Incidence and outcomes of paradoxical lymph node enlargement after anti-tuberculosis therapy in non-HIV patients

Abstract

We prospectively evaluated the incidence and outcomes of post-treatment lymphadenopathy in 154 patients with newly diagnosed lymph node Tuberculosis (TB) and in 12 patients previously treated for TB (group 2). Post-treatment lymphadenopathy occurred in 24 (15.6%) patients of group 1 and in 12 patients of group 2. Re-hospitalization was performed in 23 of these 36 patients. AFB test was positive in four (17.4%) cases, and TBC-PCR was positive in 11 (45.8%), but all samples were sterile (no microbiological recurrence). Granuloma was present in 12 (52.2%) histological specimens. Thirty-three (91.7%) of the 36 patients with post-treatment lymphadenopathy improved spontaneously (post-treatment paradoxical response (PR)) and 3 (8.6%) were improved with retreatment (clinical recurrence). The overall incidence of post-treatment PR in patients with lymph node TB (group 1) was 8.6 per 100 person-years (95% CI, 5.6±6.7). In conclusion, a substantial proportion of lymphadenopathies after TB treatment are more likely to be associated with post-treatment PR than with microbiological recurrence. Patients with negative re-hospitalization cultures who complied with the initial therapy should be monitored until the PR resolves. To avoid unnecessary re-treatment with anti-TB.

Introduction

Paradoxical deterioration of TB during anti-TB therapy has been well documented in HIV-infected patients, but it is also not uncommon in non-HIV patients, especially in those with lymph node TB. It has been observed both during and after effective TB treatment. The latter cases are more complicated because lymphadenopathy after completing TB treatment need to be differentiated from microbiological recurrence. Because of the risks associated with anti-TB prophylaxis, some physicians sometimes decide in favor of retreatment. However, lymphadenopathy after anti-TB therapy may be an immunologically mediated PR and may improve spontaneously.

Little is known about the incidence and outcomes of post-treatment lymphadenopathy, and we do not know how many cases are due to microbiological recurrence of TB and how many to post-treatment PR. We prospectively assessed the incidence, clinical characteristics, and outcomes of post-treatment lymph node enlargement in HIV and non-HIV patients with TB. We hypothesized that paradoxical expansion of lymph node lesions can also occur in patients previously treated for TB at another site (e.g., pulmonary TB). Therefore, we also evaluated the characteristics and outcomes of previously treated TB patients who visited our clinic with suspected lymph node TB.

Methods

We included all adult patients newly diagnosed with lymph node TB between May 2008 and April 2012 (group 1). Additionally, we also included patients previously treated for TB who visited our clinics with suspected lymph node TB during the same study period (group 2). “Post-treatment PR” was defined as deterioration of pre-existing lymph nodes and/or the development of new lymph nodes in patients who had received TB treatment for at least two weeks and who seemed to be improving initially. The outcome of post-treatment lymphadenopathy was classified as due to microbiological recurrence, clinical recurrence, and post-treatment PR. “Microbiological recurrence” was defined as care following anti-TB therapy, followed by reappearance of bacteria after completion of treatment as confirmed by repeat cultures. “Clinical recurrence” was defined as (1) no microbiological recurrence, and (2) regression of post-treatment lymphadenopathy with further TB treatment. “Post-treatment PR” was defined as (1) no microbiological recurrence, and (2) spontaneous regression of post-treatment lymphadenopathy without further TB treatment (i.e., TB medication and/or lymph node excision).

Results

During the study period, 154 patients with newly diagnosed lymph node TB (group 1) and 12 patients previously treated for TB (group 2) were included. Post-treatment lymphadenopathy occurred in 24 (15.6%) patients of group 1 and in 12 patients of group 2. Re-hospitalization was performed in 23 of these 36 patients. AFB test was positive in four (17.4%) cases, and TBC-PCR was positive in 11 (45.8%), but all samples were sterile (no microbiological recurrence). Granuloma was present in 12 (52.2%) histological specimens.

Thirty-three (91.7%) of the 36 patients with post-treatment lymphadenopathy improved spontaneously (post-treatment paradoxical response (PR)) and 3 (8.6%) were improved with retreatment (clinical recurrence). The overall incidence of post-treatment PR in patients with lymph node TB (group 1) was 8.6 per 100 person-years (95% CI, 5.6±12.7).

Discussion

Based on our findings, we propose a diagnostic and therapeutic algorithm for the management of lymphadenopathies that occur after anti-TB therapy (Fig. 1). After a short period of monitoring, any patients with microbiological recurrence should be re-hospitalized and samples sent for mycobacterial cultures, so that TB drug susceptibility patterns can be elucidated. Alternatively, mediastinal lymphadenopathy should be confirmed by histological examination. Rapid drug susceptibility patterns can be performed on the re-biopsied samples, which may be useful in detecting the recurrence caused by drug-resistant TB, especially when multi-drug resistant TB is prevalent.

Finally, patients with negative culture results who complied with the initial TB treatment should be monitored until the PR resolves after retreatment. If the PR persists, it may be necessary to re-treat patients again.

Conclusions

We found that a substantial proportion of lymphadenopathies after TB treatment are more likely to be associated with post-treatment PR than with microbiological recurrence.

Patients with negative re-hospitalization cultures who complied with the initial TB therapy should be monitored until the PR resolves. To avoid unnecessary re-treatment with anti-TB.

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