T cells and cytokines. The occurrence of this syndrome as part of IRIS may offer new insight into its pathogenesis.

Rheumatology key message

- Autoimmune inflammatory rheumatic syndromes can occur in HIV infection.

Disclosure statement: The authors have declared no conflicts of interest.

EDWINA LAWSON1, KATHARINE BOND1, DUNCAN CHURCHILL1, KAREN WALKER-BONE2

1 Department of Genitourinary Medicine, Royal Sussex County Hospital, Brighton and 2 Brighton and Sussex Medical School, Euan Keat Education Centre, Princess Royal Hospital, Haywards Heath, West Sussex RH16 4EX, UK. E-mail: k.walker-bone@bsms.ac.uk

Correspondence to: Karen Walker-Bone, Euan Keat Education Centre, Princess Royal Hospital, Lewes Road, Haywards Heath, West Sussex RH16 4EX, UK. E-mail: k.walker-bone@bsms.ac.uk


Rheumatology 2009;48:447–448
doi:10.1093/rheumatology/kep015
Advance Access publication 7 February 2009

A case of rituximab-induced interstitial pneumonitis observed in systemic lupus erythematosus

Sir, Rituximab (anti-CD20 mAb) depletes B lymphocytes and is widely used for the treatment of B-cell malignant lymphoma [1, 2]. The incidence of life-threatening side effects is very low, but there are some case reports of rituximab-induced interstitial pneumonitis (IP) in patients with haematological disorders [3]. We report the first case of rituximab-induced IP observed in SLE.

A 24-year-old woman was diagnosed as SLE based on the presence of malar rash, oral ulcers, leucopenia (1500/μl), thrombocytopenia (6.9 × 109/μl), hypocomplementaemia (C3, 61 mg/dl; C4, 9 mg/dl), positive test for ANA (1:640), anti-Sm antibody (158 U/ml) and anti-dsDNA antibody (10 U/ml) and CNS involvement. MRI of the brain showed areas with high intensity by T2-weighted image and low intensity by T1-weighted image in the white matter bilaterally. She was treated with 1000 mg rituximab with pre-treatment of 125 mg methylprednisolone, because of lack of response to intravenous methylprednisolone pulse and 1 mg/kg/day oral prednisolone. Before rituximab administration, chest radiograph and CT was normal (Fig. 1A–C). After finishing infusion of rituximab, she developed dry cough, but breath sounds were normal with an oxygen saturation of 99% and normal chest X-ray. Four days after the administration, chest X-ray revealed interstitial opacities in the lung base bilaterally (Fig. 1D). Chest CT revealed diffuse ground-glass attenuation in non-specific areas of both lungs without any structural distortion (Fig. 1E and F). Congestive heart failure was excluded by normal study of ultrasound cardiography and normal level of serum brain natriuretic peptide. The case was diagnosed as rituximab-induced IP based on the bronchoalveolar lavages fluid examination (increased total cell count, 1.26 × 106; increased lymphocytes, 68.9%; non-detection of eosinophils and neutrophils; low CD4/CD8 ratio, 0.19; negative PCR test for Pneumocystis jiroveci DNA and Mycobacterium DNA; and negative culture test for bacteria, fungus and Mycobacterium), negative examination for serum anti-Chlamydia antibody, CMV-antigenemia and Legionella urinary antigen and ground-glass appearance on chest CT. She had no allergic history, and was not taking any medication. Treatment with 1 mg/kg/day of prednisolone was continued. Seven days after the diagnosis, dry cough subsided and chest X-ray and CT findings disappeared (Fig. 1G–I). Lupus-related symptoms, such as malar rash and oral ulcers disappeared, the numbers of leucocyte and platelet were increased to normal ranges, and titres of serum anti-Sm antibody and anti-dsDNA antibody were decreased. The dosage of prednisolone was tapered to 10 mg/day without any exacerbation.

