Bacille Calmette-Guérin (BCG) Meningitis in an AIDS Patient 12 Years After Vaccination with BCG

Vaccination with BCG, a live attenuated strain of Mycobacterium bovis, is used on a large scale throughout the world. Concern has been raised about the administration of live vaccines to persons infected with HIV. However, the number of reported HIV-related complications of BCG vaccination appears to be limited. The majority of cases have occurred in infants previously infected with HIV, and the intervals between vaccination and the appearance of BCG-related symptoms (mostly localized) have been relatively short [1]. We describe a case of meningitis caused by BCG in an adult patient with AIDS, which occurred 12 years after BCG vaccination.

A 30-year-old native-born Dutch homosexual male was found to have high-grade Burkitt's-like non-Hodgkin's lymphoma (stage IIIBE) in November 1993. Antibodies to HIV-1 were detected with use of an ELISA and confirmed by western blot. Chemotherapy was started, resulting in a short complete clinical remission. In March 1994, meningitis lymphomatosa was diagnosed. Intrathecal chemotherapy was initiated after an Ommaya reservoir was implanted, resulting in complete clinical and cytological remission.

In June 1994, the patient was readmitted to the hospital because of high fever, headache, and neck stiffness. Analysis of the CSF showed pleocytosis (cell count, 1,335/mm^3), an elevated protein concentration (1.38 g/L), a normal glucose level (2.9 mmol/L), and no relapse of the lymphoma. A few colonies of Propionibacterium acnes were isolated from the CSF, possibly representing skin contamination of the specimen; no acid-fast bacilli were found on Ziehl-Neelsen staining. Treatment with amoxicillin and flucloxacillin was started, but the patient's clinical condition deteriorated. A CT scan of the head was obtained, and the findings suggested abscess formation around the drain of the Ommaya reservoir, which was subsequently removed. The reservoir contained purulent material, and Ziehl-Neelsen staining showed numerous acid-fast bacilli. Tuberculous meningitis was diagnosed, and treatment with isoniazid, rifampin, and pyrazinamide was initiated. However, his condition further deteriorated, and he died 11 days later.

![restriction fragment length polymorphism typing of the mycobacterial strain isolated from the CSF of a patient with BCG meningitis](https://academic.oup.com/cid/article-abstract/22/5/870/361159/1)

Figure 1. Restriction fragment length polymorphism typing of the mycobacterial strain isolated from the CSF of a patient with BCG meningitis. DNA from the mycobacterial isolates from the patient and from controls was digested using the restriction enzyme PvuII. After electrophoresis and Southern blotting were done, the blot was subjected to three probes: IS986 (a), IS1081 (b), and MPB64 (c). Lane 1: Mycobacterium tuberculosis isolate; lane 2: the Brazilian BCG vaccine strain; lane 3: the Dutch BCG vaccine strain; lane 4: the mycobacterial isolate from the patient; lane 5: Mycobacterium bovis isolate; lane 6: M. tuberculosis reference strain H37Rv; lane 7: M. tuberculosis reference strain Mt 14323. A represents IS986 fingerprints; BCG strains contain either one or two copies of this insertion sequence [2]. B represents IS1081 fingerprints; hybridization on an 8-kb fragment is specific for BCG [3]. C represents MPB64 gene fingerprints; this gene is absent in a subset of BCG strains [4]. Lane numbers refer to la, lb, and lc.

Mycobacteria were isolated from CSF obtained on the first and the ninth days of the patient's last hospitalization. The isolated strain was identified as BCG on the basis of results of restriction fragment length polymorphism (RFLP) typing with three probes (figure 1). The patient had been vaccinated with BCG when he served in the Dutch Army Medical Corps in 1982.
We believe that our patient’s meningitis was caused by late reactivation of BCG 12 years after BCG vaccination. BCG was isolated from the CSF, and identification of the organism was confirmed by analysis of the RFLP patterns of the mycobacterial isolate. To our knowledge, our patient represents the first case of BCG meningitis that occurred as an HIV-related complication of BCG vaccination. The 12-year interval between vaccination and the appearance of his symptoms suggests that he was probably not infected with HIV when he was vaccinated with BCG and that progressive immunodeficiency due to HIV infection and, possibly, transient additional immunosuppression as a result of chemotherapy led to late reactivation of the bacillus.

BCG vaccination at birth or soon after is an important strategy for the control of tuberculosis in developing countries. In some of these countries, the prevalence of HIV infection is high; thus it is surprising that the number of reported HIV-related complications of BCG vaccination among infants and adults has been limited until now [1]. However, it is difficult to differentiate BCG from other Mycobacterium tuberculosis—complex isolates, particularly in areas where diagnostic facilities are limited. In countries where the risk of tuberculosis is low, BCG should not be given to individuals who are infected with HIV or who are suspected of being infected with HIV, in accordance with World Health Organization guidelines [5]. We recommend caution with respect to BCG vaccination of persons at risk for HIV infection.

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References

Pulmonary Chest Wall Swelling Due to Tubercular Mediastinal Lymphadenopathy in a Patient with Human Immunodeficiency Virus Infection and Syphilis

The clinical features of tuberculosis have largely changed in recent years for a variety of reasons [1]. Unusual clinical signs may be encountered, thereby posing a diagnostic dilemma. In patients with HIV infection and tuberculosis, there is more frequent involvement of lower lobes, an increased occurrence of dissemination, and a tendency toward early abscess formation [2]. Mediastinal lymphadenopathy is common in certain racial groups including Asians, Africans, and Haitians [3]. This disease may cause clinical features due to compression of adjacent structures in the mediastinum, but more often it is seen as a mass on a chest x-ray. We describe a patient with HIV infection who had a pulsatile swelling in the right upper parasternal region due to tubercular mediastinal lymphadenopathy. He also had syphilis.

A 40-year-old man presented with a 2-week history of high-grade intermittent fever and cough with blood-tined sputum. He also had a 1-week history of dull continuous pain in the right upper parasternal region. He had had multiple unprotected sexual encounters with prostitutes 13 years ago. Physical examination revealed an ill-looking individual with a temperature of 102°F, pallor, digital clubbing and signs of consolidation in the left infraclavicular area. The rest of the findings were unremarkable. Laboratory studies disclosed the following values: hemoglobin, 9.3 g/dL; total leukocytes, 8.4 x 10^9/L (65% polymorphonuclear cells); and erythrocyte sedimentation rate (Wintrobe method), 20 mm/h. A chest roentgenogram showed a homogeneous opacity with an air bronchogram in left lower lobe and slight widening of the superior mediastinum. Examinations of sputum for acid-fast bacilli were repeatedly negative. Blood and sputum cultures were sterile. An

Figure 1. A CT scan of the chest of an HIV-infected patient with syphilis and a pulsatile chest wall swelling due to tubercular mediastinal lymphadenopathy shows hypodense lesions with ring enhancement in the superior mediastinum and a lesion of similar density without enhancement anterior to the sternum on the right side.