Disseminated BCG in HIV infection

J NINANE,* A GRYMONPREZ,* G BURTONBOY,† A FRANCOIS,* AND G CORNU*

Departments of *Paediatric Haematology and Oncology and †Experimental Virology, Cliniques Universitaires Saint-Luc, Brussels, Belgium

SUMMARY A boy, born to a mother with AIDS related complex, was immunised with BCG on the 10th day of life. At the age of 4 months he presented with a local enlarged lymph node, fever, hypotonia, and diarrhoea. *Mycobacterium bovis*, BCG strain, was grown from the lymph node and cerebrospinal fluid; this proved dissemination.

The increasing prevalence of HIV infection in children, associated with immune deficiency, has led to concern about the efficacy and complications of immunisation among these children.^{1 2} The problem of whether children infected with HIV should receive live vaccines is complex: the risk of vaccination must be balanced against the risk of infection in the non-vaccinated child.

There is evidence that HIV infection is responsible for the increased frequency of infection with tuberculosis and for morbidity with this micro-organism.³ Patients with AIDS and tuberculosis are more likely to have extrapulmonary disease,⁴ although bacteraemia in disseminated *Mycobacterium tuberculosis* is rare. In patients with AIDS related complex infection due to *M tuberculosis* is of poor prognosis, accelerating the transition to AIDS even if tuberculosis is only restricted to the lungs.⁴

These problems with HIV infection and tuberculosis prompted us to explore the use of BCG vaccine in children who were HIV positive. Some cases of local adenitis after BCG immunisation have been reported.¹ Although a few case reports suggest a generalised infection due to BCG in patients infected with HIV, dissemination has never been clearly proved, except for the isolation of *M bovis* in one reported case from blood culture in an adult with AIDS and Kaposi's sarcoma.⁵

We report here a case of disseminated infection caused by *M bovis* after BCG vaccination in an infant infected with HIV who presented with generalised lymphadenopathy, hypotonia, fever, diarrhoea, and raised liver enzyme activities.

Case report

A boy, born in Zaïre to a mother with AIDS related

complex, was immunised with BCG on the 10th day of life. Between the age of 1 and 2 months, he presented with repeated urinary tract infections, mucocutaneous candidiasis, and high fever. He was transferred to our hospital at the age of 4 months, for persistent fever, weakness, fatigue, anorexia, and diarrhoea.

On admission, he was an ill looking baby with a body temperature of 38.8°C. His weight was 4600 g (10th centile), height 58 cm (5th centile), and head circumference 39.5 cm (5th centile). He had an enlarged lymph node in the left axilla (diameter >2 cm) near the BCG vaccination site, hepatosplenomegaly, and hypotonia. The erythrocyte sedimentation rate was >150 mm in the first hour, fibrinogen concentration 2.86 g/l, and the C reactive protein concentration 0.246 g/l. His white cell count was $5 \times 10^9/l$ (30% lymphocytes) and haemoglobin concentration 80 g/l. His liver enzyme activities were raised: serum aspartate transaminase, 110 IU/l (normal <40); serum alanine transaminase, 50 IU/l (normal <40); alkaline phosphatase, 385 IU/l (normal range 80–280); lactate dehydrogenase, 1200 IU/l (normal range 140–300); and γ glutamyl transferase, 1300 IU/l. Plasma gammaglobulin concentration was 65 g/l and the T4/T8 ratio was 1.4 (T4, $0.269 \times 10^9/l$; T8, $0.190 \times 10^9/l$). The in vitro response of lymphocytes to mitogens (phytohaemagglutinin, pokeweed, concanavalin A), and OKT3 was extremely reduced.

Although antibodies against HIV-1 were not detected in the serum either by two commercial enzyme linked immunoadsorbent assays (ELISA) (Pasteur production and Abbott env/core recombinant EIA) or by immunofluorescence, further investigations were performed as the mother was known to be seropositive. Another ELISA test (Wellcome) was found to give a weak positive result and Western blot analysis showed a low level of antibodies against GP 120. Moreover, HIV-1 antigen was detected repeatedly in six serum samples from the patient (Abbott HTLV-III antigen EIA). A search for infection showed *Candida albicans* and enterococci in a throat swab, but no bacterial infection was found in blood, stools, or urine. No viral, fungal, or protozoal infection was found. Culture of cerebrospinal fluid, however,

grew colonies of an acid fast bacillus, identified as *M bovis*, BCG strain. *M bovis* could not be isolated from blood or from a nasogastric tube, but was grown in pus from the enlarged lymph node. A chest radiograph was normal apart from showing an enlarged heart. Cardiac ultrasonography excluded a pericardial effusion. Examination of the optic fundus, electroencephalography, and cerebral ultrasonography gave normal results. Abdominal ultrasound showed normal kidneys but the liver was appreciably enlarged. A liver biopsy was attempted but unfortunately failed to produce liver tissue.

The child was treated with rifampicin 15 mg/kg/day, isoniazid 10 mg/kg/day, and ethambutol 20 mg/kg/day. His general condition improved dramatically and he became afebrile on the third day of treatment, and the local inflammatory signs disappeared around the affected lymph node. The results of his blood tests also showed a rapid improvement: the erythrocyte sedimentation rate fell from 150 mm in the first hour to 50 mm on the fifth day of treatment, the liver enzymes returned to normal values. The in vitro response of lymphocytes to mitogens remained low, however, and the T4/T8 ratio fell to 0.33 at the age of 5 months (T4, $0.072 \times 10^9/l$; T8, $0.215 \times 10^9/l$). Hepatosplenomegaly became more prominent and hypotonia persisted, although it was less pronounced. The child returned to Zaïre at the age of 5 months. He died two months later, probably from bacterial infection.

Discussion

The World Health Organisation recommends avoidance of the use of BCG in children infected with HIV who have symptoms as the efficacy is disputed in these children,⁶ and because dissemination has been described in an adult patient.⁵ In the case reported here of *M bovis* dissemination, the infant who was infected with HIV was vaccinated on the

10th day of life, before he had any clinical symptoms of HIV infection. Dissemination was proved in our patient by culture of *M bovis*, BCG strain, in the cerebrospinal fluid and in the lymph node (local inflammation due to BCG).

Although tuberculosis represents a real problem in Africa, and despite the fact that the frequency and the gravity of tuberculosis is increased in subjects infected with HIV³ with a great propensity for extension to extrapulmonary sites,⁴ our observation clearly shows that it is not advisable to vaccinate infants born to mothers infected with HIV with BCG, unless HIV infection can be ruled out in the child.

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Correspondence and requests for reprints to Dr J Ninane, Department of Paediatrics, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, B-1200 Brussels, Belgium.

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