Letters to the Editors

Rituximab in ankylosing spondylitis: a promising option when other treatments are not viable

Sirs,

Ankylosing spondylitis (AS) is a complex autoimmune condition affecting the axial skeleton. Its pathogenesis remains unclear, complicating subgroup categorisation and targeted treatment development. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment for axial involvement, with anti-TNF, anti-IL-17, and JAK inhibitors used for patients unresponsive to NSAIDs (1, 2). Rituximab is widely used in rheumatology to treat autoimmune diseases by reducing B cell numbers. Controversies remain over rituximab use in AS treatment, though it has shown benefits in some cases (3). This report discusses RTX use in an AS patient unable to use anti-TNF or JAK inhibitors and unresponsive to anti-IL-17 therapy.

A 55-year-old woman diagnosed with AS at the age of 37 while abroad was treated with NSAIDs and sulfasalazine for about 10 years, with a good response. At 47, after moving to our country, she had 15 minutes of morning stiffness, a global disease score of 4, Bath AS disease activity index (BASDAI) of 2.6, AS disease activity score (ASDAS) of 2.3, CRP of 4.6 mg/L, ESR of 22 mm/h, creatinine of 1.6 mg/dL, and GFR of 52. NSAIDs were stopped due to kidney function, but three months later, her symptoms worsened, with two hours of morning stiffness and CRP of 20 mg/L, ESR of 42 mm/h, and higher disease scores. Adalimumab was planned due to the inefficacy of sulfasalazine and stomach complaints. After two months, hoarseness led to its discontinuation, and biopsy confirmed high-grade dysplasia on the vocal cords. Secukinumab was initiated but showed no improvement by six months, despite symptomatic glucocorticoid treatment that increased blood pressure. After secukinumab, ESR was 36 mm/h, CRP 32 mg/L, BASDAI 7, ASDAS 7.2, and global score 7.5, leading to its discontinuation. During follow-up, symptoms and spinal mobility worsened, and she developed pulmonary thromboembolism after four years. JAK inhibitors were deemed unsuitable due to stable pulmonary care and malignancy risk. In the fifth year, RTX treatment was started with 1-gram IV infusions two weeks apart, followed by a dose six months later. By the third month, the patient's BASDAI decreased to 5, ASDAS to 4.3, CRP to 14 mg/L, and ESR to 21 mm/h, supporting continuation of RTX. After three years, she remains stable regarding AS and vocal cord dysplasia, with a BASDAI of 3.1 and stable immunoglobulin levels. Laboratory parameters, including liver and kidney function, inflammatory markers, haemoglobin, and neutrophils, showed no deterioration with RTX.

TNF blockers are effective treatment options for AS. There are some concerns regarding the use of TNF blockers in relation to malignancies (4). Additionally, JAK inhibitors carry a black box warning regarding clotting conditions and malignancies. JAK inhibitors and TNF inhibitors were not considered appropriate for this patient. Several publications discuss RTX use in RA; however, reports on its use in AS are limited (5). Rodríguez-Escalera *et al*. administered RTX to an AS patient who had not received anti-TNF therapy, observing significant improvement (3). In a study by Song *et al*. involving 20 patients, RTX showed success in TNF-naive AS patients (6). Other studies report success with RTX in AS patients with contraindications to TNF therapy, and Al Dhaheri *et al*. also noted success in an AS patient (7, 8). A 1-year prospective clinical study in India in 2021 followed 15 AS patients for 48 weeks, concluding that RTX is safe and effective for AS (9) (Table I).

The efficacy of RTX in AS is associated with its blockade of pro-inflammatory cytokines (TNF-alpha, IL-1, IL-6) via CD20 B cell depletion. No specific autoantibody has been identified in AS pathogenesis, though B cells may enhance the effectiveness of RTX as antigen-presenting cells (10). Based on this case and existing literature, RTX may be a valuable alternative for AS patients when TNF blockers are contraindicated and JAK inhibitors, anti-IL-17 therapies, and NSAIDs are unsuitable. However, further research is needed for confirmation due to the limited case series and small studies currently available.

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Table I. Features of AS patients treated with rituximab in the literature.

Study/Case no.	Patient details	Other details	Treatment details	Outcomes
Rodríguez-Escalera C. *et al*. (3).	42-year-old female with hepatitis B; prior NSAIDs, sulfasalazine, methotrexate, leflunomide	Contraindication to TNF due to patient preference	RTX with lamivudine; NSAID discontinuation; maintained on metamizole	Improvement with RTX, no hepatitis B reactivation
Song IH. *et al*. (6).	20 AS patients (10 TNF-naive, 10 TNF non-responders) AS	Evaluating RTX efficacy in TNF-naive and TNF-experienced	RTX administered; ASAS 20 goal assessed at 6 months	50% ASAS 20 response in TNF-naive group; no response in TNF non-responders
Kobak Ş. *et al*. (8).	43-year-old male with long-standing AS and RA; prior hip replacement, multiple DMARDs	Active disease despite anti-TNF, suspected RA overlap	RTX added to MTX after anti-TNF discontinuation; remission in RA, partial AS response	Partial response in AS; ESR/CRP decreased; no change in spinal measures
AlDhaheri F. *et al*. (7).	38-year-old male with AS, uveitis, and Achilles tendonitis; family history of AS	Malignancy after etanercept; contraindication to further TNF	RTX 375 mg/m² initially, then every 6 months	Clinical improvement; BASDAI and CRP reduced
Gantait K. *et al*.(9).	15 patients (13 male, 2 female); predominantly axial (12) and peripheral (3) involvement	Exploring CD20+ cells as therapeutic target; contraindications to TNF-alpha inhibitors	Two doses of RTX with pre-medication; 48-week follow-up	Significant improvement (>50% in BASDAI); no major side effects

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