

Case in Point

Arthritis, Infectious Tenosynovitis, and Tendon Rupture in a Patient With Rheumatoid Arthritis and Psoriasis

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Multiple comorbidities, advanced age, tobacco use, and alcohol abuse made a proper diagnosis difficult in a patient with polyarticular septic arthritis, infectious tenosynovitis, and ruptures in the tendons of both thumbs.

Compared with monoarticular arthritis, polyarticular arthritis may yield an initially narrower differential diagnosis that focuses on systemic inflammatory conditions, such as rheumatoid arthritis (RA). Approximately 15% to 30% of septic arthritis is polyarticular, of which about 45% is associated with underlying RA.^{1,2} Regardless of the number of joints involved, septic (infectious) arthritis is a valid consideration given the morbidity and mortality.

In a retrospective study in the United Kingdom (UK) between 1982 and 1991, the morbidity and mortality of septic arthritis was 31.6% and 11.5%, respectively, and 16% of the study population had RA.³ A review of the literature by Dubost and colleagues found that polyarticular septic arthritis (PASA) has a mortality

of 31% to 42% compared with 4% to 8% for monoarticular septic arthritis, and RA was present in 67% of the PASA fatalities.¹

Rheumatoid arthritis and its treatment predispose patients to septic arthritis. Septic arthritis in the UK general population is 0.42 per 100 patient-years for patients with RA on antitumor necrosis factor therapy.^{3,4} In a retrospective study in the U.S., the incidence of septic arthritis was 0.40 per 100 patient-years for patients with RA compared with 0.02 per 100 patient-years for patients without RA.⁵

Other complications of RA include infectious tenosynovitis and tendon rupture. The incidence and prevalence of infectious tenosynovitis and tendon rupture in RA are not firmly established in the literature.

We present a patient with RA and psoriasis who responded initially to acute management for RA but subsequently was diagnosed with culture-negative polyarticular arthritis and infectious tenosynovitis associated with beta hemolytic group G *Streptococcus* (GGS), a part of *Streptococcus*

milleri (*S. milleri*). During surgery, he was also found to have bilateral extensor pollicis longus (EPL) tendon rupture. Given the possible morbidity, the authors believe this patient may be of interest to the medical community.

CASE PRESENTATION

A 69-year-old African American male presented with 3 to 4 days of swelling and pain of bilateral wrists, bilateral hands, and the left ankle with subjective, but resolved, fevers and chills. His medical history was significant for seropositive erosive RA, psoriasis, hypertension, hyperlipidemia, alcohol abuse, chronic tobacco use, osteoporosis, and glaucoma. He did not have diabetes, reported no IV drug abuse, and except for the immunosuppressive effects of his medications, was not otherwise immunocompromised.

For 2 years in the outpatient setting, the rheumatology clinic had been managing the patient's rheumatoid factor (RF) positive and anticyclic citrullinated peptide (CCP) antibody positive erosive RA with

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etanercept 25 mg subcutaneously twice a week. The RA affected his hands, wrists, shoulders, and ankles bilaterally but was successfully controlled. The dermatology clinic was managing the patient's psoriasis with calcipotriene cream 0.005% twice a week and clobetasol ointment 0.05% twice a week. Psoriatic plaques were noted on bilateral elbows, bilateral dorsal hands, and bilateral dorsal feet.

Initial Evaluation

At evaluation, the patient's vital signs revealed a temperature of 36.3°C (97.3°F), pulse of 102 beats per minute, respiratory rate of 16 breaths per minute, oxygen saturation of 99% on room air, and blood pressure of 102/70 mm Hg. He was found to have edema, tenderness, and erythema of the wrists bilaterally and left metacarpophalangeal joints (MCPs) and edematous right MCPs and left medial ankle.

The patient had been nonadherent with etanercept for 5 months and restarted taking the medication only 2 weeks before presentation. He had noticed worsening arthritis for at least 1 month. His last RA flare was approximately 1 year before presentation. Additional symptoms included 4 days of nausea, nonbloody and nonbilious emesis, left lower quadrant pain, and diarrhea without melena or hematochezia.

Initial laboratory studies found 3.2 k/μL white blood cells (WBCs) with a differential of 11.9% lymphocytes, 4.2% monocytes, 83.3% neutrophils, 0.5% eosinophils, and 0.1% basophils; 165 k/μL platelets; 96 mm/h erythrocyte sedimentation rate (ESR); and 45 mg/dL C-reactive protein. The patient was diagnosed with viral gastroenteritis and RA flare and was admitted for inpatient management secondary to limited ability to care for himself.

