AN EPIDEMIC OF COMPLICATIONS OF BCG VACCINATION

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Abstract

A total of 633 patients presented with adverse effects of BCG vaccine in different health facilities in Khartoum within a period of five months. This coincided with the introduction of two new strains of the vaccine (Pasteur and Connaught). 557(89%) of the cases were infants under nine months, 79% of whom were vaccinated within the first three months of age. The adverse effects developed as early as one week following inoculation. 601(95%) and 147(23%) of the cases presented with adenitis and undue vaccination lesion, respectively. There was one case of disseminated BCGitis who survived, but another one died. Change of the vaccine strains may be responsible for the outbreak.

Introduction

Although BCG vaccines are amongst the most widely used, they are the most controversial with respect to their protective effects. In contrast to the findings of the large-scale trial in south India, which showed that administration of BCG vaccine had no protective effect, recent studies proved that BCG immunization of the newborn and young infants produced significant level (52-90%) of protection against tuberculosis in childhood, especially against tuberculous meningitis where the protective effect may be as high as 95%[1-3]. This has increased the tendency for more uptake of the BCG vaccines in vaccination programmes particularly in countries where the incidence of tuberculosis is not falling[4].

In Sudan, the estimated risk of infection with tuberculosis is 3.4% and the case fatality rate amounts up to 10% in some hospitals[5-7]. Accelerated programme of immunization was started in 1985 which improved the BCG vaccination coverage from 8% in 1984 to 54% in 1988 to 60% in 1992[4].

Early in 1990, it was noted that there were many cases of adverse effects of the BCG vaccine. This occurred few months after reintroduction of Pasteur strain of the vaccine in late 1989. The strain was then withdrawn and replaced in September 1990 with the Connaught strain. This is a report of a surveillance conducted in the national capital- Khartoum, during the period between September 1990 and January 1991.

Patients and Methods

Paediatricians and medical practitioners in 20 accessible health centres in Khartoum, were requested to complete a typed questionnaire for every case they attend with complications due to BCG vaccination during the period between the first of September 1990 and the 31st of January 1991. The data was collected with the help of the Disease Surveillance Department of Expanded Programme of Immunization (EPI). Simple tabulation was done using the computer software Epi Info (8). The Chi square test was used to the 5% significance level.

Results

A total of 633 children with adverse effects due to BCG vaccination were reported by paediatricians and medical practitioners in the three districts of the national capital, namely Khartoum, Khartoum North and Omdurman, during the five-month period of the study. Four cases were excluded because the data was incomplete. There were 331(53%) cases seen in hospitals, 171(27%) in private clinics and 127(20%) in health centres. Their ages ranged from six days to two years: 557(89%) of the patients were under nine months (Table 1). The male to female ratio was 1.2:1.0 The majority (79%) of the children received the BCG vaccine before they were three months old and by the age of nine months, 98% of

them were vaccinated (Figure). Out of 629, 381(61%) and 248(39%) of the cases received Pasteur and Connaught strains, respectively: 55% were vaccinated in health centres, 30% in hospitals, 8% in private clinics, 7% in primary health care units, dispensaries or by mobile vaccination teams. The vaccines were administered by vaccination officers, nurses, midwives, health visitors or doctors. Out of 629, 407(77%) of cases were brought for medical advice before they were three months old and this correlated well with the age at which these children were vaccinated (Figure). The duration of symptoms ranged from 6 to 240 days: 154(25%), 275(44%) and 118(19%) of the cases were seen within one, two and three months of the start of the symptoms, respectively.

Lymphadenitis was seen in 601(95%) of cases, all on the same side of vaccination - the vaccine being administered on the proximal left forearm. Involvement of the left axillary group of glands occurred in 452(75%) cases; and together with epitrochlear glands, they accounted for 546(91%) of the cases. Occipital and cervical gland involvement was observed once in each case. When the vaccine was given in the thigh, the groin glands were enlarged (3%) (Table 2). The size of the glands was estimated to be more than one centimetre in diameter in 410(68%) of cases and 258(43%) of all the glands were fluctuant.

Undue vaccination lesion was observed in 176(28%) of cases. This varied from a large induration, significant subcutaneous abscess, big ulcer or delayed healing of the scar. There was one case of keloid.

Other complications included post-vaccination fever, allergic rash and extensive dermatosis (depigmentation) which occurred in 14, 8 and 2 of the cases, respectively. There was one case of cough, nocturnal fever, loss of weight and radiological changes suggestive of tuberculosis. There was also one case of generalised lymphadenopathy with septicaemia who survived and a similar case had fatal BCGitis.

