

Infective Endocarditis in Congenital Heart Disease Patients: It's Time to Pay More Attention!

Chung Il Noh, MD

Department of Pediatrics, College of Medicine, Seoul National University, Seoul, Korea

Infective endocarditis (IE) is the result of endovascular microbial infection. Due to the growing patient population suffering with pre- and postoperative congenital heart disease (CHD), the increased placement of prosthetic valves, vascular grafts and patches in the heart and also the improvement of intensive cardiac care, IE that is related to CHD is showing continuously changing features. In general, IE can be better classified by referring to the activity of the disease, the diagnostic status (definite/possible), the anatomic site (right/left side), the underlying disease (native valve/prosthetic valve/other foreign material), the microbiology of the disease (the causative microorganism and the culture/serology/PCR/histology) and the patient population (CHD, nosocomial IE, drug users, hemodialysis, etc.).¹⁾

p318-323 참조

Because of the endothelial lining of the heart and valves, only highly virulent organisms (e.g., *S aureus*) are capable of infecting the normal healthy heart. Therefore, almost all of the IE is the result of complex interactions between the host's immune and coagulation systems, structural cardiac disease, microorganisms and procedures that can cause bacteremia. The steps in the development of lesion are 1) endothelial injury with the resultant coagulum (that contains large amounts of fibrinogen-fibrin, fibronectin, plasma protein and platelet protein) and inflammation-induced expression of $\beta 1$ integrins by the endothelial cells (that results in fibronectin binding to the endothelial surface via the $\beta 1$ integrins), 2) pathogen adherence to the coagulum via MSCRAMMS (microbial surface components recognizing adhesive matrix molecules) and the fibronectin-binding protein on their surface and the additional adherence of the pathogens to the fibrin matrix, and 3) vegetation formation with the proliferating patho-

gens (infected coagulum). The infected vegetation increases with the binding of pathogens to the coagulum, the initiation of monocyte activation and the cytokine and tissue factor production. This cycle of adherence, organism growth and platelet-fibrin deposition can start to repeat by itself. Fibronectin-binding protein and MSCRAMMS are on the surface of *S. aureus*, *Streptococcus viridans*, *Streptococcus pneumoniae*, group A, C and G streptococci, and *Candida albicans*.²⁾³⁾

About 10-20% of IE is associated with preexisting CHD. Besides those patients with isolated ASD, postoperative ASD or PDA without residue beyond 6 months postoperatively, and the mitral valve prolapse without valvular regurgitation, most of the CHD patients have a risk of incurring IE and so lifelong antibiotic prophylaxis is recommended.⁴⁾ There is no general agreement about instituting antibiotic prophylaxis for postoperative VSD, well repaired TOF and for the post-intervention state of ASD, VSD and PDA.⁵⁾ IE among CHD patients has a high mortality rate (up to 10%). VSD, PDA, aortic valve abnormalities and TOF are usually considered the common preoperative defects for IE. The diseases and factors for IE in the high risk group include complex cyanotic CHD (e.g., single ventricle, transposition or TOF), aortopulmonary shunt, complex intracardiac repairs with conduit, patches or prosthetic valve, and a history of previous IE.⁶⁾ Even in the simple CHD patient group, surgery itself is an important risk factor to IE. In cases of prolonged intensive care after cardiac repair with prosthetic valves or conduits, IE can develop immediately during the postoperative period (the first 2 weeks after surgery).⁷⁾

Diagnosis of IE is based on the combination of persistent bacteremia and anatomical lesions in the heart. The Duke criteria, which contain echocardiographic evidences of IE, have a high sensitivity and a high negative predictive value. The sensitivity of the Duke criteria can be further increased by performing transesophageal echocardiography. TEE should be done in the patients with a doubtful transthoracic echo, the patients with prosthetic valve and pacemaker IE, and the patients with

Correspondence : Chung Il Noh, MD, Department of Pediatrics, College of Medicine, Seoul National University, 28 Yeongeong-dong, Jongro-gu, Seoul 110-744, Korea
Tel: 82-2-2072-3632, Fax: 82-2-743-3455
E-mail: ohungnoh@plaza.snu.ac.kr

suspected abscess. However, a negative blood culture or a negative echo does not exclude IE. Culture negative IE can occur in about 10% of the overall cases. Culture-negative IE can occur if antibiotic administration was done within the previous 2 weeks, or if there is the presence of fastidious or intracellular pathogens (*Brucella* spp., *C burnetti*, *Bartonella* spp., *Chlamydia* spp., *Mycoplasma* spp., *Legionella* spp., *T whipplei*). PCR is useful in the culture-negative cases, as it can show a positive result even after long-term treatment with antibiotics.⁸⁾

IE is a serious problem with a high complication rate and high mortality (about 10%) in population with CHD. Increasing numbers of the patients are currently being operated on with using foreign materials such as prosthetic valves, patches or conduits. These patients are at the lifelong risk of IE and this risk increases with age. The risk factors to IE are chronic hypoxia, previous cardiovascular operation, repair with foreign material, cardiac interventional procedures and dental procedures.⁹⁾ Predisposing events (e.g., dental, oral and respiratory tract procedures, pneumonia, atopic dermatitis, skin infection and skin piercing) can be identified in about 50% of IE patients. For the perioperative cases, a prolonged ICU stay after recent operation with using foreign material is the most common event.⁷⁾ Staphylococcal or streptococcal species are the common causative microorganisms, although infection with Gram negative bacilli, MRSA or fungi is recently increasing.¹⁰⁾ Patients with cyanotic CHD are susceptible to gingival colonization by bacteria of the HACEK group.⁹⁾

