Unusual Complication of B.C.G. Vaccination

SYLVIA M. WATKINS

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Complications of B.C.G. vaccination are uncommon (Medical Research Council, 1956; Horwitz and Meyer, 1957; Youmans *et al.*, 1957; Anderson *et al.*, 1959), and rare overdoses of vaccine have been recorded (Griffith, 1963, 1964). An accidental overdose of the magnitude of 40 times the normal dose does not appear to have been previously reported in the literature.

Case Report

A man aged 26 had three Mantoux tests in France in January, March, and June 1966; they were negative and he was therefore advised to have a B.C.G. vaccination six months later. On 6 January 1967 he attended the casualty department of another hospital with an ampoule of B.C.G. vaccine (designed for percutaneous multiple puncture) from the Institut Pasteur. This is more than 10 times stronger than the English intradermal vaccine, and the instructions recommend that it should be given by scarification of three sites of the skin of the deltoid region: 2 to 4 drops on each site, separated by 1.5 cm, with a maximum total length of scratch of 20 cm. The casualty officer misinterpreted the French instructions and injected 0.4 ml intradermally into three separate areas over the right deltoid, thus giving a dose 40 times greater than that contained in the usual 0.1 ml of English vaccine.

Over the next few weeks the patient's arm became inflamed, swollen, and painful, with pronounced axillary and supraclavicular lymphadenopathy. On 10 February he developed erythema nodosum, and four days later was admitted to the Royal Free Hospital.

On examination he was pyrexial (38.5°C). There were three pustules, each 1 cm in diameter, in the right deltoid region surrounded by an area of erythema and induration, up to a total area of 12 by 12 cm. Right axillary and supraclavicular lymphadenopathy was present with glands up to 4 cm in diameter. There was erythema nodosum of both legs. No other abnormalities were found.

Investigations.—Chest x-ray examination showed nothing abnormal. Mantoux reaction was 1:100,000 positive; a swab from the lesions yielded a growth of *Staphylococcus epidermidis* only; no acid-fast bacilli were seen and no mycobacteria were grown in culture. The E.S.R. was 35 mm in one hour (Westergren). Haemoglobin, white cell count, platelet count, blood urea, and urine were all normal.

After a course of ampicillin some of the swelling and induration improved, possibly due to regression of secondary infection. He was started on isoniazid, 100 mg three times a day and during the next few weeks he gradually improved. In May 1967, however, he noticed a swelling in the right infraclavicular region, which was slightly tender. Apart from some lack of energy, he was otherwise well. On examination he was afebrile; a soft fluctuant swelling 4 cm in diameter was found just below the right clavicle; a lymph node 1 cm in diameter was palpable in the right supraclavicular region; and there was induration of the right axilla without definite lymphadenopathy. Three small depressed scars were seen at the site of the original vaccination. Haemoglobin, white cell count, E.S.R., blood urea, and electrolytes were all normal. Pus aspirated from the cold abscess showed pus cells and a few Gram-positive cocci, but there was no growth on culture. No acid-fast bacilli were seen, no mycobacteria were grown on culture, and guinea-pig inoculation was negative. He was started on full doses of strep-

tomycin para-aminosalicylic acid (PAS), and isoniazid, and the cold abscess was aspirated on three occasions by Mr. Lionel Gracey; on each occasion about 20 ml of pus was removed, but after the third aspiration it did not reaccumulate.

The patient was discharged on PAS 12 g daily, isoniazid 300 mg daily, and streptomycin 1 g daily. He subsequently returned to France with instructions to continue treatment with PAS and isoniazid for a total of two years.

Comment

B.C.G. vaccination is a remarkably safe procedure, and complications when using normal doses are rare. Generalized B.C.G. infection, which may be fatal, was reported by Horwitz and Mayer (1957), who reviewed other cases in the literature. Only two cases of erythema nodosum were reported in a total of 14,100 vaccinations in the M.R.C. (1956) trial. Other specific complications of B.C.G. vaccination reported include regional adenitis with or without caseation (cold abscess formation), lupus vulgaris, subcutaneous cold abscesses, scrofuloderma, lymphadenitis, tuberculid and tuberculosis verrucosa cutis at the site of the injection, ocular lesions (including phlyctenular conjunctivitis), and "lighting up" of underlying tuberculous infection, all of which are very uncommon (M.R.C., 1956; Horwitz and Meyer, 1957; Anderson *et al.*, 1959). Provocation of sarcoidosis (Ellman and Andrews, 1959) may possibly also be a complication of B.C.G. vaccination. Rare non-specific complications include keloid, eczema, epithelial cysts, and granuloma in the vaccination ulcer. Some workers (Youmans *et al.*, 1957) have found a lower rate of complications when the percutaneous multiple-puncture technique is used; on the other hand, the results of a 15-year survey in France showed that the intradermal technique was preferable to scarification from the point of view of both incidence of complications and results of vaccination (Edwards, 1963).

Reports of B.C.G. overdoses are rare. Griffith (1963, 1964) reported on 10 children who were given an intradermal inoculation of a strong vaccine, designed for percutaneous multiple puncture. Each child received 12 to 15 times the usual dose, but the mistake was immediately realized; the children were treated with isoniazid and there were no complications. Even our patient had a surprisingly mild reaction considering the magnitude of the overdosage.

Since the most dramatic features of his illness were local lesions at the site of the massive inoculation of B.C.G. it would seem that the likeliest diagnosis was B.C.G. tuberculosis, though bacteriological proof was lacking. The alternative possibility of activation of underlying tuberculous infection seems unlikely in view of both the clinical features and his repeatedly negative Mantoux tests (though these had not been performed within the six months preceding vaccination).

This case is of interest because its very rarity serves to illustrate the exceptional safety of B.C.G. vaccinations; furthermore, it points the moral that foreign drugs should not be used unless their nature and all the relevant instructions are understood perfectly.

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Royal Free Hospital, London W.C.1

SYLVIA M. WATKINS, B.M., M.R.C.P., Senior Medical Registrar