Original Article

RECENT PROBLEM OF SKIN LESIONS INDUCED BY BCG VACCINATION

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Abstract [Purpose] To study the recent trends of occurrence of skin lesions as adverse reactions of vaccination with Bacillus Calmette-Guérin.

[Materials and Methods] The Reports of Vaccination Adverse Reaction Notification by Ministry of Health, Labour & Welfare, and literature retrieved from the Japan Medical Abstract (Centra Medicina Revuo Japana) were reviewed and analysed.

[Results and Discussion] There has recently been an increasing incidence of skin tuberculosis-like lesions as adverse reactions of infants in Japan due to BCG vaccination. According to the reporting system of the adverse reaction of vaccinations, the incidence rate per one million vaccinations was 1.7 from 1995 to 2002 but raised to 11.8 from 2003 to 2005. A similar trend is also seen in case reports in publications. A total of 102 cases were reported in the journals and conferences, out of which 74 were 1) generalized skin rash and 23 were 2) localized skin lesions (the remaining five could not be categorized). Type 1) and type 2) lesions roughly correspond to tuberculids and true skin cutaneous tuberculosis (including wart and lupus), respectively, for skin tuberculosis due to *Mycobacterium tuberculosis*. The recent increase of these reactions is mostly attributed to the increase in the former type of lesions, which may be associated with the concentration of the BCG vaccination among infants especially after 2005 since when the vaccination has been targeted only at those aged less than 6 months under the new vaccination policy. The prognosis of both lesions is quite good. The anti-tuberculosis treatment was given to only 20% of the former cases and 75% of the latter cases (including surgical procedure), and all were cured or subsided. There were several cases with serious underlying conditions such as severe combined immunodeficiency and Kawasaki disease in the former category.

[Conclusion] This type of adverse reaction warrants no serious concern; however, staff members should be able to recognize it adequately so that they can manage it properly and not seriously worry the guardians.

Key words: BCG, Tuberculid, Skin tuberculosis, Adverse reaction

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Original Article

THE FUNDAMENTAL EVALUATION OF COBAS®TaqMan48 USING CLINICAL SPECIMENS

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Abstract [Purpose] When smear test is positive for acid-fast bacilli, it is important to differentiate between *Mycobacterium tuberculosis* complex and nontuberculosis mycobacteria (NTM) in healthcare associated infection (HAI) control. The aim of this study is to evaluate between COBAS® TaqMan48 (TaqMan) and COBAS® Amplicor (COBAS).

[Material and method] Tenfold dilution series of 5×10^4 cfu/mL of *Mycobacterium bovis* (ATCC19210) were used for evaluating the limit of detection (LOD) and reproducibility.

73 frozen clinical specimens (34 *M. tuberculosis* complex and 39 NTM) stored at below −20℃ before its use that were treated with NALC-NaOH were used to determine the agreement between two methods.

Divided reaction reagents (include Master mix solution, Internal control and Mg^{2+}) of TaqMan for 3 and 6 tests per batch used to evaluate reagents stability.

[Result] The LOD of both kits were 5×10^2 cfu/mL. Regarding reproducibility, the same result was obtained when tested 3 times.

The agreement rate between TaqMan and culture method was 58.8%, and between COBAS and culture method was 67.6%. When limited to smear positive eleven specimens, the agreement between TaqMan and culture method was 81.8%, and between COBAS and culture method was 90.9%. Reagents divided for 3 tests and 6 tests and stored at 4℃ in dark, both test reagents stability was confirmed maximum for 16 days.

[Conclusion] As the results of the evaluation of TaqMan, the LOD, reproducibility and the agreement were similar to COBAS results. However, in low colony forming unit of clinical specimen raise the possibility that results may contain false negative.

Key words: COBAS® TaqMan48, *Mycobacterium tuberculosis* complex

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Review Article

OSTEITIS AS A COMPLICATION OF BCG VACCINATION

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Abstract [Objectives] To investigate the incidence and increasing tendency of osteitis after BCG vaccination and, in addition, its clinical features, diagnostic methods and results of treatment.

[Subjects] 22 cases of Japanese children who received BCG vaccination between 1998 and 2007 and developed osteitis, and were reported in medical journals or meetings.

[Results and discussion] Iincidence was very low, 0.2 per 100,000 vaccinations, and an increasing tendency was not seen after 2005, when the vaccination in Japan was limited to below 6 months after birth. However, it might be necessary to follow for much longer period. About 73% of cases of osteitis were seen from 9 to 18 months after receiving the vaccination. The bones of the extremities were commonly affected. Radiography usually showed the defect and cavity formation of the affected bone and often abscess around the lesion. Definitive diagnosis was made by the detection of BCG from the pus or biopsied materials. Recently, multiplex PCR method have been utilized and proved to be a rapid and reliable diagnostic method. Tuberculin reaction was positive, but QFT was negative in all tested cases; QFT will be available for the differential diagnosis of BCG and tuberculous infection. Only 2 patients had multiple lesions, and they had partial interferon-γ receptor 1 deficiency. Immunodeficiency might have some relationship to the development of osteitis after BCG vaccination. The treatment using INH and RFP was very effective and the outcome was favorable; most of the patients were cured after 6 to 12 months chemotherapy without any complications. However, there is the possibility of defects occurring in the bone and restriction of the articular movement when the diagnosis and treatment are delayed.

[Conclusion] BCG osteitis, although rare, should be considered as a possible complication of the BCG vaccination, and early diagnosis and treatment of this complication is necessary.

Key words: BCG vaccination, Osteitis, Immunodeficiency, QFT, Multiplex PCR

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The 83rd Annual Meeting Educational Lecture

NEW HORIZONS OF NEXT GENERATION CHEMOTHERAPY FOR MYCOBACTERIOSIS

Norio DOI

Abstract: Stop TB Partnership (WHO) reported "Global TB Research and Development Projects" on the basis of the annual survey (October 2007): Basic Research: 9 projects, Drug Discovery: 32 projects, Preclinical: 8 projects, Clinical Testing: 13 projects are in proceeding. Among them, promising 7 of the new Anti-TB drug candidates: Nitroimidazopyran PA-824, Moxifloxacin MFLX, Gatifloxacin GFLX, Diarylquinoline TMC-207/R207910, Nitroimidazo-oxazole OPC-67683, Pyrrole LL-3858 and Diamine SQ-109 are in progress in clinical trial Phase I−III. In 2006, Working Group on New TB Drugs (WGND)/Stop TB Partnership and Global Alliance for TB Drug Development (GATB/TB Alliance) target: by 2010, 1−2 new drugs will be registered for TB; by 2015, 7 new drugs registered for TB indication, and treatment will be shortened regimens of 3−4 months with affordable and highly effective drugs.

Key words: Anti-TB drug, Chemotherapy, M(X)DR-TB, TB/HIV co-infection case

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