Since several autoantibodies are presented in lupus patients and deposition of immune complex is shown in the affected organs, autoimmune B cells might be thought to have an important role for the pathogenesis of SLE. Rituximab has been used for the treatment of several autoimmune diseases, such as SLE [4, 5] and RA [6, 7]. So far, 16 cases with rituximab-induced IP have been reported and reviewed by Wagner et al. [3]. In all cases, rituximab was used for haematological disorders, including 12 patients with malignant lymphoma, 3 with chronic lymphocytic leukaemia and 1 with immune thrombocytopenic purpura. Analysis of the available information showed that the patients were 65.5 ± 3.1 years old (mean ± s.e.m.), the number of cycles of rituximab infusion was 4.1 ± 0.7, all patients were treated with corticosteroids and 6 out of 16 patients died during the follow-up. Our patient was relatively young (27 years) and developed IP following the first dose of rituximab. Based on the PubMed database searches, this is the first report of an SLE patient who developed IP following initiation of rituximab therapy. Recently, rituximab-induced organizing pneumonia was reported in an RA patient [8]. Although it is rare, care should be taken with pulmonary complications when rituximab is prescribed not only for malignant lymphoma, but also for the other diseases, including SLE and RA.

For this patient, infusion of rituximab was performed according to the protocol of ongoing Phase II/III trial of SLE [9] and was well managed. Regarding the dosage of rituximab, twice infusion at 2 weeks interval of each 1000 mg rituximab was used in clinical trials of SLE [4, 5], ongoing trial [9] and also RA therapy [7] approved by the Food and Drug Administration in USA. In contrast, 4 weekly infusions of 375 mg/m2 rituximab have been widely used in malignant lymphoma [2]. Therefore, an individual single dosage of rituximab is higher in SLE and RA, although total dosage is higher in lymphoma. This patient was treated with a single infusion of 1000 mg rituximab. Consequently, both individual and total dosage of rituximab may affect the development of IP. The etiology of rituximab-induced IP is unknown. It was reported that rituximab infusion was rapidly followed by activation of complements, B-lymphocyte cytolysis.
and TNF-α release [10]. These processes of infusion reaction to rituximab may provoke IP. Alternatively, this could be explained by allergic reaction to rituximab, which may not be dose related.

Rheumatology key message
- We describe the first case of interstitial pneumonitis induced by rituximab therapy in a patient with SLE.

Disclosure statement: N.M. has received research grants from Zenyaku Pharmaceutical Company/Chugai Pharmaceutical Company. All other authors have declared no conflicts of interest.

JUN KISHI1, TOSHIIRO NANKI1, KAORI WATANABE1, AKITO TAKAMURA1, NOBUYUKI MIYASAKA1

1 Department of Medicine and Rheumatology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan

Accepted 14 January 2009

Correspondence to: Toshihiro Nanki, Department of Medicine and Rheumatology, Graduate School, Tokyo Medical and Dental University, 1-5-45, Yushima, Bunkyo-ku, Tokyo, 113-8519 Japan. E-mail: nanki.rheu@tmd.ac.jp


Rheumatology 2009;48:448–450
doi:10.1093/rheumatology/kep003
Advance Access publication 16 February 2009

Anti-TNF-α therapy for rheumatoid arthritis among patients with chronic hepatitis B infection

Sir, The safety and efficacy of anti-TNF-α therapy for inflammatory arthritis among patients infected with HBV are not established. There is evidence from experimental models that TNF-α has a critical role in the clearance of HBV from infected hepatocytes [1]. High-dose immunosuppression in transplant and oncology patients causes HBV reactivation in up to 72% of chronically infected individuals. This reactivation may be asymptomatic occurring only after withdrawal of immunosuppression (immune reconstitution). There have been no randomized controlled trials using anti-viral therapies to prevent active HBV replication during or after immunosuppression but widespread use of anti-viral drugs could result in the emergence of resistant HBV strains. Published British Society of Rheumatology guidance advocates avoidance of anti-TNF-α ‘until more definitive data are available’. In contrast, however, British Society of Gastroenterology guidelines advise use with caution and frequent monitoring of aminotransferases and viral load during and for 3 months after cessation of therapy and consideration of prophylactic or early intervention strategies with nucleoside analogues if reactivation of viral replication occurs [2].

We present a case of severe RA in a chronic HBV-infected individual treated successfully and safely with anti-TNF-α alone.