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RS3PE Syndrome- Orthobiological Therapy

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Abstract

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare rheumatologic disease of the elderly characterized by joint pain in the hands and wrists, with pitting edema and tenosynovitis of the tendinous structures of the wrist and hand and may, however, extend to other joint locations with a favorable response to glucocorticoids. We describe the case of a patient diagnosed with the RS3PE entity and followed up in a Physiatry consultation, in which a treatment with activated platelet-rich plasma according to the GOLDIC ® method was proposed, with very positive results that remained after 12 months of treatment.

Keywords

RS3PE; Peripheral polyarthritis; GOLD.

Introduction

Although it was originally known as “benign rheumatoid arthritis of the elderly”, it was not until 1985, when McCarty et al. carried out a cohort study of several patients of advanced age, RS3PE was then described as a different clinical entity from seronegative rheumatoid arthritis (RA) that occurs predominantly in men over 60 years of age (2/3) with a higher incidence in Caucasians and in the rural

population.

Although there are overlapping clinical manifestations between RS3PE, rheumatoid arthritis, and polymyalgia rheumatica, RS3PE has distinct features with the following classification criteria: bilateral swelling of both hands, sudden onset of polyarthritis, age over 50 years, and rheumatoid factor (RF) seronegative. It is characterized by symmetrical polyarthritis with synovitis of the extensor and flexor tendons, severe edema with depression on the dorsum of the hands, and weakness of the pelvic and scapular girdles.

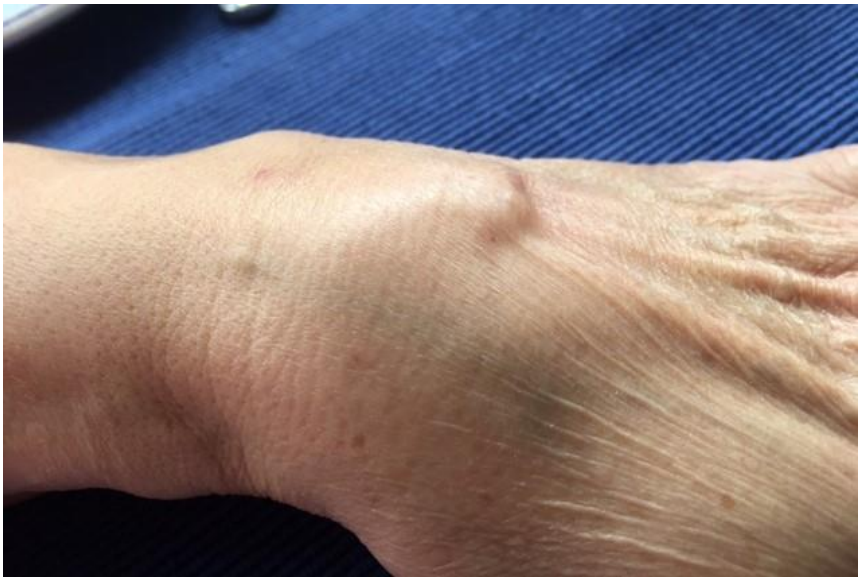
Although the cause is still unclear, RS3PE can occur in association with infectious microorganisms, various rheumatic diseases, paraneoplastic syndromes and therapy with certain drugs. The pathogenesis of RS3PE may underlie changes in vascular endothelial growth factor, interleukin-6 and infection, observed in studies based on limited data from RS3PE. The fundamental therapeutic factor, in patients with RS3PE without concomitant malignancy, is the good response to small doses of glucocorticoids, although temporary.

