

Clinical and Ultrasound Monitoring of Uveitis and Spondyloarthritis Treatment with Certolizumab Pegol- Uveitis Ultrasound Monitoring and the Use of Certolizumab

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ABSTRACT

Introduction: Ocular ultrasound has been a promising imaging method in vitritis diagnosis in patients with inflammatory arthropathy. The objective of this study was to evaluate the use of ultrasound in the monitoring of eye and joint treatment with certolizumab.

Materials and Methods: This clinical case includes a 47-year old Caucasian male patient diagnosed with Spondyloarthritis. The patient reported red eye and arthritis of the right elbow and ankle, treatment failure with other anti-TNFs and starting treatment with certolizumab. Ultrasonography with a 12 MHz high frequency linear probe was used to evaluate the eye and a frequency of 15 to 18 MHz for the evaluation of the joints.

Outcome: The patient showed improvement in the gray scale (GS) and power Doppler (PD) evaluation of posterior tibial tenosynovitis and synovial recess of right posterior elbow, in 3 months, with remission of left eye uveitis within 7 months of ultrasound monitoring.

Conclusion: Ultrasound detected improvement, in a short time, of inflammatory changes in the eyeball and joint, with the use of certolizumab.

Keywords: Certolizumab pegol, Ultrasound, Uveitis, Arthritis

INTRODUCTION

Ocular ultrasound is an imaging method that has been increasingly explored by ophthalmologists; in addition radiologists are also becoming involved with this procedure that offers excellent images of unchanged anterior and posterior eye chambers and also of eyes with uveitis [1].

In spondyloarthritis, anterior uveitis is reported with more frequency, but there is also involvement of intermediate uveitis and the degree of topographic impairment varies according to the subtype of these inflammatory arthropathies [2].

Synovial fluid within the joint space, likewise the content of the aqueous and vitreous humor, can exhibit a very large amount of cytokines, in the case of an ocular inflammatory process [3].

In our clinical practice, we observed many vitritis echographic changes in patients with psoriatic arthritis and axial and peripheral spondyloarthritis [4]. There is no

description in the literature of the evaluation of ultrasound, ocular and joint monitoring in spondyloarthritis patients treated with an immunobiological agent. The objective of this study was to monitor certolizumab treatment effects through clinic and ultrasound exams of the eyes and joints, using a high-frequency linear probe.

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MATERIALS & METHODS

Patients, clinical and laboratory characteristics and physical examination

This is the case of a 47-year old patient, Caucasian, male, engineer, with 12 years spondyloarthritis diagnosis and negative HLAB27; however, his sibling tested positive for HLAB27 the patient reported a chronic history of circadian rhythm inflammatory cervicalgia, with important morning stiffness and difficulty in lateralizing the neck since the beginning of the clinical condition. Magnetic resonance imaging showed osteodegenerative changes; rhythm inflammation low back pain occurring only at the onset of the patient's clinical condition without alteration of radiographic and non-radiographic sacroiliitis. He was affected with right elbow and ankle arthritis for the last 6 months and he also reported concomitant red left eye, uveitis free, in the ophthalmic evaluation; He did not present with any other extra-articular manifestations. He had bilateral hip prosthesis. The patient had already used infliximab, adalimumab, and had been using etanercept for 1 year. Since the patient presented with clinical ocular and articular alterations, with changes in the physical examination using etanercept, subcutaneous certolizumab 400 mg weekly treatment was instituted at weeks 0, 2 and 4, with an induction dose; subsequently, every 4 weeks a maintenance drug dose was used. The clinical follow-up assessment was performed using the visual analog scale (VAS); 28-joint Disease Activity Score (DAS28); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) [5,6].

Ultrasound evaluations

The patient signed a written free and informed consent form for evaluation at the Rheumatology Ultrasound Clinic in Campinas, São Paulo State. Patient's ultrasound evaluation was performed by a single rheumatologist with 12 years exams' experience. A MyLab 25 Gold ultrasound (EsaoteSpA, São Paulo, Brazil) with a 12 MHz high frequency linear probe was used to evaluate the eyes and a frequency of 15 to 18 MHz for the investigation of the joints, with a PD frequency of 6.6 to 8 MHz, pulse repetition frequency that varied from 0.5 Hz to 1.0 MHz and low filter. The ocular ultrasound evaluation was performed with the patient's eyes closed covered with a large amount of gel and without pressing the eyes structures; the patient was asked to move the eyes latero-medially; the probe was positioned longitudinally. All images of the joints were performed using GS and PD techniques to detect eco-structural damage, following the OMERACT ultrasound guidelines for musculoskeletal assessment [7]. The left eye ultrasound was performed at baseline and after 7 months treatment; the joint evaluation was performed after 3 months treatment.