DISCUSSION

Intradermal inoculation of a live BCG vaccine, normally results, after three weeks, in a bluish red papule at the site of injection. The lesion reaches its maximum size in six weeks, when the skin overlying it becomes shiny and ulcerates. The ulcer is typically about five millimetres in diameter and usually heals by the thirteenth week[9]. The vaccine is recommended to be given from the first day of life and almost all the patients in this series received it by the age of nine months; globally, 88% of the children received the vaccine by the first year[4].

Unlike most previous studies, the patients in this series showed wide spectrum of complications and these started as early as one week following vaccination. Sporadic cases of BCG vaccine complications had been reported since the vaccine was first introduced in 1921[10]. Undue local ulceration, abscess formation at the vaccination site and swelling of the regional lymph nodes are the most common complications[11-22]. Less frequent complications include osteitis, skin reactions, disseminated BCGitis, meningitis and polyneuritis[23-31].

Lymphadenitis was a major adverse effect in this series. This is not surprising since four-fifth of the children were below six months of age and adenitis is known to be common in the neonates and occurs exclusively in children under two years of age[32]. There was also frequent involvement of the epitrochlear glands. The findings of large and suppurative adenitis was in agreement with other studies[11-20].

Although undue reaction at the vaccination site occurred in just over a quarter of the cases in this series, yet many participants in the study believed that this figure was an underestimation[33]. Quite a few mothers did not present their babies because of excessive vaccination lesion and the condition was picked up during examination either for adenitis or any other reason for seeking medical attention. Moreover, there were cases dealt with by surgical units and those were not included in the surveillance. Localized subcutaneous abscesses, big ulcers and depigmented skin lesions of the type seen in this series were also reported elsewhere[22,23].

Only two cases of disseminated BCGitis were seen in this study, one of whom died with septicaemia-like illness and the diagnosis was based on clinical grounds, unlike other studies where facilities were readily available for confirmation[26-28].

Very few epidemics of complications due to BCG vaccination were reported in literature. An epidemic of subcutaneous abscesses after BCG vaccination was reported amongst school children and was attributed to faulty vaccination technique[34] Poor vaccination technique, high potency or virulence of the vaccine, wrong dose or wrong mixing, were all

incriminated in the causation of these adverse effects[10,32,34,35]. In this study, Pasteur strain was used in three-fifth while the Connaught was used in the remainder of the cases and each of them was responsible for an equal number of cases of adenitis (p=0.91) and undue vaccination lesion (p=0.24, Table 2). On the other hand, the vaccines were administered by trained medical staff who had been doing the same job long before the epidemic, and therefore bad technique would certainly not account for most of the cases. On the other hand, the rates of adverse reactions following BCG vaccination is said to be directly related to the prevalence of tuberculosis in the community and these vary from 0.1% to 4.3% - knowing that Sudan is classified among the high prevalent countries for tuberculosis[4-7,36].

Since the epidemic coincided with the introduction of new strains of the vaccine, perhaps a more appropriate explanation is the phenomenon reported from Zimbabwe, where it was shown that the rate of adverse reaction to BCG rose rapidly with introduction of a different strain of the vaccine[37]. Moreover, it is documented that different strains of vaccine have different risks of complications[32]. Unfortunately at this point of the study, it would be difficult to pinpoint exactly where things went wrong but it may be true that change of the vaccine strain may have caused the outbreak and further detailed search is mandatory. Management and follow up of the case will be dealt with in another report.

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References

1. Tuberculosis prevention trial, Madras. Trial of BCG vaccines in south India for tuberculosis prevention. Indian J Med Res 1980;72:Suppl,1--74.

2. BCG vaccination in the newborn and young infants. Wkly Epidemiol Rec 1980;55:1-3.

3. Efficacy of infants' BCG immunization. Wkly Epidemiol Rec 1986;61(28):216-218.

4. Expanded Programme on Immunisation Information system. Summary of the WHO Eastern Mediterranean Region. WHO/EPI/CEIS/96.03.

5. Zaki AM. A community-based study on tuberculosis control at the primary health care level in the Red Sea Area - Sudan. MD Thesis. University of Khartoum 1995.

6. Ibrahim SA, Karrar ZA, Bashar S. The pattern of Childhood tuberculosis in Khartoum. Sudan Med J 1993;31(2):1-15.

7. Ministry of Health. Annual Statistical Report. Health Statistic and Research Department. Khartoum 1993.

8. Epi Info version 5. USD Incorporated, 2075A West Park Place, Stone Mountain, GA 30087.

9. Irvine KN. BCG and Vole Vaccination. A practical handbook. London, National Association for the Prevention of Tuberculosis, 1957.