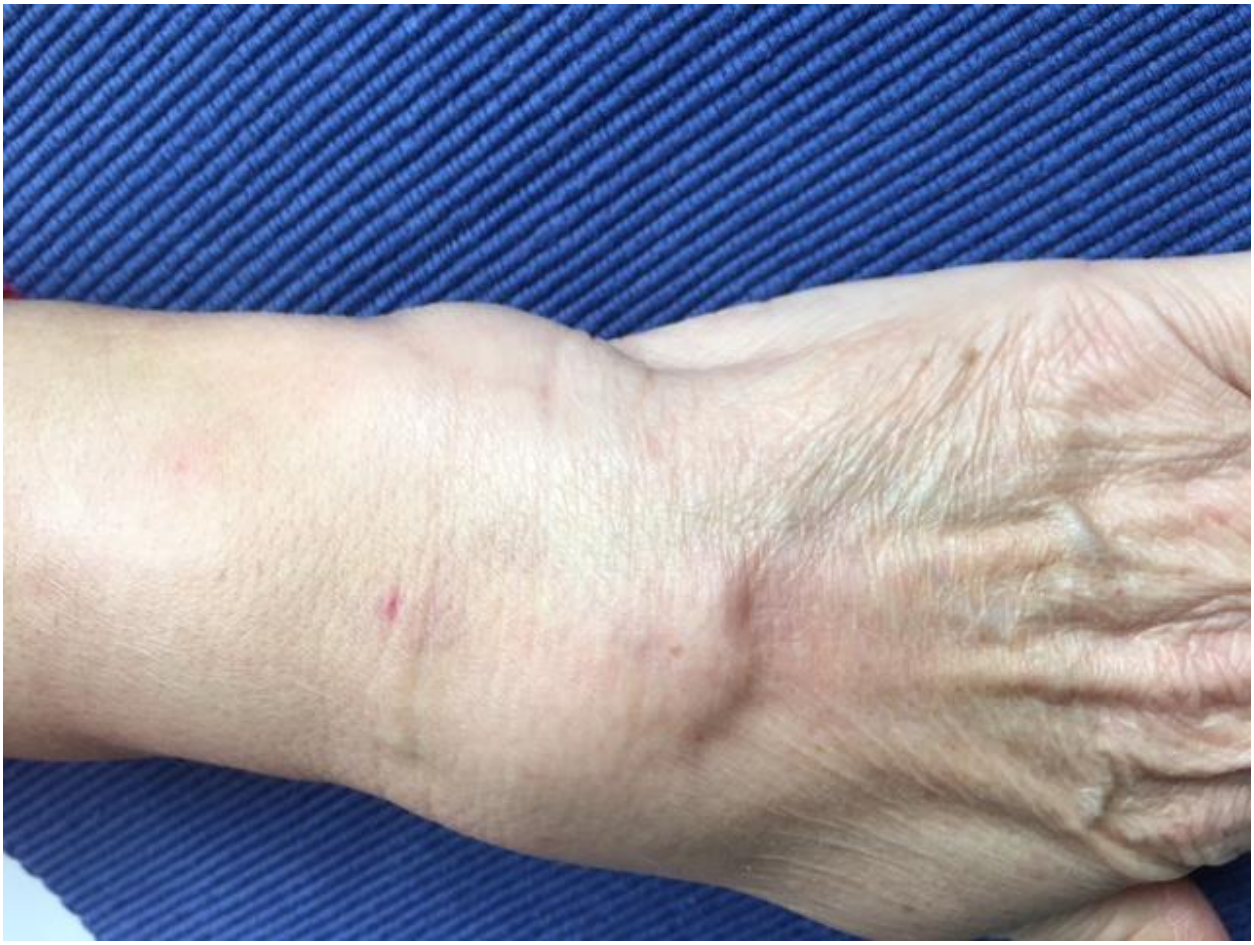
Clinical Case

In the present case, we present a 67-year-old female patient, Caucasian, residing in a city, with the professional occupation of manager/entrepreneur.

She started insidiously for 6 years a clinical picture of polyarthralgia, with polyarthritis of the upper limbs involving the left shoulder, both hands, wrists and both feet, predominantly on the left.

Observed several times in a period of crisis, the painful involvement compromised joint functionality, with swelling due to synovitis but without a permanent “deficit”: functional impotence, swelling in the back and fingers of both hands, with pain on palpation in the radio-articular joints. carpicas, carpo-metacarpicas, metacarpophalangeal and interphalangeal, in the paths of the extensor tendons (Figure1).





