Clinical patterns of cutaneous tuberculosis at King Fahad Hospital of the University in Al-Khobar, Saudi Arabia over 13 years

To the Editor

I read the interesting article by Bukhari[1] on "Clinical Patterns of Cutaneous Tuberculosis at King Fahad Hospital of the University in Al-Khobar, Saudi Arabia over 13 years." Tuberculosis (TB) continues to be a major health problem in developing countries. The development of resistance to anti-tuberculous drugs, and the increase in diseases and conditions associated with immunodeficiency, such as acquired immunodeficiency syndrome (AIDS) and chemotherapy have caused TB to increase recently. As a result, the incidence of cutaneous tuberculosis (CT) has been increasing as well. Moreover, CT continues to be one of the most elusive and more difficult diagnoses to make for dermatologists practicing in developing countries. Not only because they have to consider wider differential diagnoses (leishmaniasis, leprosy, actinomycosis, deep fungal infections, and so forth), but also because of the difficulty in obtaining a microbiological confirmation. I have 7 comments considering the aforementioned study.

First, the diagnosis of CT remains a matter of challenge as a clear-cut demonstration of acid-fast bacilli is the only solid proof. Though purified protein derivative test (PPDT) has been extensively adopted as a diagnostic tool for TB, its interpretation might be confounding, particularly in developing countries where TB is still a prevailing health threat. The PPDT is subject to reader variability, and lacks sensitivity in immunocompromised patients, recently infected persons, and very young children. It lacks specificity because many antigens in PPD cross-react with antigens found in environmental mycobacteria, leading to doubling of the risk of a false positive result in some geographical locations. In addition, PPDT may not be stable over time, that is, the size of the reaction may increase with serial tests in individuals with prior sensitization to mycobacteria, or the test may over time revert to a negative result. Prior Bacille Calmette Guérin (BCG) vaccination and exposure to patients with active TB might alter the response to PPDT, thus, makes interpretations of the reading of PPDT more difficult.[2] The PPDT performed in the studied patients showed variable results. Meanwhile, the positive BCG scar that was only detected in 2 out of 7 patients enrolled in the study is further confounding our concern on their prior BCG vaccination status. On the other hand, Ziehl-Neelsen stain of suspected smear is rarely capable of demonstrating acid-fast bacilli due to paucity of bacillary load in comparison to pulmonary TB, an observation that was further documented in the studied patients. Nowadays, polymerase chain reaction (PCR) system provides rapid and sensitive detection of *Mycobacterium tuberculosis (M. tuberculosis)* deoxyribonucleic acid (DNA) in formalin-fixed, paraffin-embedded tissue specimens.[3] Although it is very useful, the cost and the technique involved might limit its use, particularly in developing countries.

Second, the suggested epidemiologic, clinical, and histopathologic profiles of CT in difficult cases without clear-cut demonstration of acid-fast bacilli might necessitate the need to provisionally regard them as CT. Initiation of combined anti-tuberculous therapy on empirical basis and assessing the clinical responses might be justifiable. Response to treatment at 5 weeks often helps in substantiating the diagnosis of CT in these doubtful cases.[4] I presume that the studied patients were provisionally diagnosed as CT on the aforementioned criteria. Meanwhile, I wonder whether the studied patients showed prompt responses to combined anti-tuberculous therapy.

Third, due to small number of patients involved in the study, the author was unable to demonstrate concomitant diseases with CT. It is well-known that many diseases could be associated with or disclose underlying TB, namely leukocytoclastic vasculitis, erythema nodosum, rheumatoid arthritis, systemic lupus erythematosus (SLE), IgA nephropathy, and idiopathic thrombocytopenic purpura. Abnormal cell-mediated hyper-response to *M. tuberculosis* might contribute to these associations.

