

Editorial



The Necessity of a Nationwide Surveillance System of Serious BCG Adverse Reactions

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OPEN ACCESS

Received: Dec 19, 2018

Accepted: Dec 29, 2018

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Disclosure

The author has no potential conflicts of
interest to disclose.

► See the article “*Mycobacterium bovis* osteitis following immunization with Bacille Calmette-Guérin (BCG) in Korea” in volume 34, e3.

Since the Bacille Calmette-Guérin (BCG) vaccine was first used in 1921, it has been administered safely to billions of people all over the world. Local adverse reactions such as skin reaction and regional lymphadenopathy are common after BCG vaccination, but most of these recover without sequelae. BCG osteitis and generalized BCG infection after BCG vaccination are very rare. The risk of osteitis after BCG vaccination has varied from 0.01 to 300 per million doses, depending on the skill and method of administration, the strain, dose, gender, age, and immune status of the recipient.¹

In the current issue of *Journal of Korean Medical Science*, Choi et al.² demonstrated the clinical characteristics of 21 children diagnosed with BCG osteitis during 2007–2018. Although it was reported from a single referral center, it is the first report in Korea that reported a number of cases that occurred over a relatively long period. The clinical features of the patients were comparable to those reported from other countries.³ BCG osteitis mainly occurred in children less than 5 years of age and was rarely accompanied by fever $\geq 38^{\circ}\text{C}$. The bones of the limbs, especially lower limbs, were mainly involved rather than the axial bones. Some patients were diagnosed only after a few months after the onset of symptoms, and the authors emphasized the importance of clinical suspicion based on clinical features of BCG osteitis.² There is no national data on the incidence of BCG osteitis in Korea. In their study, the incidence of BCG osteitis following the percutaneous BCG vaccination (Tokyo-172 strain) in Korea was estimated at 4.44 cases per million based on the results of the study. In Taiwan, the isolated extrapulmonary tuberculosis (TB) strains and pathologic specimens collected from children < 5 years of age have been sent to the national mycobacterial laboratory for detection of BCG strain since 2008. After this active surveillance, the incidence of BCG osteitis increased from 3.7 cases per million doses during 2002–2006 to 30.1 per million during 2008–2012.³

In Korea, BCG vaccination is recommended for all newborns within 4 weeks of age, with an immunization rate of up to 99%⁴; and only intradermal BCG vaccine is included in the national immunization program but percutaneous BCG vaccine is not. Therefore, although the immunization rate of the percutaneous vaccine is more than twice that of the intradermal vaccine, BCG osteitis following percutaneous BCG vaccination has been not reported to the

vaccination adverse event reporting system. Also, BCG vaccination is being administered to all newborns in Korea without any screening test for severe combined immunodeficiency syndrome (SCID), which is a high-risk condition of disseminated BCG infection. In Taiwan, the timing of BCG vaccination was delayed from 24 hours after birth to 5 months of age in 2012, when SCID screening test is available nationwide, in order to be able to obtain screening results prior to vaccination. In addition, there was a decrease in the TB incidence in Taiwan (48 cases per 100,000 population in 2014), and the schedule of BCG immunization was revised to recommend for infants aged 5–8 months to further decrease the risk of BCG-related severe adverse reactions.⁵ In Japan, the incidence of osteitis after BCG vaccination was reported as two per million doses during 1998–2007.⁶ In 2013, the recommended age of BCG vaccination was delayed to 5–7 months of age to lower serious complications after the BCG vaccination.

According to the criteria proposed by the International Union against Tuberculosis and Lung Disease, the BCG vaccination policy can be considered to change from routine universal BCG vaccination to selective vaccination of high-risk groups in countries that meet the following conditions.⁷ An efficient notification system should be in place, and one or more of the following three must be met: either the average annual notification rate of smear-positive pulmonary TB is less than five per 100,000 population per year, or the average annual notification rate of TB meningitis in children < 5 years of age is less than one per 10 million population over the previous 5 years, or the average annual risk of TB infection is less than 0.1%. Under the multifaceted efforts of healthcare providers and public health authorities, the overall incidence of TB has been gradually decreasing over the past decade in Korea. However, the TB incidence in 2017 is about 70 per 100,000 population,⁸ which is higher than other developed countries and requires routine universal BCG immunization. Therefore, the nationwide incidence of severe adverse reactions following BCG vaccination should be monitored to determine the optimal timing of BCG vaccination.

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