

## CASE REPORT

### AN IATROGENIC COMPLICATION IN A PATIENT WITH RHEUMATOID ARTHRITIS

Claudia COBILINSCHI<sup>1,2</sup>, Flavia DUMITRU<sup>3</sup>, Ruxandra IONESCU<sup>1</sup>

<sup>1</sup>Sf. Maria Clinical Hospital, Bucharest, Romania

<sup>2</sup>University of Medicine and Pharmacy, Bucharest, Romania

<sup>3</sup>Department of Radiotherapy, Coltea Clinical Hospital

**Address for correspondence:** Claudia Cobilinschi, University of Medicine and Pharmacy, Bucharest, Dionisie Lupu 37, 020022, Romania. E-mail: claudiadeaconu1@yahoo.com.

#### Abstract

*Rheumatoid arthritis (RA) is the most encountered chronic inflammatory rheumatic condition with a predominance in middle-aged women. If inadequately controlled and in the presence of risk factors, RA can lead to complications such as septic arthritis. The case presentation displays a 55-year-old female patient with a long history of RA that developed infection of the knee after repeated arthrocentesis for persistent arthritis. Empirical double parenteral antibiotherapy and methylprednisolone were initiated leading to favorable patient outcome before irreversible damage occurred. Septic arthritis should be considered in patients having chronic inflammatory diseases, especially if under immunosuppressive drugs and corticosteroids. Prompt intervention can decrease morbidity in RA patients.*

**Keywords:** rheumatoid arthritis, septic arthritis, arthrocentesis, biologics, immunosuppression.

**DOI** <https://doi.org/10.56082/annalsarscimed.2021.1.25>

#### Introduction

Rheumatoid arthritis (RA) is the most frequent chronic inflammatory condition that symmetrically affects small joints of the hands and feet but also large joints causing pain and swelling. The progressive joint destructions are irreversible and lead to damage accrual and patient disability [1].

The prevalence of RA can reach up to 1% of the population, with higher rates in northern Europe and America and it mostly affects middle-aged women [2].

Despite being incompletely known, etiopathogenesis is multifactorial with genetic and environmental factors involved, including infections, smoking or hormonal status [3].

Treatment of RA has largely diversified with the discovery of biologics targeting

cytokines like tumor necrosis factor (TNF)- $\alpha$ , interleukins (IL)-6 or the anti-CD20 rituximab but also the newer molecules like targeted synthetic disease modifying antirheumatic drugs (tsDMARDs) like tofacitinib or baricitinib [4]. In 2019, the European League against Rheumatism (EULAR) issues updated recommendations for management in patients with RA, including indications for all these agents and following the treat-to-target strategy in order to obtain prompt control of disease activity [5]. Implementing this strategy is still challenging in clinicians' daily practice.

However, in some patients, complications can occur during the disease and treatment should be adjusted accordingly. Due to long-term immunosuppression drugs and variable dose of corticosteroids, patients are at risk of

developing infectious events that can make the RA management more difficult to handle.

Septic arthritis is an infection of the joint tissue or fluid. Joints can be targeted through the bloodstream, directly from trauma, surgeries or local injections [6]. Left untreated, it rapidly leads to joint destruction, deformity and further disability, thus whenever suspected, empirical antibiotherapy is mandatory [7].

Joints suffering from chronic conditions such as RA are more prone to contracting infections regardless of disease treatment, probably to the modified joint structure that allows microorganisms to avoid phagocytosis [8].

The risk of septic arthritis in RA patients is up to 14-fold higher than in the general population. Known risk factors are age, joint prosthetics and joint anomalies [8].

The aim of this article is to describe a case of RA patient that develops iatrogenic septic arthritis after multiple knee punctions.

### Case presentation

A 55-year-old female patient is admitted to the Emergency Department for red, painful swelling of her right knee with acute onset that intensified in the last three days. Her medical report confirmed a diagnosis of seropositive rheumatoid arthritis for twelve years for which she was on chronic treatment with leflunomide, hydroxychloroquine and a medium dose of corticosteroids. Patient was also overweight, hypertensive and diagnosed with osteoarthritis of the spine and hip.