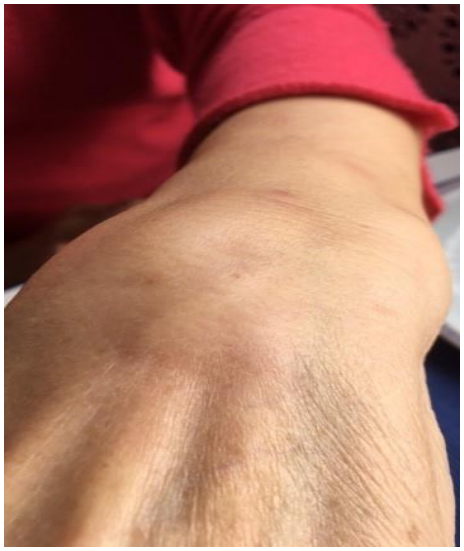


Figure 1: Hand2, Hand3, Hand5.

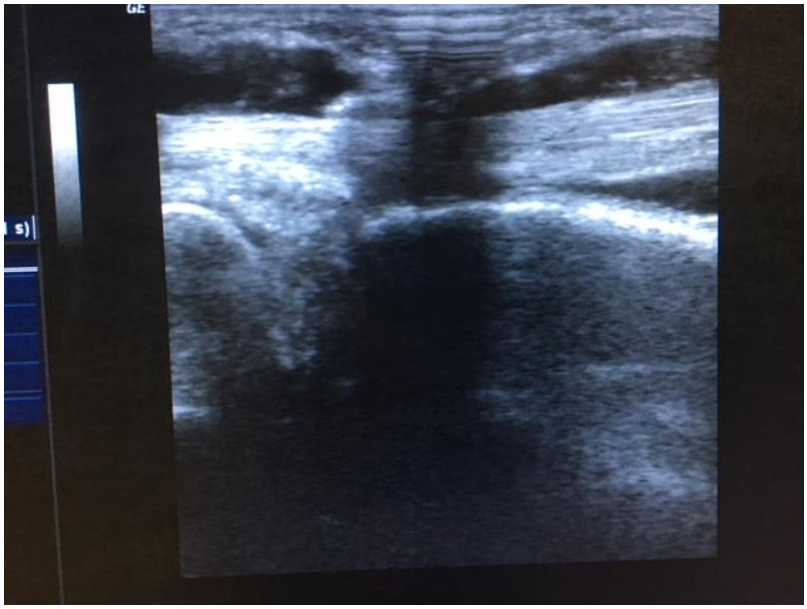
No Raynaud's phenomenon

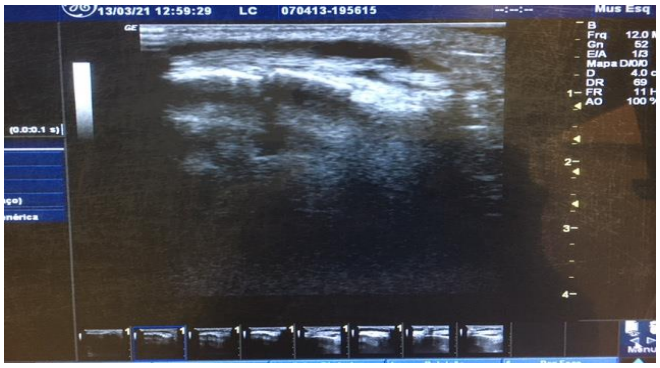
The serological study performed by several analytical tests on blood and urine showed results within normal parameters, namely blood count, SV, CRP, transaminases, alkaline phosphatase, CPK, protein electrophoresis, urea, creatinine, total cholesterol, HDL, LDL, triglycerides and LDH.

Researched tumor markers, namely CEA, AFP, Ca 19.9, Ca 12.5 and Ca 15.3 negative.

Absence of positivity of rheumatic markers such as AgHLA B27, anti-cyclic citrullinated peptide (anti-CCP), rheumatoid factor, IgA and IgM, core autoantibodies (ANA), antiDNA autoantibodies, DsDNS, U1-snRPN, SM, histone, Ro/ SS-A, La/SS-B, Scl70 and Jo1.

In an ultrasound imaging study of the hands and wrists, the images were characteristic of synovitis, with accentuated synovial effusion, causing pain and anatomical swelling of the wrist, namely on the left (Figure 2).

