prevalent involvement of the left side valves. Altered hemodynamics, due to preexisting valve damage, may predispose to endothelial damage and platelet deposition, thus increasing the likelihood of endocarditis during bacteriemia. Entry of microorganisms into circulation, due to focal infection or trauma, ultimately converts thrombotic non bacterial endocarditis into infective endocarditis. Events that traumatize the oral mucosa, particularly the gingiva, the genitourinary and gastrointestinal tracts are associated with an increased risk of bacteriemia. The adherence propensity of some microorganisms to non bacterial thrombotic deposits plays a major role, and fibronectin, a glycoprotein that is the main surface constituent of mammalian cells, has been identified as an important factor in this process (5). Decrease of host defenses mechanisms most probably plays a major role as well. The local blood flow pattern changes, as a result of alteration of the valve's geometry, concur

to thrombus formation (non infective thrombotic endocarditis), microorganisms adhesion during bacteremia and onset of infective endocarditis (injury-thrombus-infection theory. The microorganisms then can grow and induce further thrombus formation and neutrophils chemiotaxis. Thus, underlying disease with deformed valve is the main risk factor of infective endocarditis. Likewise, jet or friction lesions of the endocardium, as seen on the left ventricular outflow tract in aortic incompetence and hypertrophic cardiomyopathy, are a well known site of infective colonization.

However, studies of experimental endocarditis showed that injury to the endocardium and vascular endothelium may serve as a focus of infection even before the development of sterile thrombotic vegetations (6).

Most of gram + bacteria are resistant to the bactericidal activity of the serum, whereas gram - are not. This explain why gram + bacteria are more likely to be a cause of infective endocarditis.

Pathology and complications of native valve endocarditis.

The pathology of infective endocarditis may be local, including valvular and perivalvular destruction (7), and distal, due to detachment of septic vegetations with embolism, metastatic infection and septicemia (2).

As far as the *distal complications*, they differ whether endocarditis is right-sided or left-sided, and whether emboli from vegetations are septic or bland. Right-sided endocarditis may be complicated with pulmonary artery embolism and infarcts, pneumonia and lung abscesses. Left-sided endocarditis may be complicated with systemic embolism and cerebral, myocardial, kidney, splenic, intestinal infarcts and/or abscesses. Embolic events are the most common extracardiac complication associated with infective endocarditis, with the incidence ranging from 22 to 43% (8). Valvular vegetations seem to be a significant risk factor for embolism only in case of infection with *Streptococcus viridans* (8). Cerebrovascular accidents occur in nearly 10% of infective endocarditis of the left-sided heart and a similar incidence was found in patients receiving anticoagulants and in patients who did not (9). Paradoxical emboli may occur in congenital heart disease with intracardiac shunt.

Metastatic infection may lead to apoplegic meningitis, myocarditis and pyelonephritis. Splenic abscesses are at risk of rupture, so abdominal computed tomography is indicated for monitoring splenic involvement (10). Septicemia may stimulate disseminated intravascular coagulation. Deposition of circulating complexes

may account for diffuse or focal glomerulonephritis. Mycotic aneurysms may involve both the large-medium size arteries and the small vessels (Osler's nodes) (11).

Local complications of infective endocarditis occur in the valve itself or in the perivalvular region, and they also vary, whether atrioventricular or semilunar valves are affected. Vegetations are usually attached to atrial aspect of atrioventricular valves and to ventricular aspects of semilunar valves, at the valve line closure. Infective endocarditis of the aortic valve may present with vegetations of various size, which in the acute phase consist of septic thrombus entrapping microorganisms and neutrophil infiltrates. Sometime, they are so small as to be overlooked by the pathologist. Echocardiography can demonstrate only lesions 2-3 mm or more in size. In subacute-chronic phase, microorganisms may disappear, granulomatous inflammation including giant cells occurs and vegetations may transform into coarse calcific deposits. Cusp disruption with loss of substance account for tearing, fraying, perforation and bulging, especially when the microorganism is staphylococcus. Valve incompetence with left ventricular decompensation and congestive heart failure is the usual hemodynamic complication. It may be associated with some degree of functional stenosis, if vegetations are remarkable. Local spread of infection includes extension to the aortic wall that may lead to development of sinus of Valsalva aneurysms, ring abscess, tunnels and fistulae to the surrounding cardiac chambers (right and left atria, right and left ventricles) and pericardial cavity itself with cardiac rupture and tamponade. Transesophageal echocardiography is highly accurate in the detection of complications, such as paravalvular abscesses or mycotic aneurysms. Aortic root complications carry an increased operative mortality and a high incidence of postoperative regurgitation (12). Extension of the infective endocarditis from the aortic to the mitral valve occurs through mitro-aortic fibrous continuity. A marker of such complication is the development of a septic aneurysm in the anterior leaflet of the mitral valve (satellite infection or kiss lesion), with or without perforation. Involvement of the atrioventricular conduction system may account for atrioventricular block. Rupture of the membranous septum may induce acquired ventricular septal defect.

A part from cusp vegetations and perforations, which do not differ substantially from those occurring at semilunar valve level, infective endocarditis of atrioventricular valves are peculiar in so far as the subvalvular apparatus (chordae tendinae and papillary muscle) may be also affected. Chordal rupture may occur in the setting of infective disruption. Papillary muscle rupture may also occur, either due to septic

localization on the tip or to myocardial necrosis because of coronary embolism. Perivalvular extension of the infection and ring abscesses are exceptional at atrioventricular valve level.

Healed endocarditis is marked by indentation of the free margin of a cusp, perforation of the body of the cusp with thick edges, cusp aneurysms, ruptured chordae tendinae and healed fistulae.

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