Upon presentation in the Rheumatology Department the patient was afebrile, a blood pressure of 170/90 mmHg and a pulse of 110 beats per minute. She had an intensely red, warm right knee, exhibiting extreme pain if mobilized. Clinical examination also confirmed tender and swollen joints in small joints and wrists of both hands. Blood tests were remarkable through high inflammatory markers (erythrocyte sedimentation rate 90 mm/h and C-reactive protein (CRP) 110 mg/L), leukocytosis, negative procalcitonin

and positive rheumatoid factor RF and anti-citrullinated protein antibodies ACPA.

Ultrasound confirmed a medium quantity of liquid in the suprapatellar bursa and synovitis in both radiocarpal joints, while knee plain X-ray showed signs of secondary osteoarthritis with asymmetrical narrowing of the joint space and few typical erosions of the carpal and proximal interphalangeal joints.



**Figure 1.** Bilateral knee and hand plain X-rays

Reviewing the anamnesis, the patient confirmed multiple knee arthrocentesis in the past two months for recurrent episodes of arthritis. During her long period of inflammatory rheumatic disease, she had had methotrexate treatment for one year that she stopped because of digestive intolerance, followed by sulfasalazine that caused her liver enzymes. Thus, combination treatment with leflunomide and hydroxychloroquine was

preferred with an increase of corticosteroid dose during disease flares.

The clinician that assessed her in follow-up visits confirmed knee effusion and decided to perform repeated arthrocentesis with local corticosteroid injection. The procedure conducted prior to admission in our department extracted 20 ml of greenish, viscous synovial fluid resembling pus.

Considering the patient's description of the extraction and the clinical setting with inflammatory features of the joint, septic arthritis of the right knee was considered and double intravenous empirical antibiotherapy with vancomycin and ceftriaxone was initiated.

Aiming for a confirmation of the diagnosis, ultrasound-guided arthrocentesis was done with the extraction of 3ml yellowish, opalescent liquid. This proved to be an exudate with 89% polymorphonuclear cells, low glucose level and high titer rheumatoid factor. The microscopical examination of the fluid confirmed very frequent neutrophils, lymphocytes and no crystals. However, cultures could not isolate any germ from the liquid and blood cultures were negative.

The RA flare confirmed through the number of tender and swollen joints, ultrasound confirmed synovitis and a high disease activity score (DAS28 4.61), intravenous methylprednisolone was added with significant improvement of the joint swelling.

After two weeks of parenteral antibiotics, the patient was discharged with significant regression of the knee swelling, no pain and no inflammatory syndrome on laboratory reevaluation. Double oral antibiotherapy was continued at home for four more weeks according to available published guidelines together with chronic RA treatment and readjustment of corticosteroid regimen.



**Figure 2.** Knee arthrocentesis and synovial fluid appearance

Meanwhile, reassessing patient's rheumatic condition, an insufficient control of the disease was confirmed with multiple flares despite undergoing all conventional synthetic disease modifying antirheumatic drugs (csDMARDs). Following the recommended treat-to-target strategy, the patient was considered as candidate for biological therapy, and she was tested for hepatitis B, C and tuberculosis (TB). Unfortunately, the Quantiferon test came back positive and the pneumologist confirmed latent TB and initiated isoniazid 300mg daily. According to national regulation, isoniazid treatment is required for at least one month prior to commencing biological or targeted synthetic (ts)DMARDs, so patient was delayed access to other therapies.

During her follow-up visit and after ensuring she is safe from an infectious relapse, the patient was initiated on tsDMARD tofacitinib for prompter action and following EULAR's recommendation for management in RA in monotherapy. Two weeks later, patient had no tender or swollen joints and corticosteroid dose was progressively reduced.

### Discussion

Septic arthritis can occur more frequently in RA patients, its incidence being estimated at 70 cases per 100,000 person-years, leading to an increased morbi-mortality. Correctly recognizing an infection of the joint and differentiating it from a rheumatic flare or a crystal-induced arthropathy is essential since treatment strategy is different and prompt initiation of antibiotics is required to avoid substantial joint damage. Initially empirical antibiotic stewardship should later be adjusted according to cultures and patient's clinical and biological evolution. Moreover, drainage of the joint is recommended either surgically, arthroscopically or through needle aspiration [9].