The patient was started on prednisone 40 mg orally once a day (for 5 days) for empiric treatment of an RA flare and continued on etanercept. The inpatient rheumatology service was consulted. Further evaluation later that day found involvement of the proximal interphalangeal joints and elbows and tenderness of the tendons of the dorsal hand bilaterally. Over the next 2 days, the patient remained afebrile and WBCs were within normal limits. Edema, erythema, and tenderness of the involved joints somewhat improved, but tenderness along the tendons of the dorsal hand worsened, which concerned the managing teams for infectious tenosynovitis.

By day 4, the patient was afebrile and had a leukocytosis of 12.9 k/μL with neutrophils 86.7%, but improvement of erythema, pain, and range of motion of involved joints and no tenderness to palpation of tendons was noted. The inpatient orthopedic surgery service evaluated the patient and did not find sufficient evidence necessitating surgical intervention.

Worsening Condition

On day 6, arthrocentesis of the left wrist was performed secondary to worsening of erythema and edema. The patient experienced new edema of the left shoulder and leukocytosis continued to trend upward (15.7 k/μL on day 6). Purulent aspirate (1.5 mL) was obtained from the fluctuance and tenosynovium of the left wrist. Empiric vancomycin 1 g IV twice daily and ceftriaxone 2 g IV daily were started and continued for 3 days. By this point in his hospital course, the patient had received 1 dose of etanercept. Prednisone and etanercept were previously discontinued because of the discovered infection. Blood cultures were drawn

and had no growth (Table). Gastroenterology studies were limited to stool cultures and did not include colonoscopy. Leukocytosis began trending down.

On day 8, antibiotics were tailored to penicillin G 4 million units IV every 4 hours following growth of GGS from the sample of the left wrist. Subsequently, synovial fluid (3 mL) from the left shoulder was obtained following initiation of antibiotic therapy and had no growth. Magnetic resonance imaging (MRI) found tenosynovitis of the left ankle and right wrist.

On day 9, transthoracic echocardiography was performed and found no evidence of infectious endocarditis. Later that night, the patient was taken to surgery for incision and drainage/debridement of bilateral wrists and left ankle, synovectomy of right wrist, and aspiration of right shoulder. Findings included abscess in the left wrist and inflammatory synovitis and bilateral EPL tendon rupture consistent with RA. Pus from the left ankle had few gram-positive cocci in chains with no growth, and the specimens from both wrists grew GGS. Aspirate from the left ankle was an opaque yellow fluid with 14,900/mm³ WBC, 30,000/mm³ red blood cells (RBC), 97% neutrophils, 1% macrophages, 2% lymphocytes, and 0% monocytes. Aspirate from the right shoulder was an opaque bloody fluid with 10,100/mm³ WBC, 40,000/mm³ RBC, 95% neutrophils, 2% macrophages, 1% lymphocytes, and 1% monocytes. On day 10, sulfasalazine 500 mg twice a day was initiated for RA.

Following surgery and continued antibiotics, the patient's leukocytosis resolved, and improvement was seen in all joints with decreased edema, erythema, and pain and increased range of motion. Postop-

Table. Microbiology

Hospital Day Collected	Sample	Source of Sample	Result
6	Aspirate	Left wrist	No growth
6	Pus (aspirate)	Tenosynovium at left wrist	Group G <i>Streptococcus</i>
6	Stool	Feces	No growth
7	Blood (x 2)	Blood	No growth
8	Aspirate	Left shoulder	No growth
9	Surgical specimen	Superficial left wrist	Group G <i>Streptococcus</i>
9	Pus (surgical specimen)	Deep left wrist	Group G <i>Streptococcus</i>
9	Surgical specimen	Right wrist	Group G <i>Streptococcus</i>
9	Opaque yellow aspirate (surgical specimen)	Left ankle	Few gram-positive cocci in chains
9	Opaque bloody aspirate (surgical specimen)	Right shoulder	No growth
22	Blood (x 2)	Blood	No growth
24	Urine	Urine	<i>Candida albicans</i>

erative recovery was complicated by ileus, urinary retention, and fungal (*Candida albicans*) urinary tract infection, all of which resolved without significant complications. The inpatient rheumatology service restarted prednisone at a lower dose of 20 mg. The patient became afebrile and sufficiently stable for transfer to a lower level of care with continued physical therapy and IV antibiotics for another 3 weeks.