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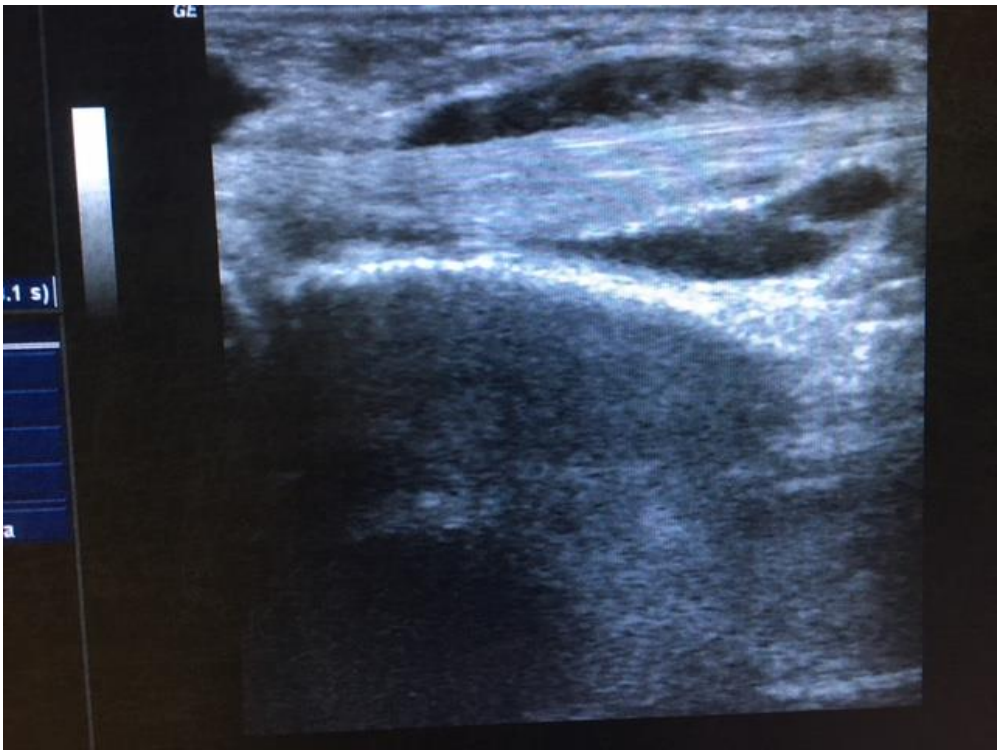


Figure 2: ECO MAO 1, ECO MAO 5, ECO MAO 8.

In more recent radiological examinations, degenerative joint changes begin to appear, specifically metacarpop-pyramidal (in this case interpreted as a degenerative change associated with age group.

In the personal history there is no history of rheumatic pathology. Absence of diabetes mellitus, gastrointestinal, renal and cardiopulmonary pathology and only mild hypertension controlled with ibersartan 150 mg once daily.

