Brief Communications

Paradoxical response to anti tuberculous drugs

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Enlargement of tuberculous lymph nodes or tuberculoma of the brain on antituberculous drugs is referred to as a paradoxical response (PR).[1,2] Paradoxical response causes anxiety during treatment, and the patient may be blamed for compliance or considered as treatment failure.[2-4] In this study, 6 patients with tuberculosis (TB) (5 lymphatic and one pulmonary) that showed PR to anti-TB drugs from 1996 to 2001 in the Basrah Military Hospital, Iraq, were reported. Medical records were reviewed to collect the demographic information and ways of diagnosis of TB, so treatment was given. Tuberculosis was diagnosed on the bases of history with lymph node (LN) biopsy showing caseating granuloma, sputum positive for acid fast bacilli (AFB), or biopsy for cold abscesses. All the patients were males. Most of them were presented with a classic picture of TB of LN or lungs, or both. Demographic, clinical features and PR were summarized in **Table 1**. One patient presented with pyrexia of unknown origin (PUO) for 2 months, and was given a therapeutic trial of anti-TB, but 2 months later he started to show right supraclavicular LN enlargement that was treated with excisional biopsy which proved to be tuberculous based on the presence of caseating granuloma. Again, this patient, after 4 months of treatment started to show 4 cold abscesses over the chest wall and feet that were treated by drainage and he was cured after a total of 6 months of treatment. The other patient presented with left supraclavicular LN enlargement. The excisional biopsy showed caseating granuloma, and in the 9th month of treatment he again started to show new LN enlargement in the left side of the neck, were biopsy was taken and showed the features of TB, and treated for another 6 months with no relapse. The 3rd patient was presented with left supraclavicular LN enlargement that measured 2x6 cm. Aspiration of which showed caseous material and excisional biopsy was consistent with TB. The PR occurred 2 weeks after treatment as an increase of the LN size; therefore, another excisional biopsy was carried out and treatment continued for a total of 6 months with no later relapse. Another patient presented with right supraclavicular LN enlargement of 3x3 cm for 6 months duration. The chest x-ray (CXR) showed right hilar LN enlargement. The excisional biopsy of LN was classic for TB, with erythrocyte sedimentation rate (ESR) of 80 mm/hour. During treatment, he improved and the ESR dropped to 15 mm/hour. After 4 months, the ESR increased to 94 mm/hour, and new CXR showed right paratracheal new LN appearance with enlargement of hilar LN. The same treatment continued and one month later the ESR dropped to 32 mm/hour and LN size in the mediastinum were regressed. Treatment continued for 6 months with no relapse after 2-years of follow up. The 5th patient presented with fever, cough, night sweating and chest pain of 2 weeks duration. The CXR showed left upper zone infiltrated with positive sputum for AFB and ESR of 120. Treated with anti-TB, and in the 4th month of treatment he started to have left supraclavicular LN enlargement that measured 2x2 cm, excisional biopsy of which was consistent with TB. Erythrocyte sedimentation rate was 60 mm/hour, with CXR showing minimal right apical fibrosis. Anti-TB continued for a total of 8 months. There was no relapse after 2 years of treatment. Another patient presented with 10 days cough and hemoptysis. Clinical examination showed left upper zone dullness with bronchial breath sound. The chest x-ray showed left upper zone thinned wall cavity with nearby infiltrate. Erythrocyte sedimentation rate was 8 mm/hour and repeated sputum AFB were negative, and bronchoscopy was carried out that was reported as normal with wash showing heavy growth of *Pseudomonas* infection that has treated with antibiotics and he was discharged home. Two months later he was readmitted to the hospital for unresolved left upper zone cavity with infiltrate. Investigations were ESR 10 mm/hour and sputum positive for AFB, and was given anti-TB drugs. One month later CXR showed new right upper opacity involving the whole lobe, with increased left upper lobe lesion. The same treatment was continued, and after 2 months of starting treatment, sputum was negative for AFB and both apical opacities were decreasing in size. The treatment continued for 6 months with no later relapse after one year of follow up. The PR was reported in 30% of cervical lymphadenitis and 16% of intracranial tuberculoma.[1,2,5] The exact cause of PR is still obscure and result from hypersensitivity to tuberculoprotein (antigenic load) of dead bacilli.[2] It seems that a combination of host immunity, virulence of bacilli, the site of infection, the antigenic load and the effect of chemotherapy may play a role in the pathogenesis.[1] Tuberculoma of the brain may increase in size or appear as new lesions while the patients on treatment, and clinical deterioration may occur and the patients may die.[2] The PR of tuberculoma in the brain can mimic brain tumors. The use of steroid for prevention of this phenomenon is still controversial. The PR may occur in sites away from the original site of tuberculosis.[1] This was obvious in patients one,

5 and 6. One of our patients with PR in 2 sites (first LN and later in the skin). Though it is mentioned that the PR will appear during the early weeks,[3] this is not always the case, as we have seen in our patients. One patient appears within 2 weeks, one patient appeared after one month, one after 2 months, 3 after 4 months and one patient appeared after 9 months. Despite the anxiety induced by PR the lesions eventually will improve with anti-TB therapy and there is no need to change the line of treatment,[4] but in our patients, we tried excision of lymph nodes whenever it was feasible. This was carried out in the first 5 patients.

In conclusion, PR is an immunologic phenomenon that causes anxiety to the treating physician, but eventually there will be a response to anti-TB therapy.

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