DISCUSSION

The patient had 2 underlying systemic inflammatory conditions: RA and psoriasis. The underlying chronic arthritis was likely caused by RA, not psoriatic arthritis (PsA). The patient met the 2010 American College of Rheumatology criteria but

failed to meet the classification criteria for PsA.^{6,7} However, the clinical features of RA and PsA overlap. Rheumatoid factor and CCP can be positive laboratory findings in both RA and PsA.⁸⁻¹⁴ Tenosynovitis is found in about half of RA patients and PsA patients ($P > .05$).¹⁵ In its evaluation of the patient, the inpatient rheumatology service suspected that the patient may have had RA with components of PsA.

Rheumatoid arthritis complicates the diagnosis of septic arthritis. In a study by Nolla and colleagues, a mean of 7.3 days (range 3 to 18 days) elapsed before a diagnosis of septic arthritis was made in 10 patients with RA on corticosteroids.² Consideration of risk factors such as increasing age, male sex, tobacco

use, extra-articular manifestations of RA, positive RF, rheumatoid nodules, poor functional capacity, high ESR, leukopenia, comorbidities (chronic lung disease, alcoholism, organic brain disease, and diabetes), and the use of corticosteroids may expedite the diagnosis of infections in patients with RA.¹⁶ In this case, the patient had some of these risk factors: age, male sex, alcoholism, chronic tobacco use, positive RF, high ESR, and leukopenia (at presentation).

The history of medication nonadherence of etanercept with progressively worsening arthritis and early clinical improvement (reduction in erythema, edema, and pain and temporary loss of signs of tenosynovitis on examination) while on prednisone suggested that the patient had a

RA flare. The prednisone likely alleviated the inflammatory process but created an immunosuppressed state that allowed GGS to invade and possibly disseminate. Alternately, the patient may have been infected before presentation. The lack of a definitive time line for his case prevented the authors from forming conclusions about a possible causal relationship between the infection and medications. The subjective fevers before admission were nonspecific and could have been caused by RA, presumed gastroenteritis, or other undiagnosed infectious processes. The observed leukocytosis may have been initially corticosteroid-induced.¹⁷

Septic Arthritis

The suspicion of septic arthritis and infectious tenosynovitis substantially increased on day 6 with worsening symptoms, involvement of additional joints, and spiking fevers. Group G *Streptococcus* was obtained from the aspirate of the left wrist and from the surgical specimens from the bilateral wrists. The clinical presentation, MRI imaging studies, and surgical and nonsurgical specimens supported a diagnosis of GGS tenosynovitis. However, there was no clear evidence (ie, positive culture with identified organism) of septic arthritis, likely secondary to early septic arthritis and initiation of antibiotics before joint aspirations. The aspirate from the left ankle was yellow and opaque, but the culture was negative.

The pathogenic organism in the patient was GGS. Group G *Streptococcus* is normal flora of the oral cavity, gastrointestinal (GI) tract, upper respiratory tract, genital tract, and skin, which were all possible sources of seeding.¹⁸ Streptococcal species account for about 20% of septic arthritis, and GGS arthritis accounts for 4% to 19% of streptococcal ar-

thritis.¹⁹⁻²² From a review of the literature, 2 cases of GGS tenosynovitis have been published.^{23,24} However, in an ultrasound study and MRI study, 49% and 43%, respectively, of patients with RA had tenosynovitis of the tendons of the hands.^{15,25}

GGS Demographics

About three-quarters (71%) of patients with GGS arthritis are male.¹⁹ The analysis of the literature by Bronze and colleagues found that chronic joint disease and alcoholism are present in 34% and 14% of patients with GGS arthritis, respectively. One-quarter (23% from Dubost and colleagues) to one-third (32% from Schattner and colleagues) of patients with GGS arthritis have RA.^{19,26}

Fever is present in less than half (43%) of patients with GGS arthritis.¹⁹ Positive synovial fluid is expected in 90% of patients.¹⁹ Leukocytosis and elevated ESR need not be present.^{27,28} The arthritis is polyarticular in one-quarter of patients (24% from Bronze and colleagues and 26% from Dubost and colleagues).^{19,26}

Positive blood cultures can be expected in one-fourth (26%) of patients with GGS arthritis.¹⁹ The patient's blood cultures were negative. Blood cultures drawn before initiation of antibiotics yielded no growth, so if the spread was hematogenous, the bacteremia was transient or intermittent. Before and after initiation of antibiotics, specimens from the shoulders did not grow colonies, whereas specimens from the wrists did. If the shoulders were truly infected, these findings and the notably later involvement of the shoulders suggest that the shoulders may have been seeded later in the hospital course.