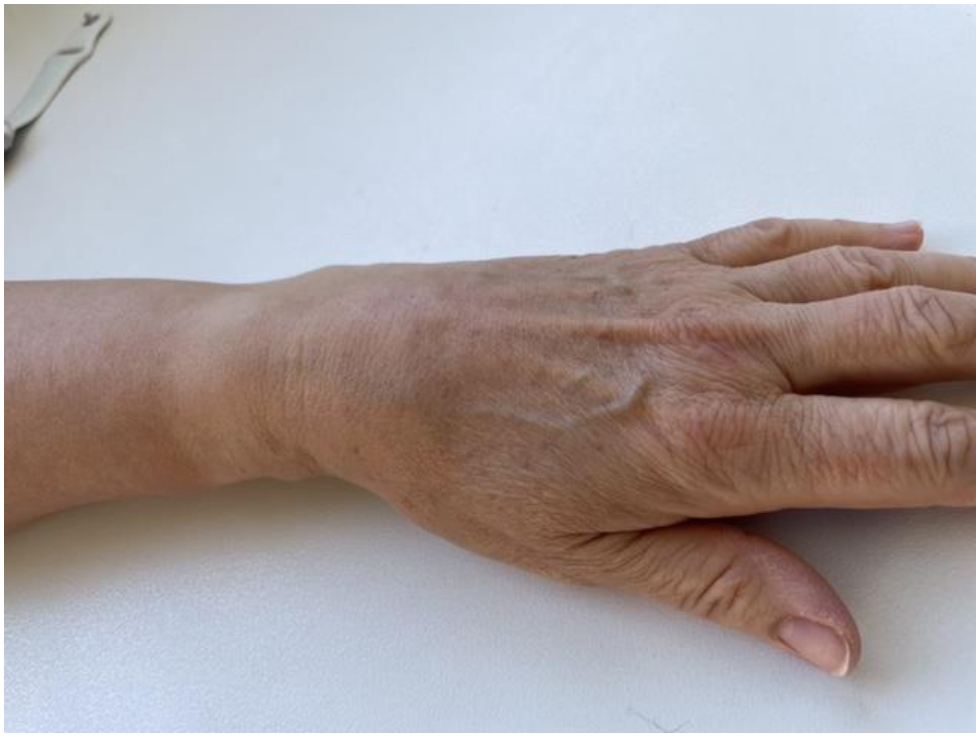
She underwent surgical intervention in 2008, by arthroscopy, to the right knee due to a meniscus injury and in 2018 due to carpal tunnel syndrome on the left.

She was initially treated with NSAIDs without significant response and with a single depot injection corticosteroid (betamethasone) with a good response, leading to the absence of clinical inflammatory semiology and without pain but with a fluctuating duration of 1 to 2 months.

Thus, given the clinical characteristics described, with a negative serological study and rapid response with corticosteroids, we can say that this is a clinical picture with a rheumatologic profile of Remitting Seronegative Synovitis Synovitis Syndrome with Depressible Edema (RS3PE), fulfilling the criteria proposed by Olivo et al.: patient over 65 years old, morning stiffness, apparent symmetric polyarthritis with involvement of the wrists, metacarpophalangeal and interphalangeal joints , synovial involvement of the tendon sheaths of the hand extensors with pitting edema in the affected areas, negative

rheumatoid factor and absence of other diseases.

However, the present clinical picture suffered a year ago a sudden worsening with exuberant synovitis on the back of the hands/wrists, painful and disabling with no response to NSAIDs and even corticosteroids, so the protocol of ultrasound-guided infiltration procedure, with growth factors and anti-inflammatory cytokines – GOLDIC (r) technique, every 5 days, four previously prepared injections of autologous plasma. Improvement would appear after the second injection, with a marked decrease in edema and inflammatory aspects of the involved synovial structures (Figure 3).



