

CLINICAL VIGNETTE

A 28-Year-Old Male with Acute Onset Inflammatory Arthritis

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Case Summary

A 28-year-old male presented to rheumatology with three days of pain in the left knee, left Achilles tendon, and bilateral wrists, starting one day after an intense cycling workout. He also had isolated pain and swelling in his left 2nd metacarpophalangeal joint. His right wrist in particular had become swollen and painful such that he had significant difficulty sleeping, typing, or using a mouse.

He had no prior history of arthritic complaints. There was no personal history of back pain, inflammatory eye disease, or significant enthesitis (aside from occasional tendinitis after over-exertion). There was no personal or family history of inflammatory bowel disease or psoriasis. There were no preceding infections and he denied fevers, rashes, dysuria, abdominal symptoms, or diarrhea. He had an unprotected sexual encounter approximately 6 weeks prior to presentation, with a male partner, and had history of syphilis four years prior to presentation. He had traveled to India for two weeks, returning three weeks prior to presentation.

Since symptom onset he had tried round the clock ibuprofen 600 mg every 6 hours without relief. He also tried acetaminophen and naproxen without benefit. On the day of presentation, he started a methylprednisolone taper, without initial benefit.

Past medical history included depression, gastroesophageal reflux disease, seasonal allergies, and sleep apnea. Surgical history included removal of an osteochondroma in the past. There was no relevant family history. He was a non-smoker, but drank five glasses of wine per week. He was homosexual with multiple partners. He underwent screening for sexually transmitted diseases every three months. Last screening was 3 months prior to presentation, and negative.

He had no allergies. Medications included emtricitabine-tenofovir which he took for pre-exposure prophylaxis for HIV prevention, methylprednisolone taper, tretinoin topical cream, and bimatoprost ophthalmic solution.

On physical exam, he appeared uncomfortable due to wrist pain. Temperature was 98.5 F, pulse 96, blood pressure 138/79, respirations 18, oxygen saturation 99% on room air. He had exquisite pain with active ranging of the right wrist, and mild pain with passive ranging. He had notable swelling, tenderness, warmth, and mild to moderate erythema about the right wrist, dorsal hand, proximal fingers, left elbow, and left 2nd metacar-

pophalangeal joint. There was mild tenderness about the left knee joint line and left Achilles tendon. The rest of the physical exam was unremarkable.

Initial labs were notable for white blood cell count of 11.8, with 91% neutrophils, and c-reactive protein 16.5 mg/dL. Anti-nuclear, rheumatoid factor, cyclic citrulline, and SSA/SSB antibodies were negative. Screening blood tests for HIV, syphilis, and hepatitis B/C were negative. Uric acid was 3.4. Urine polymerase chain reaction (PCR) testing was negative for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. HLA-B27 was negative.

Right wrist x-ray showed soft tissue swelling but was otherwise negative.

Right wrist aspiration yielded 2 mL of cloudy blood tinged fluid, that was sent for cell count with differential, crystal analysis, and gram stain/ culture. Intra-articular steroid injection was deferred while awaiting further work-up. Initial synovial fluid analysis showed negative gram stain with numerous white blood cells. Cell count could not be performed due to clotted sample (though it did demonstrate 93% neutrophils). Crystal analysis was negative.

He was started on prednisone 40 mg per day, for presumptive treatment of non-specific inflammatory arthritis. By the following day he had had minimal clinical improvement, so urgent referral was made to Infectious Disease (ID) for further evaluation. His throat was swabbed for culture and gonorrhea/chlamydia PCR. Patient declined rectal swab or urethral swab. Blood cultures were sent.

Two days following his initial presentation, *Neisseria gonorrhoeae* PCR from throat swab returned positive. He was started on ceftriaxone one gram intravenously daily, and given azithromycin one gram orally for one dose, for treatment of disseminated gonococcal infection. On the third day following presentation, *Neisseria gonorrhoeae* PCR returned positive from right wrist synovial fluid, and synovial fluid culture grew gram negative diplococci (which were later confirmed as *Neisseria gonorrhoeae*.)

