Chronic myeloid leukaemia and tuberculosis in a patient with rheumatoid arthritis treated with infliximab

F Broussais, M Kawashima, H Marotte, P Miossec

Cases of lymphoma and tuberculosis (TB) have been described in patients receiving tumour necrosis factor α (TNFα) inhibitors. We report a case of chronic myeloid leukaemia (CML) and TB, where molecular markers could be followed in a rheumatoid patient treated with infliximab.

CASE REPORT
A 56 year old white woman, with a 2 year history of refractory and destructive rheumatoid arthritis (RA), had been treated with methotrexate (MTX, 10 mg/week). As this was not effective, MTX was increased to 15 mg/week, and she received a total amount of about 1250 mg. Because of persistent active disease and high erythrocyte sedimentation rate (44 mm/1st h) with high platelet count at 0.6 × 10^12/l, infliximab was combined with MTX (15 mg/week) in August 2001 at 3 mg/kg every 8 weeks.

Although the disease improved, thrombocytosis, first considered as possibly related to inflammation, increased up to 1.1 × 10^12/l in January 2002. Bone marrow aspiration demonstrated typical features of CML with the (9; 22) (q34; q11) translocation. Infliximab was stopped. After a month of treatment with hydroxy carbamide (500 mg, three times a day), the platelet count decreased to 0.5 × 10^12/l. Hydroxy carbamide was stopped and interferon alfa (IFNα) was started in April 2002 at 8 million units a day, until August 2002. Such treatment was not well tolerated, and a weight loss of more than 10% of body weight, mild fever, and persistent bronchitis ensued, which were first thought possibly to be related to the IFNα.

In June 2002, because of cachexia and lung symptoms a chest x ray examination was carried out, which showed extensive caverns of typical TB. Some of these lesions were already evident on a film taken in 1993, strongly suggesting that the TB had been reactivated in a patient who should have received antibiotics before starting infliximab. Mycobacterium tuberculosis was grown from three consecutive sputum analyses. A four drug regimen was initiated for 2 months, followed by isoniazide and rifampicin for 4 months. Because of persistent anorexia and depression, IFNα treatment was replaced by STI 571 at 600 mg/day. At the time of writing, the patient remains in haematological remission. Joint manifestations are limited to arthralgia, treated with non-steroidal anti-inflammatory drugs.

bcr-abl transcript was detected by reverse transcriptase-polymerase chain reaction at the time of CML diagnosis at a level of 0.5 × 10^-2. This level decreased with myelosuppressive agents to 0.5 × 10^-4. In addition, using RNA collected from this patient before infliximab treatment, the transcript could be detected at 0.5 × 10^-3 before the first infusion, indicating that CML was present before infliximab treatment. Its rate of expression appeared to increase during infliximab treatment, suggesting that such treatment has an effect on clonal expansion, although the mutation was already detected before treatment was started (fig 1).

To our knowledge, this is the first description of a diagnosis of CML during infliximab treatment. Available data are insufficient to draw conclusions as to whether CML developed as part of the natural history of the underlying medical conditions, or whether it occurred as a complication related to a cell mediated immune defect.

Figure 1 Clinical course and main biological variables for TB and CML diagnosis. (A) The course of the platelet count during infliximab infusions and treatment against CML. (B) Body weight is shown. (C) Kinetics of the bcr-abl transcript expression.
Muscarinic acetylcholine receptor autoantibodies in patients with Sjögren’s syndrome

Y Naito, I Matsumoto, E Wakamatsu, D Goto, T Sugiyama, R Matsumura, S Ito, A Tsutsumi, T Sumida

Sjögren’s syndrome (SS) is an autoimmune disease characterised by lymphocytic infiltration into the lacrimal and salivary glands, leading to dry eyes and mouth. Infiltration is also found in the kidneys, lungs, thyroid, and liver. Immunohistochemical studies have shown that most infiltrating lymphocytes around the labial salivary and lacrimal glands, and kidneys are CD4 positive γδ T cells. Previous studies with polymerase chain reaction provide evidence about the T cell receptor Vδ and Vγ genes on these T cells, and sequence analysis of the CDR3 region indicates some conserved amino acid motifs, supporting the notion that infiltrating T cells recognise relatively few epitopes on autoantigens. Candidate autoantigens recognised by T cells infiltrating the labial salivary glands of patients with SS have been analysed, and Ro/SSA 52 kDa, α-amylase, heat shock protein, and T cell receptor BV6 have been identified. However, there is no direct evidence that these reactive T cells really attack and destroy the salivary glands. In contrast, the presence of autoantibodies (Abs) against M3 muscarinic acetylcholine receptor (M3R) has been reported, and it is suggested that an immune reaction to M3R plays a crucial part in the generation of SS. Robinson, et al demonstrated that human anti-M3R Abs reduce the secretory function in NOD.lgnull mice. Moreover, Bacman et al clearly showed that human Abs against the second extracellular loop of M3R could

REFERENCES