Correspondence

Multiple splenic macronodular tuberculomas: MRI characteristics under treatment

Tuberculous involvement of the liver and spleen is uncommon, especially in the absence of pulmonary manifestations.\(^1\) Magnetic resonance imaging (MRI) characteristics of multiple tuberculous splenic lesions have not been described so far. Also, to the best of our knowledge, MRI changes of macronodular tuberculomas under treatment have not been described.

An 18-year-old immunocompetent man with fever, nausea, vomiting, diarrhoea and weight loss was admitted to hospital. Chest radiography was unremarkable. Computed tomography (CT) exhibited multiple splenic lesions and mesenteric lymphadenopathy with rim enhancement. Abdominal MRI confirmed the multiple splenic lesions and disclosed two hepatic nodules. Colonoscopy with biopsy revealed non-specific inflammatory changes at caecum. Surgical biopsy of mesenteric lymph node and PCR test from myelogram disclosed *Mycobacterium tuberculosis.* Anti-tuberculosis treatment was initiated and was considered successful on clinical grounds. On 5- and 10-month follow-up, MRI lymphadenopathy progressively regressed and most of the splenic lesions rendered low signal intensity, although few lesions completely resolved.

According to the MR characteristics, three types of splenic tuberculomas were observed in our case. Type I lesions had a target appearance on T1WI, with a hypointense centre, hyperintense inner rim and hypointense outer rim. On post-gadolinium T1WI, the inner rim enhanced mildly. On T2WI, these lesions were comparable to liver tuberculomas, as described by Kawamori et al.\(^1\) They were hyperintense with a hypointense rim corresponding to active lesions with central caseation necrosis and peripheral granulomatous tissue (Figure 1). Type I splenic foci became smaller, and T2 iso- or hypointense 5 months post-treatment initiation, while they did not enhance and were T2WI hypointense (Figure 2A) and ‘black’ on gradient-echo sequence on 10-month follow-up (Figure 2B), possibly representing fibrotic/calcified granulomas. Type II lesions were homogeneously hypointense on T1WI, hyperintense on T2WI, exhibited a mild thin rim enhancement and had a similar appearance with the two hepatic lesions. These nodules were presumably at a different stage of evolution during the course of the disease as compared with type I lesions, and the obvious granulomatous reaction might be ab-

**Figure 1** T2WI with fat saturation shows four splenic lesions (arrows) with increased signal intensity and a hypointense rim (type I lesions). Note that there is one posterior splenic lesion (arrowhead) that exhibits homogeneously low signal intensity (type III lesions).

**Figure 2** Follow-up MRI 10 months after initiation of treatment. A. T2WI at the same level as in figure 1 shows that the lesions became hypointense and decreased in size. B. T2 star images at the same level as in Figure 1 show marked hypointensity and ‘blooming’ artefact at the lesions, probably representing fibrosis/calcifications.
sent at that time. To confirm, they had completely resolved on 5- and 10-month follow-up MRI, as opposed to the prolonged appearance of type I lesions. Type III lesions presented with decreased signal intensity on both T1 and T2WI (Figure 1), did not change on 5- and 10-month follow-up and were identical to the final stage of type I lesions (Figure 2A and B).

Tuberculous involvement of the spleen may be manifested by multiple nodules; they may exhibit variable appearance on MRI that presumably reflects different stages of evolution of the disease. Under successful treatment the healing process is related to the evolution stage of the lesion where treatment was initiated. Low signal intensity foci on both T1WI and T2WI after treatment probably correspond to inactive lesions. MRI is an excellent tool for disclosing and monitoring macronodular tuberculomas.

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The role of gender and literacy in the diagnosis and treatment of tuberculosis

In the June issue of the Journal, Granich and Reichler posed a question regarding patient delay and health care facility delay for illiterate PTB patients in Yemen.2 We would like to clarify how both delays differ between literates and illiterates. The median patient delay for illiterates was 4 weeks, while that for literates was 2 weeks (P = 0.130 by the Mann-Whitney test), the median health care facility delay for illiterates was 7 weeks, while that for literates was 2.5 weeks (P = 0.069 by the Mann-Whitney test). Moreover, as shown in the Figure, health care facility delay is more likely a related factor than patient delay. It is also shown in the Figure that more than 40% of illiterates, compared to less than 20% of literates, wait for 8 weeks before receiving a proper diagnosis at a health care facility. From the interview data, it is apparent that the primary reason for this delay among illiterates is that they are reluctant to seek further medical evaluation since they first received a diagnosis of a common cold or temporary inflammation, which reinforced their idea of a ‘common illness’. Hence, it is suggested that the health care facility delay may be shortened if medical staff can persuade illiterates to visit a medical facility at a specified interval after the first visit in order to consult with a doctor again.

