Letter to the Editor

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An Alarm for Pediatricians Facing BCG Vaccine Complications

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Dear Editor

The Bacillus Calmette Guérin (BCG) vaccine is an attenuated live vaccine that has been recommended since 1921 and is currently administered in over 100 countries (1). According to the National Immunization Program (NIP) of Iran, the BCG vaccine is given at birth (2) However, there is currently no national screening test for underlying immunodeficiency disorders in Iran. Therefore, despite the contraindication of administering the BCG vaccine to cases of Severe Combined Immunodeficiency(SCID) (3), most of these cases still receive the vaccine at birth. This is because they typically do not exhibit any abnormal signs or symptoms in the neonatal period or they may have no family history of congenital immunodeficiency diseases.

SCID is a hereditary disease, with an incidence of one case in 40,000-100,000 live births. Typically, SCID patients are not diagnosed until 4-7 months of age (4) when they have likely experienced several episodes of infections. The survival rate for these patients has significantly improved with hematopoietic stem cell transplantation (HSCT).

In Iran, the survival rate for SCID patients is affected by disseminated BCG infection (BCG-osis) following BCG vaccination. It is crucial for clinicians, particularly pediatricians, to be aware of the potential complications of BCG vaccination in SCID cases. Once a diagnosis of SCID is confirmed, if the patient is not yet showing symptoms, it is essential to promptly start post-exposure chemoprophylaxis to prevent the dissemination of BCG and the development of BCG-osis.

When there are no signs of local disease (known as BCGitis), the suggested post-exposure prophylaxis regimen is to initiate of a combination of rifampin and isoniazid during the pre-transplantation period and continue it during the post-transplantation period until complete immunological reconstitution occurs. This regimen should be started as soon as possible before any signs and symptoms of BCGitis develop for maximum effectiveness. Some recommend only careful observation without any chemoprophylaxis at this stage (5). However, if effective post-exposure prophylaxis against Mycobacterium bovis is not started timely, the prognosis of the patient is poor despite HSCT.

It should be noted that, unlike prevention, treatment of BCG-osis is usually unsuccessful and often leads to a poor prognosis in immunocompromised cases, especially in SCID patients.

Cases of SCID are not the only examples of inborn errors of immunity (IEI) that can result in complications from neonatal BCG vaccination. Patients with Chronic Granulomatous Disease (CGD) and Mendelian Susceptibility to Mycobacterial Diseases (MSMD) are also at risk for severe complications from BCG vaccination (6,7) .

Other IEIs such as hyper-immunoglobulin E syndrome (HIES or Job's syndrome) and X-linked hyper IgM syndrome are also at risk of BCG infection. However, complications from BCG vaccination are typically less common and severe in these diseases compared to those mentioned above (7).

It seems that the timing of BCG vaccination at birth should be reevaluated, particularly in regions where TB incidence is low. The incidence of TB has significantly decreased in recent years in Iran (8) prompting a suggestion to change the timing of BCG vaccination from birth. It is also recommended to screen for IEI before administering the BCG vaccine (9). While there are concerns about the efficacy of the BCG vaccine in tropical areas where exposure to atypical mycobacteria is common (10), it seems prudent to change the timing of BCG vaccination in non-tropical regions with low TB incidence.

It is recommended to carefully review the family history for any cases of immunodeficiency or sibling death due to infection or unknown causes before administering the BCG vaccination. In these situations, avoid administering any live vaccines until the immune system has been evaluated and potential immunodeficiency has been ruled out. It is also advised for families with a history of inherited immunodeficiency disorders to consider non-consanguineous marriage.

This letter emphasizes the importance of starting a two-drug post-exposure prophylaxis regimen as soon as possible after identifying SCID and before any signs or symptoms of BCG infection appear in infants living in regions where the BCG vaccine is administered at birth.

REFERENCES

1. Shahmohammadi S, Saffar MJ, Rezai MS. BCG-osis after BCG vaccination in immunocompromised children: Case series and review. ***Journal of Pediatrics Review*** 2014;2(1):62-74.
2. National Immunization technical advisory group of the Ministry of Health and Medical Education of Iran. Schedule and Guideline of Immunization. Iran: Unicef; 2015 [Cited 2022-October-11]. Available from: https://goums.ac.ir/files/aghala/files/4(2).pdf [In Persian].
3. American Academy of Pediatrics. [Tuberculosis.] In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book: 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics: 2021[786-814].
4. Centers for Disease Control and Prevention (CDC). Addition of severe combined immunodeficiency as a contraindication for administration of rotavirus vaccine. ***MMWR Morb Mortal Wkly Rep*** 2010;59(22):687-8.
5. Bernatowska E, Wolska-Kuśnierz B, Pac M, Kurenko-Deptuch M, Pietrucha B, Zwolska Z, et al. Clinical guidelines Risk of BCG infection in primary immunodeficiency children. Proposal of diagnostic, prophylactic and therapeutic guidelines for disseminated BCG based on experience in the Department of Immunology, Children's Memorial Health Institute in Warsaw between 1980-2006. ***Central European Journal of Immunology*** 2007;32(4):221-5.
6. Movahedi Z, Norouzi S, Mamishi S, Rezaei N. BCGiosis as a presenting feature of a child with chronic granulomatous disease. ***Braz J Infect Dis*** 2011;15(1):83-6.
7. Norouzi S, Aghamohammadi A, Mamishi S, Rosenzweig SD, Rezaei N. Bacillus Calmette-Guérin (BCG) complications associated with primary immunodeficiency diseases. ***J Infect*** 2012;64(6):543-54.
8. https://icdc.behdasht.gov.ir/TB_status/%D9%85%D8%B1%D9%88%D8%B1%DB%8C-%DA%A9%D9%88%D8%AA%D8%A7%D9%87-%D8%A8%D8%B1-%D8%B1%D9%88%D9%86%D8%AF-%D9%BE%D9%86%D8%AC-%D8%B3%D8%A7%D9%84%D9%87-%D8%B4%D8%A7%D8%AE%D8%B5-%D9%87%D8%A7%DB%8C-%D8%A8%D8%B1%D9%86%D8%A7%D9%85%D9%87-%DA%A9%D9%86%D8%AA%D8%B1%D9%84-%D8%B3%D9%84-%D8%AF%D8%B1-%DA%A9%D8%B4%D9%88%D8%B1. Accessed October 07, 2022.
9. Sayyahfar S, Esteghamati A, Rezaei N. Is It Time to Change the BCG Vaccine Administration Time in Iran? ***Tanaffos*** 2023;22(4):353-6.
10. Poyntz HC, Stylianou E, Griffiths KL, Marsay L, Checkley AM, McShane H. Non-tuberculous mycobacteria have diverse effects on BCG efficacy against Mycobacterium tuberculosis. ***Tuberculosis (Edinb)*** 2014;94(3):226-37.