Atypical Evolution of Pulmonary Tuberculosis During Treatment

To the Editor:

A recent article by Williams et al (Chest 1988; 93:836-38) presents a paradoxical type of evolution in three patients with tuberculosis primoinfection who, during correct treatment, appear to have experienced a reactivation of the disease accompanied by wheezing and bronchial inflammation. The essential contribution of this paper is that the reactivation appeared as a bronchial inflammation with asthmatic symptoms.

Some years ago we reported eight cases of this kind,\(^1\) recently we have encountered eight more.\(^2\)

This paradoxical type of evolution was first described more than 30 years ago by Choremis et al,\(^4\) although without remarking upon the probable bronchial component. Later, this type of evolution was also found in adult pulmonary\(^5\) and pleural\(^6\) tuberculosis.

Knowledge of this type of evolution of pulmonary tuberculosis is important as it often causes problems for the physician. When faced with a case like this, it is easy to think of the appearance of resistance to drugs or of an initially mistaken diagnosis. All our cases have been cured with continuance of the same treatment. In no case have we used corticoid therapy.

These facts are not easy to interpret. Choremis et al and Williams et al thought of the possibility of a Herxheimer reaction owing to the liberation of large quantities of bacillary toxins that follows the destruction by chemotherapy of a great number of tuberculous bacilli. However, we believe this interpretation is, at most, doubtful. Herxheimer reactions begin a few minutes or hours after the administration of a chemotherapy drug, whereas in the cases mentioned above and in our cases, the apparent reactivation occurred between the second and sixth weeks after the beginning of the treatment. In the three cases reported by Williams et al, this reactivation began in weeks 12, 8 and 28. We rather think that this type of reaction may be related to the changes in the immune mechanisms of the patient during antituberculosis treatment.

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admission for treatment of severe respiratory dysfunction. The time lapse between appropriate medical treatment and deterioration in our patients varied from two to seven months. Our patients also differed in having negative mycobacteria cultures in the sputum, bronchial washes and the endobronchial granuloma biopsy unlike the "reactivation" of tuberculosis which was suggested by Dr. Munoz-Gutierrez.

Late clinical disappearance, absence of mycobacteria in the endobronchial granuloma and the response to glucocorticoids indicates an inflammatory or immune response. The classic Jarisch-Herxheimer reaction (JHR) occurs within 24 h after therapy; bacterial "endotoxins" have been implicated. Glucocorticoids can suppress the severity of this JHR. The early deterioration of treated tuberculosis resembles the JHR except it occurs later than 24 h. In view of the natural life history of mycobacteria tuberculosis infection coupled to tuberculosis chemotherapy with resultant slow growth and continuing bactericidal activity, this late reaction is not surprising. Despite the late reaction in our patients, we are of the opinion that there was an altered immune response during tuberculosis chemotherapy which clinically resembled a Jarisch-Herxheimer Reaction.

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Detection of Antibodies Against Mycobacterium tuberculosis

To the Editor:

We read with interest the paper of Levy and colleagues describing the ELISA method as a tool for discriminating between sarcoidosis and tuberculosis. This diagnostic problem is still genuine, especially in cases of bacteriologically-unconfirmed tuberculosis, where the verification is often connected with invasive methods. The possibility of distinguishing between sarcoidosis and tuberculosis on the basis of serologic test results would be a really great advance in pneumologic practice.

Levy's results indicate a significant difference in the levels of antimycobacterial antibodies between sputum positive patients with pulmonary tuberculosis and patients with active sarcoidosis and healthy control group. We could presume, on the basis of this study, that the ELISA method with a crude mycobacterial antigen could even be useful for direct diagnosis of tuberculosis.

We tested this possibility in a group of 1,132 patients with recently diagnosed pulmonary disease, including 479 cases of active pulmonary tuberculosis and 11 cases of verified sarcoidosis (results prepared for publication). ELISA assay was performed in the modification described by Daniel et al and differed from Levy's test in the range of optical density.

From our preliminary results, we can conclude that false positive and false negative results do exist in every group of patients. Also, in the group of healthy persons there are sometimes increased levels of antimycobacterial antibodies. We assume that it is impossible in a heterogeneous group of patients to distinguish between individual pulmonary diseases on the basis of ELISA test results with crude mycobacterial sonicates.

These results are in agreement with other authors. The majority of authorities presented their results using large groups of patients and control subjects. Viljanen et al described a correlation between the level of antimycobacterial antibodies and activity of tuberculosis, but the possibility to use the ELISA test for diagnosis of tuberculosis still lies in the future. According to our opinion, we suggest that the ELISA method is not suitable for discrimination between sarcoidosis and tuberculosis yet.

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To the Editor:

Drs. Svarcova and Striz raise some important points regarding the ability of an ELISA assay to diagnose tuberculosis. We agree that all reported assays have had false positive and false negative results when attempting to discriminate between groups of patients. The categorization also depends on where one sets the cut-point and is therefore open to manipulation. Normal control subjects and patients with a variety of diseases can express antibody to mycobacteria which probably reflects exposure to non-tuberculous mycobacteria. The etiology of sarcoidosis remains unknown but is highly unlikely to be due to an atypical response to mycobacterial infection.