Quantiferon-Gold Tuberculosis Test Cannot Detect Latent Tuberculosis in Patients With Leprosy

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Five of 10 paucibacillary leprosy patients were Quantiferon Gold (Q-G) positive with negative chest X-rays. Forty multibacillary leprosy patients were negative. Reports have shown 100% cross-reactivity of ESAT6 and CFP10 between Mycobacterium leprae and Mycobacterium tuberculosis. The Q-G test cannot detect latent tuberculosis in patients with leprosy.

Keywords. Quantiferon gold; tuberculosis; leprosy.

Two groups have reported that the Quantiferon-Gold (Q-G) tuberculosis test can be positive in leprosy patients with negative chest X-rays [1–3]. Nagai et al suggested that the Q-G test could be used to develop a better vaccine for tuberculosis. They identified specific epitopes to 6 kDa ESAT6 and 10 kDa CFP10 proteins. Based on data provided by Geluk et al [4, 5], this approach may also be useful to develop a leprosy vaccine. Earlier work by Geluk et al showed 100% cross-reactivity of Mycobacterium tuberculosis and Mycobacterium leprae ESAT6 and CFP10, which are 2 of the antigens used in the Q-G tuberculosis test [4,5]. We have suggested that the Q-G tuberculosis test be used as a probable measure of anergy in leprosy patients [1, 2]. Here, we report 50 consecutive patients in the New York Hansen’s Disease (NYHD) Program tested for Q-G tuberculosis and pathologically classified according to the Ridley and Jopling classification [6].

MATERIAL AND METHODS

Fifty patients seen at Bellevue Hospital who were in the NYHD Program were assayed for Q-G tuberculosis test between January 2015 and April 2015. Chest X-rays were obtained on positive paucibacillary (borderline tuberculoid [BT]) patients according to the Ridley and Jopling classification [6].

This classification is an accepted histopathologic spectrum of 5 types of leprosy (tuberculoid, BT, mid-borderline, borderline lepromatous [BL], and lepromatous leprosy [LL]). This is a spectrum from least Fite-positive organisms (paucibacillary) to most Fite-positive organisms (multibacillary). Q-G tuberculosis testing was performed by Quest Laboratories (www.questdiagnostics.com). The Fischer exact 2-tailed test was used to compare the paucibacillary (BT) patients to the multibacillary (BL, LL) patients.

RESULTS

Five of 50 leprosy patients tested positive with the Q-G test (10%) and all were negative by chest X-ray (Table 1). Four were foreign born and 1 was born in Pennsylvania. All 5 positive patients were paucibacillary and classified BT according to the Ridley–Jopling classification. Five patients also classified as BT by the classification had negative Q-G tuberculosis tests. Two of the positive patients became negative during multidrug therapy based on US guidelines [7]. Forty multibacillary patients (5 BL and 35 LL) were Q-B tuberculosis negative. The Q-G gold test showed that 5 of 10 paucibacillary (BT) patients were positive. Of multibacillary (BL, LL) patients, 0 of 40 were positive by the Q-G gold test. BT positivity (5 of 10) compared to multibacillary (BL-LL; zero of 40) was statistically significant by Fisher exact 2-tailed test (P < .001).

DISCUSSION

The Centers for Disease Control and Prevention (CDC) published updated guidelines for interferon gamma (IFN-γ) release assays to detect M. tb infection [7]. Data exist show that Mycobacterium kanzassii and Mycobacterium marinum can be positive by QB tuberculosis test (oral communication; G.H. Mazurek on 15 April 2015). The Q-G tuberculosis test is a welcomed advance from the purified protein derivative skin test for assessing exposure to M. tuberculosis. It is especially useful in foreign-born patients, most of whom have been vaccinated with Bacillus of Calmette-Guerin as it fails to show cross-reactivity. However, when a patient has leprosy, the Q-G test cannot be used to detect latent tuberculosis because both the ESAT6 and CFP10 antigens of M. leprae are 100% cross-reactive...
We followed up 50 leprosy patients in the NYHD Program after Q-G tuberculosis testing. We found all multibacillary patients were Q-G negative, while BT patients were positive or negative. The Q-G test cannot detect tuberculosis in any leprosy patient regardless of Ridley–Jopling classification, as the work of Geluk et al showed 100% cross-reactivity of ESAT 6 and CFP10 [4, 5]. Thus, if tuberculoid patients who have intact cell-mediated immunity to M. leprae antigens that are positive, it may be due to the M. leprae ESAT 6 and/or CFP10 rather than the M. tb epitopes. Furthermore, in the anergic LL patients, M. leprae anergy will extend to the M. tb epitopes. In either case, the Q-G test cannot rule tuberculosis in or out in leprosy patients. While both ESAT 6 and CFP10 have significant differences in amino acid sequence and serologic specificity [8], the IFN-γ release is based on epitope presentation by Major Histocompatibility Complex class 2 to the T-cell receptor. The work of Geluk et al shows that the 3-dimensional presentation of epitopes from both M. leprae and M. tb will activate T cells to produce IFN-γ. We would like to supplement the current CDC report [7] with recommendations on use of the Q-G test in patients with leprosy. A negative chest X-ray does not rule out latent tuberculosis, so each positive test needs to be assessed on a case-by-case basis. We recommend no isoniazid therapy without known additional exposure or family history in paucibacillary leprosy patients. An amendment to the US guidelines for leprosy treatment should also be considered, as it is likely prudent to extend the treatment to disseminated Q-G–negative BT leprosy patients to the full 2 years recommended for multibacillary leprosy.

Notes

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