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The tuberculin test

We read with interest the article published by Kimura and colleagues published in a recent issue of the Journal.1 As the authors state that the distribution of erythema diameters was unimodal and the distribution of induration diameters was bimodal, we would like to raise some questions for discussion. We think these may clarify an important technical point that impacts on assay utility and interpretation of erythema test results in different settings.

First, the paper has some shortcomings. It dealt with a retrospective analysis and no information about the standardisation of the TST in this period was described. Assuming that inexperience leads to error (terminal digit preference), TST reading requires experience and care.2 In addition, no information was given about possible concurrent infection with environmental mycobacteria or BCG status among the subjects included in the analysis, the most important limitations of the TST.3,4

Second, different results might have been found if the authors had used different approaches aimed at comparing measurements of erythema and induration based on 5 mm grouping. In 1970, a correlation of erythema and induration of 7455 TSTs (1543 performed with Old Tuberculine and 5912 with PPD-RT 23) was carried out in schoolchildren in Ribeirão Preto (São Paulo State, south-east Brazil).5 A linear relationship between the erythema and induration diameters using PPD-RT23 was found, and the difference between diameters was 3 mm. In 1973, in the same city, erythema and induration diameters obtained among 930 TSTs with PPD-RT23 (2 TU) were compared in 466 tuberculosis patients.6 In that study, different results from the Kimura results were observed. The average difference between the erythema and induration diameters was only 1 mm. Similar results to ours were also recently observed by Toivgoogin et al.7

Sanches, using the Battacharya method (decomposition of frequency distribution into normal components by a graphic method) in 5912 TST results from a previous study in our setting, found three components for induration and four for erythema.8 Those results were related to a high prevalence of non-mycobacterial infection detected in the city.9

Models employing mixture analysis to estimate underlying distributions have been used successfully to estimate the prevalence of infection with M. tuberculosis among BCG-vaccinated subjects in different age groups,10 although the experience is very limited.

Achcar et al., considered the use of Bayesian methods in an analysis of 35 680 TSTs.11 They used simulation methods based in Markov chain Monte Carlo (MCMC) algorithms to obtain Bayesian quantities of interest in different age groups. Interesting uni- or bimodal distributions dependent on age group were observed.

The most appropriate approach would be the use of techniques that utilise M. tuberculosis-specific antigens that are found in neither M. bovis-BCG nor environmental mycobacteria. Recently, promising results with interferon-γ release assays (IGRA) are aiding more or less in successfully overcoming the problem of non-specific reactions attributable to BCG vaccination and infection with environmental mycobacteria.11

Finally, we concur with the approach proposed by Kimura et al. to assess the incidence of infection with M. tuberculosis in a general population, measuring the incidence of infection directly through longitudinal studies. This approach would overcome the current scarce information on TB infection in different regions. The majority of TST surveys were carried out before the impact of HIV infection could be felt, and the age group in which these surveys (schoolchildren) were carried out were beyond survival of perinatally acquired HIV infection and too young to have sexually transmitted HIV infection. In parallel, the estimation of the risk of infection among schoolchildren has not, unfortunately, become an integral part of ascertaining programme effectiveness.2 To overcome these impediments, a prospective evaluation of a close contact cohort with TST survey that includes erythema and induration measurements and IGRA test results in low- and middle-income countries with different HIV infection rates might be helpful and should be pursued by researchers and TB programme managers.

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In reply
We thank Dr. Ruffino-Netto for his interest in our article.

First, our article was a cross-sectional study and as such has no follow-up component, except for the very few days of follow-up for the hospital employees who were assessed for atopy. Nevertheless, the unique and massive data set was well worthwhile bringing to attention.

Contrary to Ruffino-Netto’s assertion, information was given in our paper about BCG status. More than 95% of the schoolchildren had been vaccinated with BCG and a sizeable minority had been revaccinated. We tried various groupings of the data and decided that 5 mm groups were the best compromise between precision and economy of space. Other groupings did not indicate any reason to change our selection of 5 mm groups.

We are surprised at Ruffino-Netto’s finding that the average diameter of erythema was only 1 mm greater than that of induration. One of us (GWC) has had long and varied experience with tuberculin testing in a variety of populations and has never seen such a small average difference. One study in Japan showed a frequency of non-tuberculous mycobacterial infections in the order of 1 per 100 000. Furthermore, the distributions of induration do not show the excess of small reactions usually associated with such infections.

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