Journal of Crohn's and Colitis (2013) 7, e499–e500

Available online at www.sciencedirect.com

ScienceDirect

## LETTER TO THE EDITOR

### Current incidence of active tuberculosis in IBD patients treated with anti-TNF agents: Still room for improvement

*Dear Sir,*

Spain is one of the European countries with the highest prevalence of tuberculosis (TB) infection. TNF-alpha plays a key role in the host response against TB so that screening of latent TB infection (LTBI) is widely recommended before starting anti-TNF therapies.[1,2] We read with interest the article by Jáuregui et al.[3] published in JCC reporting cases of active TB in patients with inflammatory bowel disease on anti-TNF agents, despite negative screening of LTBI. The authors concluded that, as far as most cases occurred early after treatment initiation, optimization of screening tools is warranted. We would like to report our experience of TB cases in a similar cohort of anti-TNF treated IBD patients in the same geographic area.

Among 330 patients treated with anti-TNF therapy in our centre, 4.5% required TB prophylaxis because of LTBI. In addition, 4 patients developed active TB while being treated with TNF antagonists. Their epidemiological and clinical data are summarised in Table 1. Two of them were diagnosed early after starting antiTNF. Of interest, one patient was immigrant from an endemic area of TB, also had HIV infection, and antiTNF therapy was started concomitantly with HAART. Another patient had a past history of active TB that was treated for at least 6 months as reported by the patient; that was the reason why no preventive measures were done despite positivity of both tuberculin skin test (TST) and interferon gamma release assay (IGRA). In the other two cases, TB infection appeared 10 and 15 months after starting anti-TNF treatment with a clear epidemiological contact in one of them and we considered these cases as *de novo* TB infection and not a reactivation of previous LTBI.

Current recommendations for LTBI screening in IBD patients include clinical anamnesis, chest X-ray, TST, and IGRA depending on local epidemiologic characteristics, measures being more rigorous among immunosuppressed patients.[4] Despite this, the incidence of active TB among anti-TNF treated patients is still about 1–2%. We agree with Jáuregui et al.[3] that current LTBI screening protocols should be revisited in order to avoid false negatives, and the search for more specific and sensitive tools is warranted. It should not be forgotten that some TB cases may occur because of a non-strict accomplishment of LTBI screening recommendations. However, beyond TB reactivations early after starting antiTNF therapy, there is also a high risk of *de novo* TB infections. In fact, almost half of the patients in both Jáuregui et al.'s and our own series developed active TB more than one year after anti-TNF was introduced. These cases highlight the need for periodical assessment of epidemiological risk factors in patients on anti-TNF therapy (travels to endemic areas, change in jobs, etc.). Moreover, the usefulness of repeating tests for LTBI is still to be established.[5]

## Conflict of interest

None declared.

## References

1. Keane J, Gershon S, Wise RP, Mirabile-Levens E, Kasznica J, Schwietertman WD, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. *N Engl J Med* 2001;**345**:1098–104.
2. Lopez-San Roman A, Muñoz P, Fortun J, Gassull MA. Recommendations on tuberculosis and treatment of inflammatory bowel disease with infliximab. 2006 update. *Gastroenterol Hepatol* 2006;**29**:81–4.
3. Jáuregui A, Turon F, Ordás I, Gallego M, Feu F, Ricart E, et al. Risk of developing tuberculosis under anti-TNF treatment despite latent infection screening. *J Crohns Colitis* 2013;**7**:208–12.
4. Cabriada JL, Vera I, Domènech E, Barreiro-de Acosta M, Esteve M, Gisbert JP, et al. Recommendations of the Spanish Group on Crohn's Disease and Ulcerative Colitis on the use of anti-tumor necrosis factor drugs in inflammatory bowel disease. *Gastroenterol Hepatol* 2013;**36**:127–46.
5. Taxonera C, Gisbert JP. Letter: recommendations for the management of latent tuberculosis infection in IBD patients may not be applicable in all settings. *Aliment Pharmacol Ther* 2013;**37**:365–6.

Míriam Mañosa*
Eugeni Domènech
Eduard Cabré
*GI & IBD Unit, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain*
*CIBERehd, Barcelona, Spain*
*Corresponding author at: GI & IBD Unit, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain.
E-mail address: mmanosa.germanstrias@gencat.cat (M. Mañosa).

23 April 2013

1873-9946/$ - see front matter 
http://dx.doi.org/10.1016/j.crohns.2013.04.021

**Table 1** Demographic and clinical characteristics of patients developing TB under anti-TNF therapy.

| Patient | Sex | Age at TB diagnosis (years) | IBD | TB risk factors | Treatment at LTBIs | TST at LTBIs | Booster at LTBIs | Chest X-ray at LTBIs | IGRA at LTBIs | Time on antiTNF at TB development (months) | TB location | Diagnosis test |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 57 | CD | Immigrant | Azathioprine | + | ND | Abnormal | + | 2 | Disseminated TB | Bacilloscopy and Lowenstein + |
| 2 | M | 47 | UIBD | No | Azathioprine and prednisone. HAART (FTC/TDF + EFV) | − | − | Normal | ND | 2 | Disseminated TB | Bacilloscopy + and Lowenstein − |
| 3 | M | 24 | CD | Familiar TB contact | None | − | ND | Normal | ND | 10 | − | No microbiological detection. TST +, ELISPOT +, epidemiological contact |
| 4 | F | 37 | CD | No | Azathioprine | − | − | Normal | ND | 15 | Disseminated TB | Microbiological genetic detection (PCR) bacilloscopy |

F: female, M: male, CD: Crohn's disease, UIBD: unclassificable colitis, LTBIs: latent TB infection screening, TST: tuberculin skin test, IGRA: interferon gamma release assay; ND: not done.