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Editorial Article

Infections in Thalassemia

Apart from anemia and bone changes secondary to ineffective erythropoiesis and hemolysis, various consequences or complications may also occur in patients with thalassemia, among them are iron overload, cardiac failure, endocrine abnormalities, infections and post-splenectomy complications. These complications occur mostly in patients with moderate disease severities which do not claim patients' early lives. Therefore, of the four common thalassemia syndromes in Thailand i.e., β-thalassemia / Hb E disease, homozygous β-thalassemia, Hb H disease and Hb Bart's hydrops fetalis, the complications occur commonly in β-thal/Hb E disease, followed by homozygous β-thalassemia. Infection has been recognized as a well-known complication in thalassemia.[1] It is also a major cause of death among patients with thalassemia. In the Mediterranean countries where β-thalassemia is prevalent and homozygous β-thalassemia is a common thalassemia syndrome, infection is second to cardiac failure as a cause of death among thalassemic patients. In Thailand, where β-thal/HbE disease is more common than homozygous β-thalassemia, infections are the leading cause of morbidity and mortality.[2] Early recognition with treatment and prevention of any predisposing factors to infections are essential components in the management of this complication in thalassemia.

Evidences from both prospective, well-controlled studies and clinical observations in Thailand suggest that thalassemic patients have more episodes of infections than normal or healthy controls i.e., thalassemic patients are susceptible to infections. The spectrum of infections in thalassemia includes mild infections, severe infections, therapy-related infections and a unique infection caused by *Pythium insidiosum*. Among the mild infections are upper respiratory tract infection, gingivitis, skin infections (impetigo and cutaneous abscess) and acute diarrhea.[3] These infections do not cause severe morbidity or mortality but may decrease sense of well-being and working ability of the patients. On the other hand severe infections are a leading cause of morbidity and mortality and also a major cause of patients' hospitalization. They are usually bacterial in etiology and include septicemia, pneumonia, biliary tract infection, salmonellosis, urinary tract infection and liver abscess.[4] About 75% of thalassemic patients who had severe bacterial infections had been previously splenectomized, suggesting that splenectomy is a predisposing factor to severe infections. Interestingly, the major organisms responsible for the severe infections were

gram-negative bacilli such as *E coli, K.pneumoniae*. Less than 20% of the etiologic agents were gram-positive bacteria with *S pneumoniae*, a well known organism responsible for post splenectomy sepsis in general was identified in only 10% of cases.

Therapy-related infections in thalassemia include transfusion-transmitted diseases and desferrioxamine-related *Yersinia enterocolitica* infection. The majorities of the former are post-transfusion hepatitis and human immunodeficiency virus (HIV) infection. Recently, hepatitis C virus (HCV) has become the major etiologic agent of post-transfusional non A, non B hepatitis in thalassemic patients since hepatitis B virus vaccination has produced a striking decrease in the incidence hepatitis B infection. In a recent survey at Division of Hematology, Department of Medicine, Siriraj Hospital, the prevalence of HCV infection as detected by anti HCV was 20% while HBs Ag was found in only 2% of 104 patients with thalassemia.[5] The presence of HCV as well as iron overload was associated with significant abnormalities of liver functions among the patients suggesting that managements of both factors, if coexist, are required in order to hamper liver damage.

Y enterocolica infection is prevalent in thalassemic patients receiving desferrioxamine (DFO).[6] The causative organisms which are gram-negative bacilli use DFO as siderophores to acquire iron necessary for their growth. The infection may be localized (benign) form i.e., tonsillitis, enteritis or severe form or septicemia. In addition to early and appropriate antibiotic therapy, DFO should be stopped during the period of infection in order to achieve an effective treatment.

Without early recognition and treatment, arteritis from a fungus-like organism, *Pythium insidiosum* can be a fatal disease.[7] This type of infection is unique for thalassemia since it does not occur in normal host and is rare in other diseases (two patients with paroxysmal nocturnal hemoglobinuria were observed). The clinical presentations are secondary to progressive ischemia from thrombosis of major arteries, usually of lower limbs i.e., claudication and gangrene, Pathological changes include ascending arteritis in the presence of hyphae in the arterial wall and thrombosis followed by a destroyed portion with fibrosis. The only effective treatment so far is amputation at the level above the infected part. It should be done before the infection ascends to the level of bifurcation of major vessels. It is likely that immunotherapy is effective.

All of the spectrum of infections described has pointed out that thalassemic patients are susceptible to infections. Among the possible predisposing factors for the increased risk of infections in thalassemia are anemia[8] and reticuloendothelial system overload by pathologic red cells, splenectomy, enhanced microbial virulence by increased iron availability in iron overload and granulocyte dysfunctions. Patterns of infections and studies from many groups do not support any major defects in lymphocytes or cell mediated immunity as predisposing factors of infections in thalassemia.[9]

Effective management of infections in thalassemia consists of both prevention and treatment. The former includes immunization with pneumococcal vaccine, oral penicillins especially in splenectomized patients and removal of predisposing factors such as gallstones, reduction of iron

burden and correction of anemia. Diagnosis and treatment of infections should be prompt especially in post-splenectomy patients. Antibiotics with coverage of gram-negative bacteria should be immediately started in splenectomized patients with clinical features of severe infections even before obtaining culture and sensitivity results.

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