A study published in 2018 evaluated the use of systemic corticosteroids in addition to antibiotics and it appears that in children it can shorten the hospital stay, the time until inflammatory markers normalize and the duration of antibiotic treatment. Results in adults are still a matter of debate, as is the administration of intra-articular depot corticosteroid while having septic arthritis [10].

Joints affected by infections are the knee, hip, ankle and followed by the wrist and most of the cases present as monoarticular involvement.

The most commonly responsible microorganism for joint infection in RA patients is *Staphylococcus aureus*, being identified in up to 80% cases. The presented case had raised suspicion of the same germ because of the arthrocentesis. However, there was no positive culture from the synovial fluid. Literature states that due to the microorganism temperature instability and potential

contamination, not all cases are confirmed through adequate culture results [11].

Imaging is of use in assessing superficial joints and identifying Doppler signal indicative of active synovitis but is of limited use in more profound joints. It can be of help in performing synovial fluid extraction. Radiographic changes in septic arthritis occur in a later phase when irreversible changes are already visible [12].

Researchers have been uncertain whether immunosuppressive drugs, biologics or corticosteroids are involved in increasing the risk of joint infection in RA patients [13].

In 2011, Galloway et al. aimed at identifying the risk of septic arthritis in RA patients treated with anti-TNFs. Data came from the British Society for Rheumatology Biologics Register and included 199 patients that had suffered from at least one joint infection. Authors concluded that TNF inhibitors augment by two-fold the risk of septic arthritis in RA but mostly in patients with joint prosthetics and during first months of therapy [14].

The presented case had an insufficiently controlled disease with recurrent knee arthritis that were addressed through fluid extraction. Aiming for a tighter control of the disease might have prevented such an unwanted complication, especially considering the wide variety of available pharmacological agents that can be used in RA up to present.

### Conclusions

In patients suffering from RA, having a swollen joint might raise a diagnostic test for the physician, since it can be linked to an episode of disease flare, a crystal-induced arthropathy or a septic arthritis. Moreover, chronic immunosuppression might lead to an impaired immune response that can be defeated in the struggle with infectious microorganisms, but it can also be responsible for a scarcity of patient clinical signs and symptoms.

Septic arthritis is a serious condition that can be responsible for joint damage or even death if left untreated, thus clinicians caring for rheumatic patients should be aware of this diagnostic challenge.

### Author Contributions:

*C.C. conceived the original draft preparation. C.C., M.D., and R.I. were responsible for conception and design of the review. C.C., M.D., and R.I. were responsible for the data acquisition. M.D., and R.I. were responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. C.C., M.D., and R.I. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.*

