LETTER TO THE EDITOR

Paradoxical Reaction: Can It Be Seen After Completion of the Anti-Tuberculous Therapy?

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Sir,

Paradoxical reaction (PR) is defined as a transient expansion (worsening) of a pre-existing tuberculous lesion or the development of new lesions under appropriate anti-tuberculous (TB) therapy (1–3). Although the pathogenesis of this reaction is not completely clear, it is generally accepted as a late hypersensitivity reaction to the tuberculoproteins released from dead bacilli. A PR can be encountered at varying rates according to given clinical forms of TB. This reaction has been reported to develop under therapy (2). It is not known whether it develops after the completion of the therapy. In this report, we describe a patient who developed PRs during, and after completion of, therapy for TB lymphadenitis; we also review the relevant literature.

A 48-y-old female was admitted with fever, fatigue, and lumps in right cervical and axillary regions experienced for 1.5 y. She had had systemic lupus erythematosus and been given hydroxychloroquine and prednisolone. Her general condition was good and temperature was 38.5° C. In right cervical and axillary regions, painless and non-fluctuating lymphadenopathies measuring 3 × 2 cm were detected. A chest X-ray and thorax CT were normal. A tuberculin skin test was positive. Right axillary lymph node sampling revealed caseating granulomatous reaction. She was prescribed quadruple anti-TB therapy (isoniazid + rifampin for 12 months, pyrazinamide + ethambutol for 2 months). She responded well within 3 months; body temperature returned to normal, fatigue regressed, and lymphadenopathies disappeared. In the fourth month of the therapy, a new hard, mobile, painless lymphadenopathy measuring 3 × 2 cm developed in the right cervical region. It was excised and histology revealed caseating granulomatous reaction with a draining sinus. Therapy was continued to 12 months without interruption and her compliance to the therapy was excellent. Three months after the completion of therapy, redness, fluctuation, and a draining sinus developed in the same cervical region and all were surgically removed. The purulent material showed scanty acid-fast bacilli (AFB) by Ziehl-Neelsen (ZN) staining. It did not culture TB bacilli. A polymerase chain reaction using IS 6110 primers detected Mycobacterium tuberculosis complex in the material. A new therapy was not initiated and the patient has been well for a follow-up period of 8 y.

PR is not unusual. It can be encountered in 6% to 30% of patients under anti-TB therapy depending on the clinical forms (2). In 75% of cases, a pre-existing lesion expands in the same localization, and in the remainder a new lesion emerges in a different anatomical localization. This reaction can develop from second week to the ninth month (>3rd month) of therapy. PR for lymph nodes is represented by development of a new lymphadenitis or enlargement of existing nodes. This reaction has been reported in 6% to 25% of patients with TB lymphadenopathy in 2 previous studies (4, 5). After PR, therapy is continued. Steroids may be added or the lymph node may be removed surgically.

PR is usually seen in the third month of therapy. A PR after therapy has not been clearly defined in the literature. In 1954, Lees and Munro (6) reported a 21-y-old male patient who developed paradoxical subcutaneous abscesses during the treatment of miliary tuberculosis. Subcutaneous lesions appeared just after the treatment and recurred for more than 2 y. They prescribed isoniazid for the recurring abscesses after completion of therapy, and the abscesses regressed. Additionally, in a comprehensive TB lymphadenopathy study including 113 cases, appearance of new lymph nodes and increase in size of nodes were encountered in 2 and 10 patients respectively (5). These lesions were reported to develop 6 and 18 months after the end of therapy, in 10 and 2 patients respectively. The study did not describe these phenomena as paradoxical. The present case seems to represent the first well-documented study reporting PR after completion of therapy. In TB lymphadenitis studies (5, 7–11), relapse is not generally encountered with appropriate anti-TB therapy; therefore, relapse is not expected within the first months after an effective anti-TB therapy for TB lymphadenitis. Instead, PR should be considered when a lymph node is enlarged within the first few months following appropriate anti-TB therapy.

Our patient first developed lymphadenopathies in the fourth month of therapy, and then in the second 3-month period after therapy. In the first situation, the histology of the removed lymphadenopathy was consistent with TB. The lesions developed when the patient was clinically well, and were considered as PR. Anti-TB therapy was continued. For the second situation, the lesions were removed surgically. While ZN staining revealed scanty AFB, TB bacilli could not be yielded, and a PCR study for M. tuberculosis complex was positive. All the data suggested a PR rather than a relapse or an infection due to non-TB mycobacteria. A medical therapy was not initiated after the surgery. The patient has been well for 8 y.

In conclusion, when newly developed TB lymphadenitis or enlargements of existing nodes are seen within the first months after an appropriate anti-TB therapy, a PR should also be considered.

REFERENCES


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