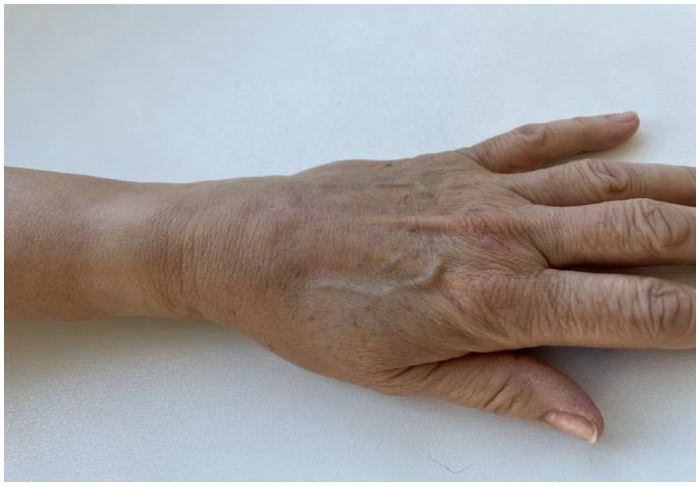
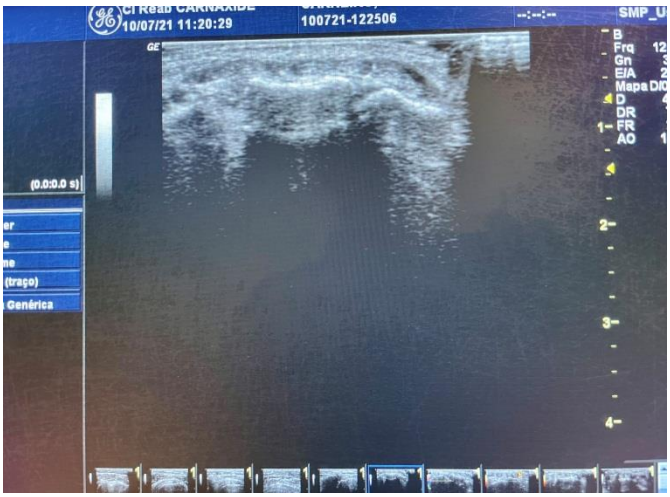
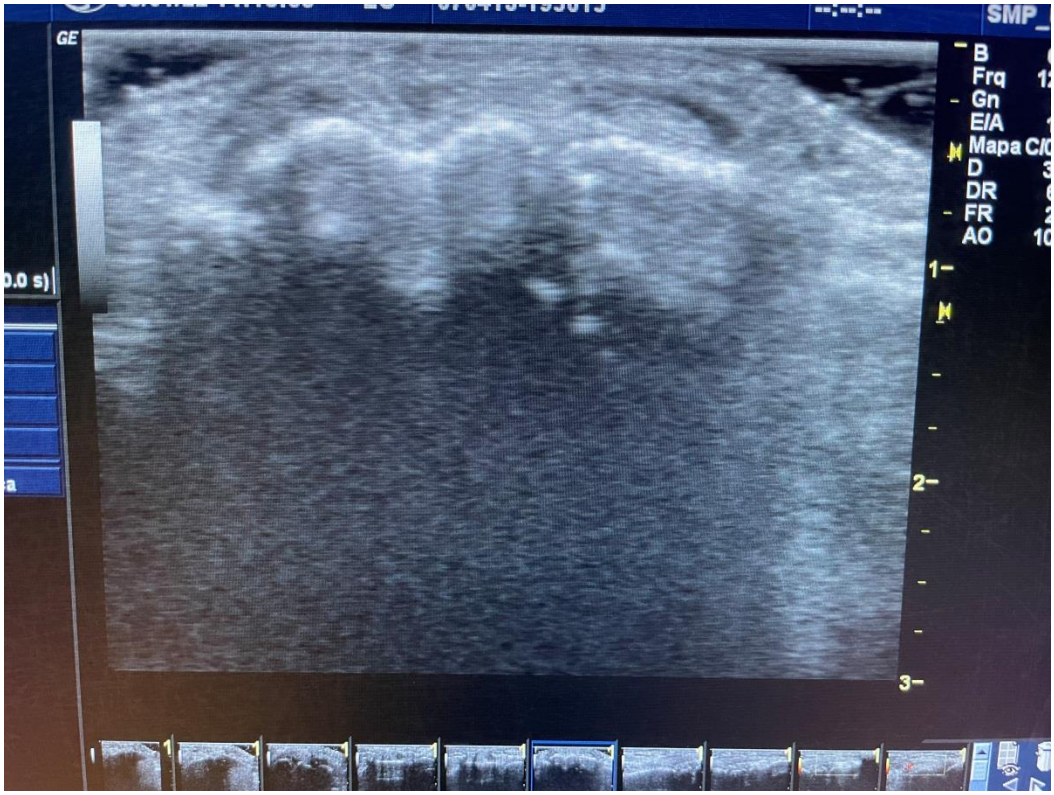


Figure 3: Hand 7, hand 8, hand 9.

The patient was monitored every three months, through consultation, clinical and ultrasound observation and analytical study (to search for a possible positive tumor marker) for a period of 12 months, namely the structures of the hands and wrists and in the observation of any new relapse, which to date has not occurred. It would have been useful to determine IL-6, VEGF (vascular endothelial growth factor), MMP-3 (metalloproteinases) and HLA B-7, which was not verified (Figure 4).