RESULTS

Clinically, there was an important improvement in metrics and laboratory tests for the C-reactive protein (**Table 1**). The ultrasound showed a total reduction of floating hypoechogenic images in the vitreous chamber of the left eye after 7 months treatment (**Figure 1**), together with an improvement in the PD of the right elbow synovitis in a posterior recess and tenosynovitis of the right posterior tibial tendon, with total reduction in tendon sheath effusion in 3 months (**Figures 2 and 3**).

Table 1. Physical and laboratory evaluation characteristics before and after 7 months of Certolizumab treatment.

Before Treatment		After Treatment
C-Reactive Protein(mg/L)	16.71	8.0
VAS (%)	100	0
DAS28	4.58	3.55
BASDAI (neck)	9.5	0.4
ASDAS	5.28	1.42

DISCUSSION

The use of ultrasound in joint inflammatory processes has been reported in several publications and this imaging method is getting increasingly established in this area. As there is no consensus as to the period of evaluation by this imaging method and since there are efficacy studies at 3-month clinical evaluation of the certolizumab treatment, we assessed the joints after 3 months. During this period an improvement of

the inflammatory activity was observed as shown in tenosynovitis and synovitis by the GS and by PD.

Papers have been published on the use of this image method for the assessment of synovitis in rheumatoid arthritis patients treated with certolizumab pegol for 12 to 52 weeks. In addition, a statistically significant correlation ($r: 0.586$, $p < 0.001$) was found between synovitis ultrasound and metalloproteinase-3 serum level increased rates. These protease enzymes are an important factor in the cartilaginous

and bone matrix degradation, which is observed in moderate to severe rheumatoid arthritis samples [8-11].

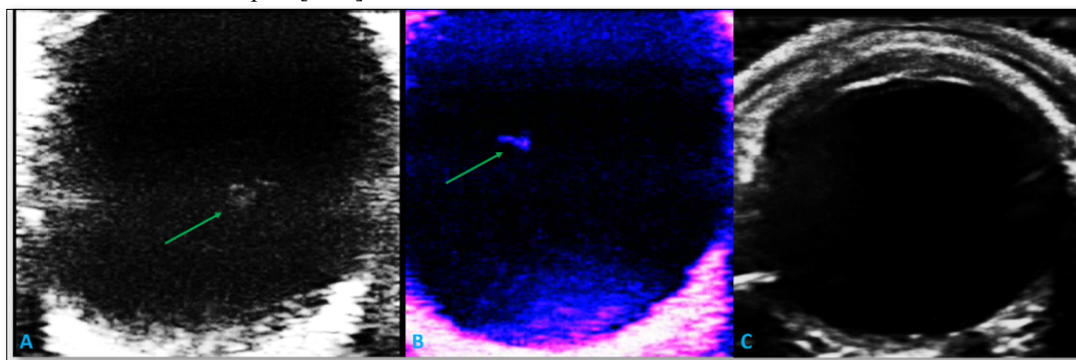


Figure 1. (A, B). The haze in the vitreous chamber in the left eye (arrow); C: Improvement of uveitis, after seven months certolizumab treatment.

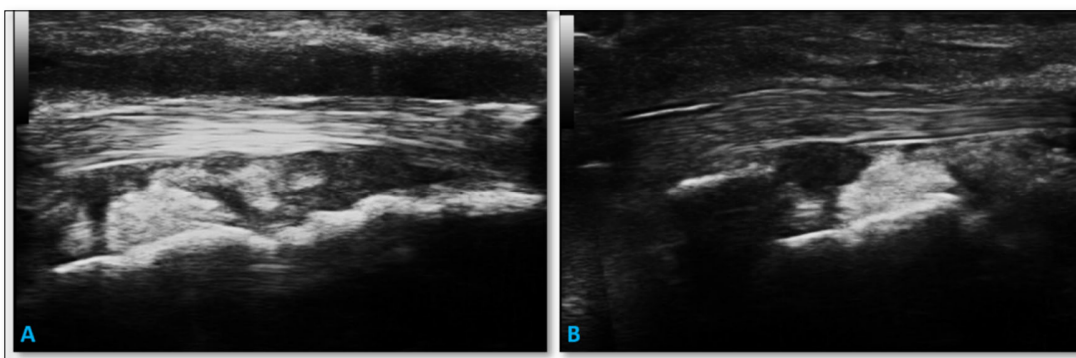


Figure 2. A. Posterior tibial tendon with intense peritendinous effusion. B. Improvement of tenosynovitis, after 3 months certolizumab treatment.