IE associated with CHD reveals a broad range of cardiac and extracardiac complications. Cardiac failure due to valve damage, inflammation or arrhythmia is a main factor for mortality. Infection of the foreign material requires surgical removal of the material and this is associated with high mortality. The mortality is related to the severity of the underlying cardiac disease, the presence of foreign materials, the type of organisms (Staphylococci, fungi), congestive heart failure and large vegetation (>15 mm). In the case of uncontrollable heart failure, persistent infection (fever and bacteremia for more than 7-10 days despite adequate antibiotics treatment), possible embolization (large and mobile vegetation >15 mm without previous embolic events), recurrent embolization (vegetation >10 mm even after an asymptomatic embolic event), fungal IE, severe and complicated perivalvar infection (abscess, valve dysfunction, conduction disturbance, large vegetation and staphylococcal infection) and infected foreign material are all indications for an operation. However, the decision for an early operation must be tailored to the individual patient.⁸⁾¹⁰⁾

Septic emboli to the CNS, spleen, pulmonary artery or renal artery are not rare (20-40%). This condition

is associated with the migration of large mobile valvar vegetation (over 10 mm), and it is more frequent in the cases with mitral valve vegetation, the changing size of vegetation under antibiotics treatment and pathogens of the *S aureus*, *Streptococcus bovis* or *Candida* species. The incidence of embolism increases after the initiation of treatment and then the incidence decreases to 10-20% after 2 weeks of treatment. Therefore, if surgery is indicated to reduce embolism, it must be done early after the initiation of antibiotics treatment.⁸⁾

An important problem related to IE is the patients' ignorance of the disease itself and their ignorance of the risk of tattoo, acupuncture, body piercing and skin infection; poor acceptance of education from the physicians during the follow up and poor abidance to preventive/treatment measures after dental procedures. There is a general false concept among both physicians and patients that prophylactic antibiotic treatment 1 hour before dental procedures can completely eliminate episodes of IE. However, many episodes of IE arise without preceding medical/surgical procedures. Because transient bacteremia from the oral cavity is possible while chewing, tooth-brushing and other normal activities, good dental hygiene becomes very important. This emphasizes the need for continuous education of the patients and general practitioners about IE.

The article by Kim et al¹¹⁾ is timely considering the increasing population of adult CHD patients in this country. The article can stimulate the physician to perform meticulous care and to educate the patients properly. However, the article did not discuss all the aspects of IE in this specific population; there was not much implication to IE early after operation or emphasizing the significance of foreign material in the heart. Both of these factors are very important in dealing with IE in this patient group. Physicians need to stay abreast of the current and changing concepts of IE among the CHD population.

We cannot really cure most CHD. However, we have made huge progress in the medical and surgical care of CHD and greatly modified the course of CHD. By performing meticulous care and education for the people with CHD, we can lend much support to the patients with CHD.

REFERENCES

- 1) Hill EE, Herijgers P, Herregods MC, Peetermans WE. *Evolving trends in infective endocarditis*. *Clin Microbiol Infect* 2006;12:5-12.
- 2) Thomas MB, Cabell C, Fowler V Jr. *Update on infective endocarditis*. *Curr Probl Cardiol* 2006;31:274-352.
- 3) Moreillon P, Que YA. *Infective endocarditis*. *Lancet* 2004;363:139-49.
- 4) Morris CD, Reller MD, Menashe VD. *Thirty-year incidence of infective endocarditis after surgery for congenital heart defect*. *JAMA* 1998;279:599-603.
- 5) Report of the British Cardiac Society Working Party. *Grown-up*

congenital heart disease: current needs and provision of service for adolescents and adults with congenital heart disease in the UK. Heart 2002;88 (Suppl 1):i1-i14.

- 6) Ferrieri P, Gewitz MH, Gerber MA, et al. *Unique features of infective endocarditis in childhood. Circulation 2002;105:2115-26.*
- 7) Li W, Somerville J. *Infective endocarditis in the grown-up congenital heart (GUCH) population. Eur Heart J 1998;19:166-73.*
- 8) Habib G. *Management of infective endocarditis. Heart 2006;92:124-30.*
- 9) Knirsch W, Haas NA, Uhlemann F, Dietz K, Lange PE. *Clinical course and complications of infective endocarditis in patients growing up with congenital heart disease. Int J Cardiol 2005;101:285-91.*
- 10) Niwa K, Nakazawa M, Tateno S, Yoshinaga M, Terai M. *Infective endocarditis in congenital heart disease: Japanese national collaboration study. Heart 2005;91:795-800.*
- 11) Kim SH, Huh J, Kang IS, et al. *Infective endocarditis in adolescents and adults with congenital heart disease. Korean Circ J 2006;36:318-323.*