Fourth, CT is an exceptional manifestation of TB that is often due to acute hematogenous dissemination of *M. tuberculosis* to the skin. Miliary or disseminated TB associated with cutaneous lesion has been rarely reported. However, with the increasing incidence of immunocompromised patients secondary to AIDS, cytotoxic therapy, and long-term use of corticosteroids, such presentation of TB might be expected to be observed more often.

Fifth, for comparative purposes, the author could not truly state the exact distribution of clinical varieties of CT due to the small number of patients recruited in the study. The studied patients were all beyond pediatric age group. Pediatric CT still represents an important health problem. It accounts for approximately 1.5% of all the cases of extrapulmonary TB. Scrofuloderma and lupus vulgaris are the 2 most common forms of CT. However, the trend in the pattern of pediatric CT is

changing, as the tuberculoid and lichen scrofulosorum, have become more common in recent years. Overall, the clinical patterns are comparable with adults. However, children can have widespread and severe involvement. Moreover, the underlying systemic involvement is more common in children, compared with adults.[5]

Sixth, physicians and dermatologists must possess high index of suspicion to diagnose CT, particularly in countries with high prevalence of TB and AIDS. They should obtain a thorough history focusing on risk behaviors for human immunodeficiency virus (HIV) infection and tuberculosis, perform proper physical examination, and adopt judicious laboratory tests. Negative smear for acid-fast bacilli, lack of granulomas on histopathologic examination, and failure to culture acid-fast bacilli must not role out the possibility of CT in highly suspected cases.

Seventh, additional multicenter studies contemplated in different parts of Kingdom is needed to determine the exact epidemiologic, clinical, bacteriologic, histopathologic, and immunologic parameters of CT. This would help assist planning certain strategic guidelines.

Mahmood D. Al-Mendalawi
Department of Pediatrics
Al-Kindy College of Medicine
Baghdad University
Baghdad, Iraq

Reply from the Author

Thank you for your interest in my article. I completely agree with your valuable comments which have added more information to the discussion. Actually, most of my cases were diagnosed based on the history and clinical presentations, ruling out other differentials that can have similar findings. Laboratory investigations were mainly suggestive, but not confirmatory of cutaneous tuberculosis in most of them. Interestingly, the complete response to treatment was the golden method to reach a confirmed final diagnosis. In the Kingdom, there are highly effective programs initiated to control tuberculosis infection with regular annual update to the World Health Organization. Finally, this study is the first in the Kingdom reporting the clinical patterns of cutaneous tuberculosis in a tertiary care hospital over a 13-year period, which calls for more similar studies in other areas and nearby countries to have a more solid view on the extent of this infection.

Iqbal Bukhari
Department of Dermatology
College of Medicine
King Faisal University
Dammam
Kingdom of Saudi Arabia

References

1. Bukhari IA. Clinical patterns of cutaneous tuberculosis at King Fahad Hospital of the University in Al-Khobar, Saudi Arabia over 13 years. ***Saudi Med J*** 2009; 30: 577-578.
2. Araujo Z, de Waard JH, de Larrea CF, Borges R, Convit J. The effect of Bacille Calmette-Guérin vaccine on tuberculin reactivity in indigenous children from communities with high prevalence of tuberculosis. ***Vaccine*** 2008; 26: 5575-5581.
3. Abdalla CM, de Oliveira ZN, Sotto MN, Leite KR, Canavez FC, de Carvalho CM. Polymerase chain reaction compared to other laboratory findings and to clinical evaluation in the diagnosis of cutaneous tuberculosis and atypical mycobacteria skin infection. ***Int J Dermatol*** 2009; 48: 27-35.
4. Ramam M, Tejasvi T, Manchanda Y, Sharma S, Mittal R. What is the appropriate duration of a therapeutic trial in cutaneous tuberculosis? Further observations. ***Indian J Dermatol Venereol Leprol*** 2007; 73: 243-246.
5. Sethuraman G, Ramesh V, Ramam M, Sharma VK. Skin tuberculosis in children: learning from India. ***Dermatol Clin*** 2008; 26: 285-294.