

# Successful Use of a Reduced Dose Regimen of Rituximab in a Case of Rheumatoid Arthritis with Raynaud's Syndrome

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**A** 44 year old man presented to the Rheumatology Department of Semey State Medical University Medical Center complaining of general weakness, joint pain (especially in the large joints and in the lumbar region), morning stiffness of up to 2 hours, loss of appetite, right sided chest pain, and fever (39°C).

He had been diagnosed with rheumatoid arthritis (RA) 9 years before and had had severe Raynaud's syndrome with digital ulcerations for the past 5 years. During the course of those 9 years he had received

parenteral gold therapy, methotrexate, glucocorticoids, chloroquine, and nonsteroidal anti-inflammatory drugs. He had also undergone sympathectomy. Physical exam revealed scarring ulcers in both hands, severely decreased movements in the large joints bilaterally, and ulnar deviation. Laboratory tests showed elevated erythrocyte sedimentation rate (ESR) at 52 mm/h, leukocytosis ( $22.7 \times 10^9/L$ ); rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (anti-CCP) were negative.

Lung ultrasound showed right pleural effusion, and about 700 ml of fluid were drained and examined for atypical cells and *Mycobacterium tuberculosis* with negative results. X-ray of the hands revealed signs of 2nd–3rd stage RA with destruction of the second right finger's metacarpal head

[Figure 1]. X-ray of the knees also demonstrated signs of 2nd stage RA.

After screening the patient for hepatitis B and C as well as for tuberculosis with negative results, rituximab was given in two 500 mg intravenous infusions 2 weeks apart. Following the rituximab infusions, the patient received methotrexate 10 mg weekly for 2 months and prednisone 5 mg daily.

In the following months, the number of tender and swollen joints markedly decreased. The patient resumed physical activity and ESR went down to normal (3 mm/h). The Das-28 score went from 6.31 to 1.61, and the severity of pain decreased to 2 from an initial score of 9–10 on the Visual Analog Scale. The patient continues to be in remission 8 years later, and an X-ray of the hands has shown stability [Figure 2].

**Figure 1.** X-ray of the hands at presentation



**Figure 2.** X-ray of the hands 8 years later



In RA cases resistant to methotrexate and anti-tumor necrosis factor agents, rituximab is generally administered at a dose of 1 gram followed by another dose after a fortnight (independent of body weight). However a meta-analysis published in 2014 showed that a lower-dose regimen (500 mg) of rituximab has similar effectiveness [1].

Considering its lower cost, we used this reduced dose in our patient with very good

outcome. Rituximab seems to be most effective in seropositive patients [2]. It worked well in our case even though the patient was seronegative, and the DAS-28 score [3] markedly decreased.

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**Capsule**

**Co-occurrence and characteristics of patients with axial spondyloarthritis who meet criteria for fibromyalgia**

**Macfarlane** and colleagues tried to estimate the proportion of patients with axial spondyloarthritis (SpA) in a UK national biologics registry who met criteria for fibromyalgia, and to delineate the characteristics of these patients. Of the patients registered in the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS), 1504 (68% male) were eligible for the current analysis, of whom 311 (20.7%) met the 2011 research criteria for fibromyalgia. Prevalence of fibromyalgia was similar between patients who fulfilled the modified New York criteria for ankylosing spondylitis (AS) (19.7%) and those who fulfilled Assessment of SpondyloArthritis international Society (ASAS) imaging criteria but not the modified New York criteria (25.2%); however, among those who fulfilled only the ASAS clinical criteria, the prevalence of FM was lower (9.5%). Patients who

met fibromyalgia criteria reported significantly worse disease activity, function, global severity scores, and quality of life, and were more likely to have moderate or severe levels of mood disorder and clinically important fatigue. Patients who met fibromyalgia criteria reported experiencing work impairment around half their working time. Meeting fibromyalgia criteria was not related to elevated C-reactive protein levels or most extraspinal manifestations, but was associated with a higher likelihood of having received biologic therapy. Developing management approaches that would address the significant unmet clinical needs of the 1 in 5 patients with axial SpA who meet criteria for FM should be a research priority.

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**Capsule**

**Cytotoxic and regulatory roles of mucosal-associated invariant T cells in type 1 diabetes**

Type 1 diabetes (T1D) is an autoimmune disease that results from the destruction of pancreatic  $\beta$ -cells by the immune system that involves innate and adaptive immune cells. Mucosal-associated invariant T cells (MAIT cells) are innate-like T-cells that recognize derivatives of precursors of bacterial riboflavin presented by the major histocompatibility complex (MHC) class I-related molecule MR1. Since T1D is associated with modification of the gut microbiota, **Rouxel** and collaborators investigated MAIT cells in this pathology. In patients with T1D and mice of the non-obese diabetic (NOD) strain, the authors detected alterations in MAIT cells, including increased production of granzyme B, which occurred

before the onset of diabetes. Analysis of NOD mice that were deficient in MR1, and therefore lacked MAIT cells, revealed a loss of gut integrity and increased anti-islet responses associated with exacerbated diabetes. Together the data highlight the role of MAIT cells in the maintenance of gut integrity and the control of anti-islet autoimmune responses. Monitoring of MAIT cells might represent a new biomarker of T1D, while manipulation of these cells might open new therapeutic strategies.

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Eitan Israeli

**“After you understand about the sun and the stars and the rotation of the earth, you may still miss the radiance of the sunset”**

Alfred North Whitehead, (1861–1947), English mathematician and philosopher best known as the defining figure of the philosophical school known as process philosophy