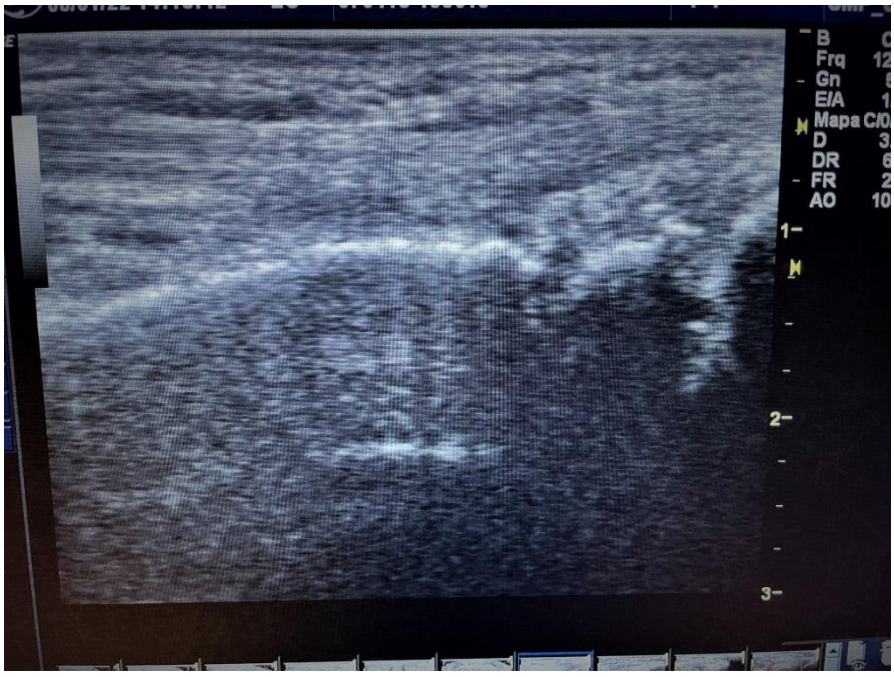


Figure 4: Echo 10, echo 15, echo 19.

Discussion

Symmetric Remitting Seronegative Synovitis with Depressive Edema (RS3PE) syndrome is a rare rheumatologic disease of the elderly characterized by joint pain in the hands, wrists, with pitting edema and tenosynovitis of the tendinous structures of the wrist, hand, favorable response to glucocorticoids and seronegative analytical pattern unless it is associated with oncological pathology.

The etiology is unknown at the moment and there are several theories in this regard that relate it to infectious agents, genetic predisposition (HLA B-7) or certain serum tumor factors such as IL-6.
The differential diagnosis should be made primarily with polymyalgia rheumatica and rheumatoid arthritis in the elderly, based on clinical manifestations, presence or absence of rheumatoid factors and erosive radiological lesions.

The prognosis is usually very good, and concomitant oncological pathology (namely lymphomas, leukemias and gastric cancer) should always be investigated.

The most appropriate treatment is with low-dose corticosteroids.

However, in the case under discussion and because an adequate response was not achieved, orthobiological therapy - GOLDIC® (Gold induced cytokines) was chosen, based on studies developed by Prof Dr Ulrich Schneider, through the technique of cell expansion by gold nanoparticles with development of cytokines responsible for immunomodulatory response, anti-inflammatory plasma proteins and cell regeneration, such as those that play an important role in immune reactions and inflammatory processes, such as interleukins (involved in the activation or suppression of the immune system in induction of division of other cells), chemokines (potent mediators or regulators of inflammation), tumor necrosis factors (TNF-α) (group of cytokines capable of causing the death of tumor cells and that have a wide range of pro-inflammatory actions).

The therapeutic protocol consisted of administering four ultrasound-guided injections of autologous plasma with an invariable volume of three cc (GOLDIC® technique), 22G needle, at the level of the synovial membranes on the dorsal side of the hand and left wrist, performed at intervals of 5 in 5 days.

This therapeutic procedure produced a rapid improvement that was observed at the third injection and sustained in the symptomatology and resolution of the synovitis for one year to date. There were no treatment-related adverse events. The author declares that there are no conflicts of interest and the study was preceded by informed consent from the patient.

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