Discussion

Disseminated gonococcal infection (DGI) results from hematogenous spread of *Neisseria gonorrhoeae*. DGI is uncommon, occurring in 0.5 to 3% of untreated mucosal infections.¹ It is most common in patients younger than 40 years of age. *Neisseria gonorrhoeae* is a rare cause of septic arthritis; in one case series in France in the 1990s it was found to be the causative organism in only 1.7% of cases.²

There are several risk factors for spread of localized gonococcal infection to joints and other tissues. Interestingly, recent symptomatic genital infection is not one of them. It is felt that asymptomatic mucosal infection delays diagnosis and therefore increases risk of dissemination.³ Other risk factors for dissemination include recent menstruation,⁴ pregnancy or immediate post-partum period,⁵ complement deficiencies,⁶ and systemic lupus erythematosus.⁷

The clinical presentation of DGI tends to follow one of two patterns, either a purulent mono- or oligoarticular arthritis, or a triad of polyarthralgias, tenosynovitis, and dermatitis. These can occur on a spectrum and there is occasionally overlap between these two presentations.⁸ Patients with purulent arthritis typically present with abrupt onset, and are afebrile. Most common joints affected include the knees, ankles, and wrists.^{1,3} Multi-joint involvement tends to be asymmetric.

In contrast, patients who present with the triad typically have fever, chills, and malaise. The fever may regress spontaneously however, so is not always present. The arthralgias are often migratory and therefore do not fit a typical pattern of septic arthritis.⁹ Likewise, tenosynovitis is uncommon in other forms of septic arthritis. In DGI, tenosynovitis tends to affect multiple tendons at once, most often about the wrist, fingers, ankles, and toes.⁹ Dermatitis is seen in approximately 75% of cases,¹ and typically presents as painless vesicular or pustular lesions¹⁰ on the distal extremities. The lesions are often transient, lasting a few days, even without treatment.

Definitive diagnosis of DGI is made by demonstration of *Neisseria gonorrhoeae* at a non-mucosal site (e.g. synovial fluid/ tissue, blood, or skin lesion) by culture or molecular testing. In the absence of this, presumptive diagnosis can be made if *Neisseria gonorrhoeae* is demonstrated at a mucosal site (rectal, urogenital, or pharyngeal), with a clinical presentation consistent with disseminated infection. If the organism is not isolated from any site, the diagnosis can still be presumed in the appropriate clinical setting, assuming no other explanation for the presentation, and appropriate response to treatment.¹¹

There are no controlled trials to inform treatment for DGI, so treatment is based largely on that for localized gonorrhea infection.¹¹ The preferred regimen is ceftriaxone 1 gram intravenously per day, with a single oral dose of azithromycin 1 gram. Cefotaxime or ceftazidime can be used as alternatives to ceftriaxone.

Duration of therapy depends on clinical presentation and response to treatment. Patients with the triad of arthralgias, tenosynovitis, and dermatitis typically respond rapidly to treatment, which is continued for a total of 7 days assuming resolution of clinical signs of infection.¹² After 24 to 48 hours of initial clinical improvement, ceftriaxone can be switched to the intramuscular formulation (250 mg IM daily) to complete the 7-day course. Alternatively, if susceptibility testing dictates, patients can be switched to oral cefixime to complete the course. Patients with purulent arthritis are treated with intravenous therapy until improvement in joint pain and effusion, typically at least 7 to 14 days. These patients often benefit from joint drainage, either serial joint aspirations or surgical drainage.¹¹

Our Patient

Our patient was started on ceftriaxone 1 gram intravenously per day, with one 1 gram of oral azithromycin given once. His right wrist was aspirated daily for 3 days, each time draining approximately 2 milliliters of cloudy yellow fluid. His symptoms did not improve significantly. Therefore, after 3 days the ceftriaxone dose was increased to 2 grams daily, which led to gradual clinical improvement. He finished a 2-week total course of intravenous ceftriaxone with near complete clinical recovery.

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