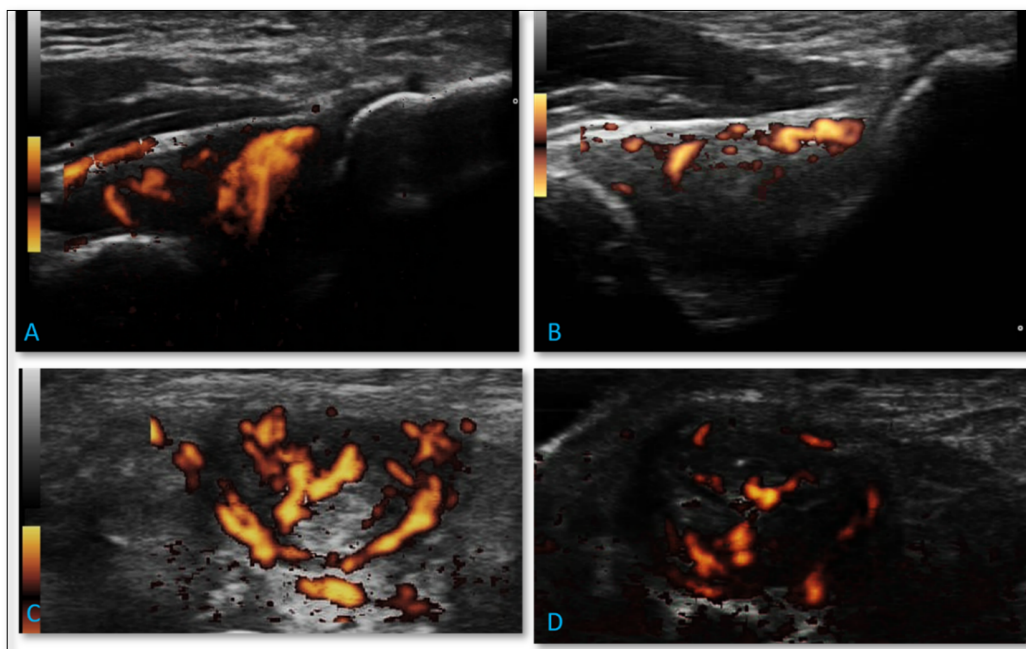


Figure 3. A. Right elbow posterior recess synovitis with important activity. **B.** Synovitis improvement, with negative signal PD, after treatment. **C.** Important tenosynovitis of the right posterior tibial tendon. **D.** Tenosynovitis improvement, after certolizumab treatment.

The ocular ultrasound assessment has shown to be a very promising method, especially in patients with an ocular inflammatory process, but still with very little information in the literature [4].

Quantification of inflammatory cells in the ophthalmological examination is still subjective, but in the future optical coherence tomography may be a promising tool. However, due to the difficulty of accessing this method, ultrasound with a linear probe may add important value to the evaluation of ocular changes. We also know that there are several factors, such as old age and infections that can alter cellularity in vitreous humor, without characterizing inflammatory eye disease; it is thus necessary to enhance the application of ultrasound to add value to this indication [12,13].

Antibodies against tumor necrosis factor, especially humanized antibodies, characterize therapeutic efficacy in uveitis in patients with spondyloarthritis, clinically assessed by ophthalmological examination. There is a study showing sustained 4-year significant reduction of uveal inflammatory activity, together with improvement in the clinical response of sacroiliitis in radiographic and non-radiographic spondyloarthritis [14].

CONCLUSION

This clinical case showed the importance of using ultrasound in the monitoring of certolizumab treatment, in the evaluation of articular and extra-articular manifestations. Further studies are still needed to validate this imaging method in patients with inflammatory process in both the eyeball and joints.

CONFLICT OF INTERESTS

None of the authors have any potential conflict of interest.

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