Trenkner and colleagues proposed that GI abnormalities provide a portal of entry for GGS, which is under the umbrella of *S. milleri*.²⁹

S. milleri is associated with abscess formation, usually of the GI tract.³⁰⁻³² In the study patient, the possible gastroenteritis may have provided such a portal of entry and subsequent seeding to the joints, and an abscess was found in the left wrist.

Tendon Rupture

Additionally, bilateral EPL tendon rupture likely occurred as a consequence of the inflammatory process from RA and infectious tenosynovitis in the patient. According to Zheng and colleagues, tenosynovitis is an inflammatory process of the synovial tendon sheath that may result in degeneration and rupture of the tendons and may contribute to bone erosions, development of joint deformities, and loss of functional capacity.³³ In a histologic study of a ruptured EPL tendon from a patient with RA, Harris observed a chronic inflammatory cellular reaction.³⁴ Harris also described a male with RA with unconfirmed bilateral EPL rupture.³⁴ Björkman and colleague identified previous injury, RA, and local or systemic steroids as important etiologic factors for EPL tendon rupture.³⁵

As in the case of this patient, the utilization of both medical and surgical therapy is not uncommon for treating GGS infection. Antibiotic therapy typically consists of penicillin (74%).²⁶ Surgical intervention is necessary in 16% to 37% of patients.^{19,26} This patient required both penicillin and incision and drainage/debridement before significant clinical improvement was noted. Prognosis of GGS arthritis is favorable with 5% mortality.²⁶

CONCLUSION

Septic arthritis and infectious tenosynovitis are readily treatable with low mortality if promptly identified.

Identification can be masked by other medical conditions, such as RA and psoriasis, and their associated immunosuppressive treatment. Bilateral EPL tendon rupture may be a complication of RA, particularly with an underlying septic arthritis and infectious tenosynovitis. ●

