CASE REPORT

Disseminated Bacillus Calmette-Guérin Disease after BCG Vaccination: A Case Report from China

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ABSTRACT

Background: Bacillus Calmette-Guérin (BCG) vaccination is recommended for newborn infants worldwide to prevent tuberculosis. However, complications do occur inevitably in a very low rate, among which the most serious is disseminated disease. The disseminated bacillus Calmette–Guérin disease is a rare disease with high fatality, and can be seen among persons with an underlying immunodeficiency. **Case presentation:** We report a 4-month-old male infant presenting with recurrent fever, an isolated left axillary massand swelling at the site of BCG inoculation. The cellular immune function analysis showed that the value of CD4/CD8 was 0.994, indicating the existence of immunodeficiency.The results of blood culture and throat swab culture showed conditional pathogen infection. He died of cardiopulmonary failure. **Conclusion:** In this case, necropsy played a significant role in the final diagnosis of disseminated pulmonary tuberculosis.

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Keywords: Bacillus Calmette-Guérin (BCG), Immunodeficiency, Pathogen infection, Tuberculosis, Vaccination

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INTRODUCTION

Bacillus Calmette-Guérin (BCG) vaccine is a live attenuated vaccine derived from *Mycobacterium bovis* (1). BCG vaccination is recommended for newborn infants worldwide, to prevent tuberculosis. The vaccine is generally considered to be safe in immunocompetent hosts (2). However, complications do occur inevitably in very low rates, among which the most serious one is disseminated disease (3). Disseminated bacillus Calmette–Guérin is a rare disease with a high fatality rate, and can be seen among people with underlying immunodeficiency (4).

THE CASE

A 4-month-old male infant presented recurrent fever, an isolated left axillary mass, and swelling at the site of BCG inoculation. Skin rashes and desquamation were seen on his whole body. At birth, he had received the hepatitis B (No. 20070101-1) and BCG (No. 2006040202) vaccines in the left deltoid muscle as a part of the routine immunization protocol in China.

The baby was brought into a pediatric hospital in Hangzhou, Zhejiang, with a marked fever of 40.2°C as the chief complaint. Laboratory measurements at the time of admission revealed an increased WBC count of 23.4×10^9/L (55.9% neutrophils ↓), decreased hemoglobin of 101g/L, increased platelet count of 523×10^9/L, and increased C-reactive protein of 66mg/L. *Stenotrophomonas maltophilia* and *Staphylococcus capitis* were seen on his blood cultures, while *Staphylococcus sciuri* was seen on the throat swab cultures. The chest radiograph and CT indicated the consolidation of the right upper lung and the infection of both lower lungs. Moreover, the cellular immune function analysis showed that the value of CD4/CD8 was 0.994, indicating the possibility of immunodeficiency. The bronchofiberscope revealed that the infant suffered from bronchial inflammatory lesions.

A presumptive diagnosis of pulmonary tuberculosis was made, and the therapy with isoniazide, rifampin, and pyrazinamide begun. However, the antituberculosis therapy did not work, and the infant remained in a serious condition with the persisted skin lesions and intermittent marked fever. Subsequently, he was brought to another hospital for further diagnosis and treatment. In that hospital, the admitting diagnosis of the infant was severe pneumonia with mold infection, toxic hepatitis, and left axilla tuberculous lymphadenitis. In consideration of fungal infection, he was given intravenous voriconazole and reduced glutathione. However, in the second morning after admission, he suddenly died of cardiopulmonary failure.

The patient`s pathologyof necropsy were as follows: 1) Several small caseous necroses were seen in the dermis and subcutaneous of anabrotic skin on the left upper arm, aroud one of which there were epithelioid cell hyperplasias. 2) A large number of caseous necroses were seen in the enlarged lymph nodes of the left axillary. 3) Large pieces of caseous necroses could be observed in the superior lobe of right lung, around which there were a small amounts of epithelioid cells and lymphocytes, without Langhans' giant cells. 4) There were hardly any normal alveolars around the lesion in the right lobus superior pulmonis. There were caseous necroses also in hilus pulmonis; and one of the caseous necroses was connected with bronchus, which formed a cavity. 5) In the left lung and inferior lobe of right lung, there were several disseminated caseous

necrosis with mononuclear macrophage and lymphocyte infiltration. (6) Several small caseous necrosis were seen in the liver and spleen.

