Letters to the Editor

Safe re-initiation of infliximab in a patient with renal tuberculosis

Sirs,

The efficiency of TNF-α blockers in the treatment of rheumatoid arthritis (RA) (1) and ankylosing spondylitis (AS) (2) has been demonstrated in large-scale trials. One of the major side effects is tuberculosis (TB) reactivation (3) leading some countries to develop recommendations (4) regarding the management of latent TB in patients who are considered for anti-TNF-α therapy. These recommendations also ask for the interruption of TNF-α blockers when TB arises under treatment. Decisions regarding the re-initiation of anti-TNF-α in the setting of active TB remain difficult.

We managed a 32-year-old Caucasian man with severe AS (BASDAI, 58mm; BASFI, 68.3mm). Numerous nonsteroidal anti-inflammatory drugs, sulphasalazine, and methotrexate failed. In October 2001, infliximab therapy, 5mg/kg every 8 weeks, was considered and produced a marked improvement in symptoms. There was no history of symptomatic TB or tuberculous contagium. Tuberculin skin test (5 units/mL), which was done before infliximab, was positive, and was ascribed to BCG vaccination during childhood. Chest radiograph and sputum cultures were normal. At the time, French recommendations (4) regarding the management of latent TB in a patient taking anti-TNF-α were not available. No TB chemoprophylaxis was given. In March 2003, the patient was admitted for asthenia, weight loss, cervical lymphadeno-pathy, and C-reactive protein at 75mg/L. Lymph-node biopsy showed *Mycobacterium tuberculosis*. Chest radiograph and sputum cultures remained normal. Acute renal failure, albuminuria and aseptic leucocyturia were noted. Urine cultures were negative. Renal biopsy showed acute interstitial nephritis with multiple non-caseating granulomas. Antituberculous tritherapy associating isoniazid (5mg/kg/d), pyrazinamid (30mg/kg/d), and rifampicin (10mg/kg/d) was started. Infliximab was stopped. After 6 weeks of TB treatment, the patient had gained weight, lymph nodes disappeared, and creatinine clearance had increased. However, in April 2003, AS flared, despite symptomatic treatment. We decided to reintroduce infliximab, after 2 months of TB treatment, with the informed consent of the patient. Soon after the first infusion, the pain resolved. After the first three months of TB tritherapy, isoniazid and rifampicin were maintained for twelve months and were then stopped. After 60 months of follow-up, no sign of TB recurrence were detected. The AS remained in remission without treatment other than infliximab.

The main interest of this case is the reintroduction of infliximab shortly after the diagnosis of TB. The re-initiation of infliximab allowed us to progressively discontinue symptomatic treatment and led to a dramatic improvement in the quality of life. It has been previously suggested that anti-TNF-α should be discontinued for the duration of active TB therapy (4). However, anti-TNF-α interruption may result in a severe flare of the underlying disease or may be responsible for a paradoxical response to antituberculous therapy (5, 6). This paradoxical reaction is the result of an excessive inflammatory response due to immune reconstitution and increased antigen exposure after receipt of TB therapy. Thus, both continuing and stopping anti-TNF-α carry the risk of an adverse clinical course. At present, it is not clear whether TNF-α blockers can be safely continued or restarted in patients with active TB. Matsumoto *et al*. described the first case of the reintroduction of anti-TNF-α after a TB flare in a patient with RA (7). The reintroduction of infliximab was performed nine months after efficient TB treatment, with one year's follow-up without a TB recurrence. Other authors have reported cases of anti-TNF-α reintroduction following TB flare, between 2 months and 3 years after the completion of TB therapy, with mean follow-up having reached 42.7 months (8, 9).

In our case, because of the severity of AS flare, infliximab was restarted after 2 months of TB treatment, first with three months tritherapy, then with isoniazid and rifampicin for twelve months. After 60 months of follow-up, AS is still in remission and there has been no TB recurrence. This suggests that the reintroduction of infliximab shortly after the start of TB treatment might be safe under strict supervision in patients with severe inflammatory diseases.

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