10. Pollock TM. BCG vaccination on man. Tubercle 1959;40:399-423.

11. Aanderson AS, Dickley LB, Durfee LB, Farber SM, Jordan LS, et al. The case against BCG. BMJ 1959;5135:1424-30.

12. Guild J, Magnus K, Tolderland K, Biering-Sorensen K, Edward PQ. Suppurative lymphadenitis following intradermal BCG vaccination of the newborn. BMJ 1955;2:1046-54.

13. Caglayau S, Yegin O, Kayran K, Timocin N, Kasirga E, et al. Is medical therapy effective for regional lymphadenitis following BCG vaccination. AJDC 1987;141:1213-4.

14. Ustevdt HJ. Usual and unusual reactions to BCG vaccination in children. Am Rev Resp Dis 1956;74:32.

15. Viskum P, Jensen CM. Allergic local and glandular response to BCG vaccination in Danish mass tuberculosis campaign of 1950-1952. Acta Tuberc Scand 1955;31:326.

16. Hsing CT. Local skin complications of BCG vaccination in preschool children and newborn babies. Bull WHO 1954;11:1023.

17. Horwitz O, Merger J. The safety record of BCG vaccination and untoward reactions. Adv Tuberc Res 1957;8:145.

18. Stopplemaqn NRH, Droin EF. Complications of intracutaneous BCG vaccination of the newborn infants. Acta Paediatr Scand 1958;47:65.

19. Chaves-carbello E, Sanchez GA. Regiional lymphadenitis following BCG vaccination. Clin Paediatr 1972;11:693.

20. DE Souza GR, Sant'Anna CC, Lapae Silva JR, Mano DP, Bethlem NM. Intradermal BCG complications: analysis of 51 cases. Tubercle 1983;64:23-37.

21. Harton W. Uncommon skin reactions after BCG vaccination. Tubercle 1959;40:265-271.

22. Dostrovsky A, Saghar F. Dermatological complications of BCG vaccination. B J Dermatol 1963;75:180-192.

23. Petello H, Salim I, Vahvanan V, Alquist J.BCG vaccination as a cause of osteomyelitis and subcutaneous abscess. Arch Dis Child 1984;59:157-161.

24. Wase-Hockert O, Beckman A, Lotte A, et al. Osteitis caused by BCG vaccination of the newborn. Bull Int Union Tuberc 1979;54:325.

25. Al-Arabi K, Alkhidir ME, Sadig S. Osteitis of the humorous following BCG vaccination. Tubercle 1984;85:305-7.

26. Bottinger M, Romanus C, Verdier Brown G. Osteitis and other complications caused by generalized BCGitis. Acta Paediatr Scand 1982;71:471-8.

27. Webster ADB, Goolamali SK. BCG'osis. J R Soc Med 1981;74:163-5.

28. Siceric S, Generalized BCG tuberculosis with fatal course in two sisters. Acta Paediatr Scand 1972;61:178-184.

29. Wallerstorm A, Enell H. Bacterial metastasis following BCG vaccination. Acta Paediatr Scand 1966;55:517-23.

30. Tardiel M, Truffot-Permatt C, Carriere JP, Dupic Y, Landriel P. Tuberculous meningitis due to BCG in two previously healthy children. Lancet 1988;Feb 27:440-1.

31. Katznelson D, Cross S, Sack J. polyneuritis following BCG revaccination. Postgrad Med J 1982;58:469-497.

32. World Health Organization. BCG vaccination of the newborn. Rationale and guidelines for country programmes. WHO Geneva 1986;WHO/TB/86:147.

33. Personal communications.

34. Public Health Laboratory Service for Communicable Disease Surveillance Centre. BCG vaccination. BMJ 1983;286:876-877.

35. Lotte A, Wasz-Hockert O. Poissen N. Dumetrescu N, Verton M, Couver E. BCG complications. Estimates of the risks among vaccinated subjects and statistical analysis of their main characteristics. Adv Tuber Res 1984; 21:107-93.

36. Vaccines used in the EPI: indications and contraindications. WHO Chronicle 1984;38(3):95-98.

37. Ray CS, Pingle D, Legg W, Mbengeranwa OL. Lymphadenitis associated with BCG vaccination: a report of an outbreak in Harare - Zimbabwe. Cent Afr J Med 1988:34(12):281-286.