DISCUSSION

Our patient first presented marked fever, and had refractory aphthous stomatitis and pulmonary infection during the early stage of the illness. Blood routine examination indicated increased WBC and platelet count, decreased hemoglobin, and increased C-reactive protein. He ,in the early stage, had axillary lymphadenectasis, and left preaxillary mass was observed during his hospitalization. Then puncture results showed caseous necrotic and a bit of skin adipose tissue.

The cause of death was clear. The necropsy showed hematogenous disseminated tuberculosis, tuberculous ulcer on the skin of the left upper arm, left axillary tuberculous lymphadenitis, caseous necrotic lung tuberculosis with the formation of cavity, obsolete pleurisy of right lung, miliary tuberculosis in the liver and spleen.

The evidences of immunodeficiency in this case are as follows: 1) The results of blood culture and throat swab culture showed conditional pathogen infection. 2) The infant had refractory aphthous stomatitis prior to the illness onset and during the early stage. 3) The necropsy revealed lung tuberculosis while there was no typical primary syndrome. And large pieces of caseous necrosis could be observed, however, there were no Langhans' giant cells around the necrosed areas and a small amount of epithelioid cells, which indicated that the immunity of the infant was poor and the reaction around the focus of infection was not substantial. 4) Though the blood test showed the values of CD4, CD8 and CD4/CD8 were within the normal range and the result of PPD test was positive, there was a lacke of evidence of macrophage viability which was closely related to immunity after tuberculosis infection. 5):The serum test showed the antibodies of 16Kda, 38Kda, and LAM were all negative. All the above proved that the infant had immune system hypofunction.

The working definition of disseminated BCG disease requires the following: a culture positive for BCG (the identification of which has been confirmed by biochemical methods at least); demonstration of dissemination by either a positive blood or bone marrow culture or evidence of infection at two or more anatomic sites beyond the region of vaccination, and signs and symptoms consistent with mycobacterial disease (5). However, it is inadequate to make a definite conclusion that the disseminated pulmonary tuberculosis in our patient was caused by BCG vaccination. The reasons are as follows: It is common to have preaxillary lymphadenectasis as the side reaction of BCG inoculation, and most of them are local lesions without systemic tuberculosis. Patients with disseminated Bacillus Calmette-Guerin disease usually have multiple lymph nodes which progress fester and suppurative without healing. Our patient had no ulcerative left axillary lymphadenitis. Besides, tubercle bacillus had not been isolated. Thus, it is difficult to conclude definitely whether the infectious pathogens of this case were BCG vaccine strains or natural bacterial strains.

The most significant evidence was the finding from necropsy, which assured the final diagnosis of disseminated pulmonary tuberculosis.

Disseminated BCG infection is the most severe complication to BCG vaccination. Therefore, the medical personnel should have a strong understanding of these rare kind of cases. Early diagnosis and promt treatment are essential to reducing deaths.

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REFERENCES

1. Rezai MS, Khotaei G, Mamishi S, Kheirkhah M, Parvaneh N. Disseminated Bacillus Calmette–Guerin Infection after BCG Vaccination. J Trop Pediatr. 2008;54:413-6.
2. Huang L-H, Shyur S-D, Weng J-D, Tzen C-Y, Huang F-Y. Disseminated Bacille Calmette-Guérin Disease as the Initial Presentation of X-linked Severe Combined Immunode-ficiency-A Case Report. Asian Pac J Allergy Immunol. 2010;23:221-6.
3. Stephan J, Vlekova V, Deist FL, Blanche S, Donadieu J, Saint-Basile GD, et al. Severe combined immunodeficiency: a retrospective single-center study of clinical presentation and outcome in 117 patients. J Pediatr. 1993;123:564-72.
4. Sadeghi-Shabestari M, Rezaei N. Disseminated bacille Calmette–Guérin in Iranian children with severe combined immunodeficiency. Int J Infect Dis. 2009;13:e420-e3.
5. Talbot EA, Perkins MD, Silva SF, Frothingham R. Disseminated bacille Calmette-Guerin disease after vaccination: case report and review. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 1997; 24:1139-46.