

## Multiple Recurrences of Tuberculosis in an HIV Infected Individual

Sir,

We report a severely immunosuppressed HIV-infected patient with multiple recurrences of tuberculosis proved to be due to re-infection by DNA fingerprinting.

A 33 years male presented with complaints of productive cough, breathlessness and high-grade fever of two months duration. He was found to be HIV-1 positive by ELISA and confirmed by Western Blot. He was anemic and CD4 count was 24 cells/mm<sup>3</sup> (4%) and the CD4:CD8 ratio was 0.06. A diagnosis of smear positive pulmonary tuberculosis was made and he was treated with WHO Category I regimen by directly observed therapy (DOT). Sputum culture and drug susceptibility testing for mycobacteria revealed *Mycobacterium tuberculosis* sensitive to all first line anti-tuberculous drugs. The patient responded well to anti-TB treatment, sputum smears and cultures became negative by the 2nd month of treatment and he was declared cured at the end of six months.

The patient developed a recurrence after two months and was treated with WHO Category II DOT. At this time his CD4 counts were still very low (4 cells per cumm, 1%). Sputum culture grew *M. tuberculosis* sensitive to all first line drugs. The patient responded well to therapy but continued to stay in the hospital for social reasons. Three months after completing Category II treatment, the patient developed a recurrence and this time the drug susceptibility results showed *M. tuberculosis* resistant to isoniazid. The patient was treated with a regimen containing streptomycin, rifampicin, ethambutol and pyrazinamide daily. The patient became sputum smear and culture positive again after eight months and this time *M. tuberculosis* resistant to isoniazid and rifampicin was isolated from the sputum. As soon as the drug

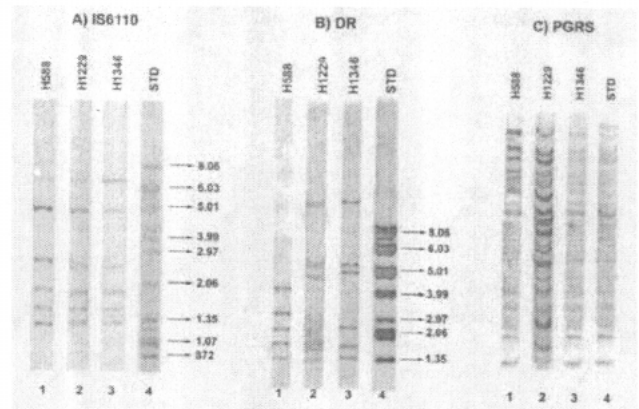


Fig. 1 : RFLP patterns of *M. tuberculosis* isolates from three episodes of tuberculosis in an HIV+ patient

Footnote: Panel A shows the RFLP pattern using IS6110 probe. Lane 1 shows the pattern of the pretreatment isolate. Lanes 2 and 3 show the RFLP patterns of isolates at relapses at 19th and 27th month. Lane 4 shows the RFLP pattern of the standard strain. Panel B and C represent the RFLP patterns of the same isolates with DR and PGRS probes respectively.

susceptibility results became available, the regimen was changed to include kanamycin, ofloxacin, ethambutol, pyrazinamide and ethionamide, with good response.

Fig. 1 shows the restriction fragment length polymorphism (RFLP) pattern using three probes IS6110, direct repeat (DR) and polymorphic GC rich sequence (PGRS) of *M. tuberculosis* isolated from the patient initially and during two of the relapses (20,28 months), using the standard protocol.

Recurrent tuberculosis might be due to either relapse or exogenous re-infection.<sup>1,2</sup> In this case, recurrent TB was due to re-infection. Though data from India is limited, previous work from this center has shown that re-activation contributes to about two-thirds of relapses in HIV negative subjects.<sup>3</sup> There have been no reports from India on TB recurrences in HIV positive individuals. One interesting finding of our report is that infection caused during the 3rd and 4th episode was by a new strain, which was identified only by DR RFLP and not by the other two probes. Although RFLP using IS6110 is the internationally accepted standard method for DNA fingerprint studies on *M. tuberculosis* strains, it has several limitations in developing countries. Multiple probes increase the sensitivity and discriminatory power of DNA fingerprinting.

Nosocomial transmission of TB has been reported to occur and is particularly frequent among immuno-suppressed individuals. A policy of separating smear positive from smear negative patients would be ideal in hospitals admitting TB patients and wherever possible HIV infected persons should be segregated from infectious TB patients. The contribution of re-infection to the epidemiology and pathogenesis of tuberculosis has important implications for tuberculosis control in India and other countries with a high burden of HIV and tuberculosis and deserves further study.

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