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

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REFERENCES

- Dubost JJ, Fis I, Denis P, et al. Polyarticular septic arthritis. *Medicine (Baltimore)*. 1993;72(5):296-310.
- Nolla JM, Gómez-Vaquero C, Fiter J, et al. Pyarthrosis in patients with rheumatoid arthritis: A detailed analysis of 10 cases and literature review. *Semin Arthritis Rheum*. 2000;30(2):121-126.
- Weston VC, Jones AC, Bradbury N, Fawthrop F, Doherty M. Clinical features and outcome of septic arthritis in a single UK Health District 1982-1991. *Ann Rheum Dis*. 1999;58(4):214-219.
- Galloway JB, Hyrich KL, Mercer LK, et al; BSR Biologics Register. 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 Dis*. 2011;70(10):1810-1814.
- Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: A population-based study. *Arthritis Rheum*. 2002;46(9):2287-2293.
- Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-2581.
- Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H; CASPAR Study Group. Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. *Arthritis Rheum*. 2006;54(8):2665-2673.
- Gladman DD, Shuckett R, Russell ML, Thorne JC, Schachter RK. Psoriatic arthritis (PSA)—An analysis of 220 patients. *Q J Med*. 1987;62(238):127-141.
- Bogliolo L, Alpini C, Caporali R, Scirè CA, Moratti R, Montecucco C. Antibodies to cyclic citrullinated peptides in psoriatic arthritis. *J Rheumatol*. 2005;32(3):511-515.
- Vander Cruyssen B, Hoffman IE, Zmierzczak H, et al. Anti-citrullinated peptide antibodies may occur in patients with psoriatic arthritis. *Ann Rheum Dis*. 2005;64(8):1145-1149.
- Alenius GM, Berglin E, Rantapää Dahlqvist S. Antibodies against cyclic citrullinated peptide (CCP) in psoriatic patients with or without joint inflammation. *Ann Rheum Dis*. 2006;65(3):398-400.
- Candia L, Marquez J, Gonzalez C, et al. Low frequency of anticyclic citrullinated peptide antibodies in psoriatic arthritis but not in cutaneous psoriasis. *J Clin Rheumatol*. 2006;12(5):226-229.
- Inanc N, Dalkilic E, Kamali S, et al. Anti-CCP antibodies in rheumatoid arthritis and psoriatic arthritis. *Clin Rheumatol*. 2007;26(1):17-23.
- Popescu C, Zofota S, Bojinca V, Ionescu R. Anticyclic citrullinated peptide antibodies in psoriatic arthritis—Cross-sectional study and literature review. *J Med Life*. 2013;6(4):376-382.
- Schoellnast H, Deutschmann HA, Hermann J, et al. Psoriatic arthritis and rheumatoid arthritis: Findings in contrast-enhanced MRI. *AJR Am J Roentgenol*. 2006;187(2):351-357.
- Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Predictors of infection in rheumatoid arthritis. *Arthritis Rheum*. 2002;46(9):2294-2300.
- Shoenfeld Y, Gurewich Y, Gallant LA, Pinkhas J. Prednisone-induced leukocytosis. Influence of dosage, method and duration of administration on the degree of leukocytosis. *Am J Med*. 1981;71(5):773-778.
- Gossling J. Occurrence and pathogenicity of the *Streptococcus milleri* group. *Rev Infect Dis*. 1988;10(2):257-285.
- Dubost JJ, Soubrier M, De Champs C, Ristori JM, Sauvezie B. Streptococcal septic arthritis in adults. A study of 55 cases with a literature review. *Joint Bone Spine*. 2004;71(4):303-311.
- Ryan MJ, Kavanagh R, Wall PG, Hazleman BL. Bacterial joint infections in England and Wales: Analysis of bacterial isolates over a four year period. *Br J Rheumatol*. 1997;36(3):370-373.
- Morgan DS, Fisher D, Merianos A, Currie BJ. An 18 year clinical review of septic arthritis from tropical Australia. *Epidemiol Infect*. 1996;117(3):423-428.
- Kaandorp CJ, Dinant HJ, van de Laar MA, Moens HJ, Prins AP, Dijkmans BA. Incidence and sources of native and prosthetic joint infection: A community based prospective survey. *Ann Rheum Dis*. 1997;56(8):470-475.
- Bradlow A, Mitchell RG, Mowat AG. Group G streptococcal arthritis. *Rheumatol Rehabil*. 1982;21(4):206-210.
- Meier JL, Gerster JC. Bursitis and tenosynovitis caused by group G streptococci. *J Rheumatol*. 1983;10(5):817-818.
- Filippucci E, Gabba A, Di Geso L, Girolimetti R, Salaffi F, Grassi W. Hand tendon involvement in rheumatoid arthritis: An ultrasound study. *Semin Arthritis Rheum*. 2012;41(6):752-760.
- Bronze MS, Whitty S, Schaberg DR. Group G streptococcal arthritis: Case report and review of the literature. *Am J Med Sci*. 1997;313(4):239-243.
- Schattner A, Vosti KL. Bacterial arthritis due to beta-hemolytic streptococci of serogroups A, B, C, F, and G. Analysis of 23 cases and a review of the literature. *Medicine (Baltimore)*. 1998;77(2):122-139.
- Gaunt PN, Seal DV. Group G streptococcal infection of joints and joint prostheses. *J Infect*. 1986;13(2):115-123.
- Trenkner SW, Braunstein EM, Lynn MD, Ike RW. Group G streptococcal arthritis and bowel disease: A rare enteropathic arthropathy. *Gastrointest Radiol*. 1987;12(3):265-267.
- Bert F, Bariou-Lancelin M, Lambert-Zechovsky N. Clinical significance of bacteremia involving the "*Streptococcus milleri*" group: 51 cases and review. *Clin Infect Dis*. 1998;27(2):385-387.
- Casarioglu E, Rodriguez A, Corredoira JC, et al. Prospective study of *Streptococcus milleri* bacteremia. *Eur J Clin Microbiol Infect Dis*. 1996;15(3):194-200.
- Jacobs JA, Pietersen HG, Stobberingh EE, Soeters PB. Bacteremia involving the "*Streptococcus milleri*" group: Analysis of 19 cases. *Clin Infect Dis*. 1994;19(4):704-713.
- Zheng S, Robinson E, Yeoman S, et al. MRI bone oedema predicts eight year tendon function at the wrist but not the requirement for orthopaedic surgery in rheumatoid arthritis. *Ann Rheum Dis*. 2006;65(5):607-611.
- Harris R. Spontaneous rupture of the tendon of extensor pollicis longus as a complication of rheumatoid arthritis. *Ann Rheum Dis*. 1951;10(3):298-306.
- Björkman A, Jörgsholm P. Rupture of the extensor pollicis longus tendon: A study of aetiological factors. *Scand J Plast Reconstr Surg Hand Surg*. 2004;38(1):32-35.