BCG vaccine and Immunodeficiency

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Abstract

Tuberculosis (TB) is considered by WHO as global health emergency in 1993. In 2011 one third of the world's population was thought to be infected with TB and 8.7 million cases of active TB annually. BCG vaccine is one of the effective control measures to prevent TB. It is in practice since 1960s where TB is highly prevalent and 120 million BCG vaccines are given annually, that is effective in preventing severe disease of extrapulmonary TB. BCG vaccine is alive attenuated vaccine that potentially could prevent TB meningitis and disseminated diseases. However, it could cause local infection, in about 1:10,000 to 1:1,000,000 in immune competent individuals and significantly higher when given to immunodeficient subjects. Immunodeficient infants who receive BCG vaccine at birth could develop disseminated BCGitis, which is associated with high morbidity and mortality. However, those who develop disseminated BCGitis usually require hospital admissions and multiple medications with high cost and low survival rate ranging between 0% to 65% worldwide. Our center; KAMC-WR, Jeddah Saudi Arabia, has 83% survival rate of treating patients with disseminated BCGitis, but with using cytokine therapy and aminoglycoside drug in addition to common anti-TB drugs.

There is high rate of primary immunodeficiency diseases (PID) in the Middle East and ministry of health in Saudi Arabia recently succeeded in moving the BGC vaccine to 6-month of age, instead of giving it at birth, in order to have time for diagnosing PID. WHO considers the development of new TB vaccines a major public health priority.

Conclusion; BCG vaccine is one of the effective preventive measures of TB, however, it could cause serious complications with low revival rate. Moving the BGC vaccine to 6-month of age will give time for diagnosing PID. Using cytokine therapy and aminoglycoside drug in addition to common anti-TB drugs will significantly reduce mortality and morbidity. There are potentials for development of new BCG vaccine.

SCID patients were categorized based on their phenotype into B- and B + group. In our cohort, 66.6% of SCID patients had B + phenotype and the rest of them demonstrated B- phenotype. Among these patients, the majority of them were T-B + NK- (40.7%), and 25.9% were T-B + NK+, 18.5% were T-B-NK + and 17.8% were T-B-NK- (Table 2). The severe BCG vaccine complications were seen in SCID patients with T-B + NK- phenotype.

The data obtained from flow cytometry showed that the lymphocyte counts in SCID patients have decreased, whereas these same cells have increased in CGD and MSMD patients ($p < 0.001$). In addition, the percentage of CD3+, CD4+, CD8+ lymphocyte has significantly increased in MSMD and CGD patients, while showing a significant reduction/absence in SCID patients ($p < 0.001$). Moreover, there was a significant difference in the percentage of CD19+ across the three groups of patients (increased in MSMD and decreased in SCID, $p = 0.002$). Evaluation of serum immunoglobulins showed increased levels of IgG, IgA, IgM, IgE in CGD patients, but decreased levels in SCID patients ($p < 0.001$).

Additionally, the total lymphocytes count and CD19+ lymphocytes were significantly lower in T-B-NK- SCID patients ($p = 0.003$ and $p = 0.004$, respectively) (Table 2). Other demographics, clinical and laboratory data were not significantly different among the four phenotypes of SCID patients ($p > 0.05$).

There was no defect regarding the anti-tetanus and anti-diphtheria immune response in CGD patients. However, impaired antibody production against tetanus and diphtheria toxoids was detected in a high proportion of SCID patients (60% and 73.3%, respectively). Data obtained from the NBT test showed that there was a defect in all the CGD patients, whereas it was normal in the MSMD and SCID patients, as expected. All laboratory information and their comparison among the three types of PIDs. PIDs can lead to BCGosis with various severities. In addition to the severity of the complications, the onset of these manifestations also varies. Overall, BCGosis in patients with SCID and CGD presents more aggressive features than other immunodeficiencies like MSMD.7 Parental consanguinity is a known risk factor for the development of an autosomal recessive form of PIDs. Since the rate of consanguineous marriage in Iran is high, many children with immunodeficiency are at risk of developing BCGosis. Thus, a regular and accurate screening program (at least discovery of SCID by counting T cell receptor excision circles in neonatal Guthrie card) in addition to the proper and early diagnosis of PIDs is needed. Perhaps, paying attention to the family history of immunodeficiency disorders, especially before BCG vaccination, seems extremely necessary. Furthermore, a manifestation of BCGosis could be an important indicator of early diagnosis of PIDs. Thus, increasing awareness of physicians about the association of BCGosis and PIDs is necessary and will lead to earlier diagnosis of these heterogeneous groups of disorders.

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