#### **Compliance with Ethics Requirements:**

*The authors declare no conflict of interest regarding this article.*

**Acknowledgements:** *None*

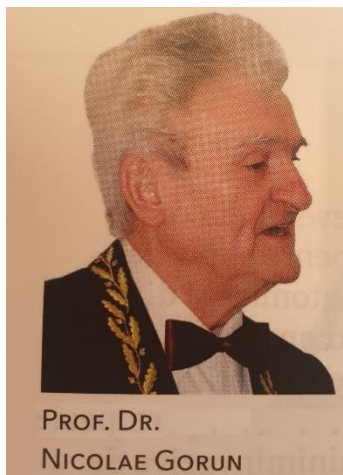
#### **References**

- [1] Mucke J, Krusche M, Burmester GR. A broad look into the future of rheumatoid arthritis. *Ther. Adv. Musculoskelet. Dis.* 2022;14:1759720X221076211.
- [2] Almutairi KB, Nossent JC, Preen DB, Keen HI, Inderjeeth CA. The Prevalence of Rheumatoid Arthritis: A Systematic Review of Population-based Studies. *J. Rheumatol.* 2021;48(5):669–676.
- [3] Koller-Smith L, Mehdi AM, March L, Tooth L, Mishra G, Thomas R. Rheumatoid arthritis is a preventable disease: 11 ways to reduce your patients' risk. *Intern. Med. J.* 2021.
- [4] Bullock J, Rizvi SSA, Saleh AM, et al. Rheumatoid arthritis: a brief overview of the treatment. *Med. Princ. Pract.* 2019;27(6):501.
- [5] Smolen JS, Landewe R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann. Rheum. Dis.* 2017;76(6):960–977.
- [6] Wallace SL, Robinson H, Masi AT, Decker, McCarty DJ. Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum* 1977;20(3):895-900.
- [7] Geirsson AJ, Statkevicius S, Víkingsson A. Septic arthritis in Iceland 1990–2002: increasing incidence due to iatrogenic infections. *Ann Rheum Dis* 2008;67(5):638–643.
- [8] Kaandorp CJE, Van Schaardenburg D, Krijnen P, Habbema PJDF, Van De Laar MAFJ. Risk factors for septic arthritis in patients with joint disease. A prospective study. *Arthritis Rheum.* 1995;38(12):1819–1825.
- [9] Gupta MN, Sturrock RD, Field M. A prospective 2-year study of 75 patients with adult-onset septic arthritis. *Rheumatology* 2001;40(1):24–30.
- [10] Qin YF, Li ZJ, Li H. Corticosteroids as adjunctive therapy with antibiotics in the treatment of children with septic arthritis: a meta-analysis. *Drug Des. Devel. Ther.* 2018;12:2277–2284.
- [11] Coakley G, Mathews C, Field M, Jones A, et al. Guidelines BSR & BHPR, BOA, RCGP and BSAC guidelines for management of the hot swollen joint in adults Guidelines for managing the hot swollen joint in adults. *Rheumatology* 2006;45(8):1039-1041.
- [12] Kumar A, Marwaha V, Grover R. Emergencies in rheumatology. *J. Indian Med. Assoc.* 2017;101(9):520-524.
- [13] Listing J, Strangfeld A, Kary S, Rau R, et al. Infections in patients with rheumatoid arthritis treated with biologic agents. *Arthritis Rheum.* 2005;52(1):3403–3412.
- [14] Galloway JB, Hyrich KL, Mercer LK, et al. Risk of septic arthritis in patients with rheumatoid arthritis and the effect of anti-TNF therapy: results from the British Society for Rheumatology Biologics Register. *Ann. Rheum.* 2011;70(10):1810–1814.

## Opening speech at “The XIIIth Congress of the Romanian Society of Orthopedics and Traumatology (SOROT)”, October 19-22, 2021

Nicolae GORUN<sup>1</sup>

<sup>1</sup> Academy of Romanian Scientists, Bucharest, Romania



Between October 19-22, 2021, in very special conditions (Coronavirus 19 pandemic), the XIII<sup>th</sup> SOROT Congress took place online, with a full success and unanimous appreciation.

Perhaps more than ever, it is now necessary to remember some very important moments in the history of this medical specialty, eminently conservative and restorative, which deals with the treatment of injuries of the support and movement apparatus (Junghans) of genetic causes and mesological (physical, mechanical, chemical and biological factors) (Draper's peristasis).

In the broad field of orthopedics, osteoarticular trauma (vertebral, thoracic, pelvic and limb) is included. Muscle, joint, ligament, tendon, vascular and nerve injuries must be included in limb injuries. In turn, injuries to the pelvis, bony chest and spine can also include injuries to the organs they harbor.

Obviously, these associated injuries can only be solved by complex teams.

The history of orthopedics and osteoarticular traumatology is multimillennial in chronological dimension and marked by numerous events and personalities.

On prehistoric skeletons, sequelae of fractures, bone tumors, tuberculosis, Paget's disease, etc. were found. Sequelae from various bone diseases and fractures have been found on mummies in Egyptian graves (Mega el Dar Cemetery). In the oldest collection of laws, the Hammurabi Code (1792-1750 BC), there are laws regarding the reward that the bone surgeon must receive in case of success, as well as the forms of sanction for the failure of the operation or the death of the patient.

Important evidence has been brought to Persia, China, India, Egypt, Greece (with the famous medical schools of Rhodes, Kos, and Knidos). The great Hippocrates left to posterity an extensive work on fractures and dislocations, congenital osteoarticular deformities, such as congenital crooked foot, congenital hip dislocation, kyphosis and scoliosis, as well as many other acquired