

A Veteran With Recurrent, Painful Knee Effusion

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Case Presentation: A 39-year-old Air Force veteran was admitted to the US Department of Veterans Affairs Boston Healthcare System (VABHS) for evaluation of recurrent, painful right knee effusions. On presentation, his vital signs were stable, and the examination was significant for a right knee with a large effusion and tenderness to palpation without erythema or warmth. His white blood cell count was 12.0 cells/L with an erythrocyte sedimentation rate of 23 mm/h and C-reactive protein of 11.87 mg/L. He was in remission from alcohol use but had relapsed on alcohol in the past day to treat the pain. He had a history of IV drug use but was in remission. He was previously active and enjoyed long hikes. Nine months prior to presentation, he developed his first large right knee effusion associated with pain. He reported no antecedent trauma. At that time, he presented to another hospital and underwent arthrocentesis with orthopedic surgery, but this did not lead to a diagnosis, and the effusion reaccumulated within 24 hours. Four months later, he received a corticosteroid injection that provided only minor, temporary relief. He received 5 additional arthrocenteses over 9 months, all without definitive diagnosis and with rapid reaccumulation of the fluid. His most recent arthrocentesis was 3 weeks before admission.

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► **Lauren E. Merz, MD, MSc, Chief Medical Resident, VABHS:** Dr. Jindal, what is your approach and differential diagnosis for joint effusions in hospitalized patients?

► **Shivani Jindal, MD, MPH, Hospitalist, VABHS, Instructor in Medicine, Boston University School of Medicine (BUSM):** A thorough history and physical examination are important. I specifically ask about chronicity, pain, and trauma. A medical history of potential infectious exposures and the history of the present illness are also important, such as the risk of sexually transmitted infections, exposure to Lyme disease or other viral illnesses. Gonococcal arthritis is one of the most common causes of nontraumatic monoarthritis in young adults but can also present as a migratory polyarthritis.¹

It sounds like he was quite active and liked to hike so a history of tick exposure is important to ascertain. I would also ask about eye inflammation and back pain to assess possible ankylosing spondylitis. Other inflammatory etiologies, such as gout are common, but it would be surprising to miss this diagnosis on repeated arthrocenteses. A physical examination can confirm monoarthritis over polyarthritis and assess for signs of inflammatory arthritis (eg, warmth and er-

ythema). The most important etiology to assess for and rule out in a person admitted to the hospital is septic arthritis. The severe pain, mild leukocytosis, and mildly elevated inflammatory markers could be consistent with this diagnosis but are nonspecific. However, the chronicity of this patient's presentation and hemodynamic stability make septic arthritis less likely overall and a more indolent infection or other inflammatory process more likely.

► **Dr. Merz:** The patient's medical history included posttraumatic stress disorder (PTSD) and antisocial personality disorder with multiple prior suicide attempts. He also had a history of opioid use disorder (OUD) with prior overdose and alcohol use disorder (AUD). Given his stated preference to avoid opioids and normal liver function and liver chemistry testing, the initial treatment was with acetaminophen. After this failed to provide satisfactory pain control, IV hydromorphone was added.

Dr. Jindal, how do you approach pain control in the hospital for musculoskeletal issues like this?

► **Dr. Jindal:** Typically, nonsteroidal anti-inflammatory medications (NSAIDs) are most

effective for musculoskeletal pain, often in the form of ketorolac or ibuprofen. However, we are often limited in our NSAID use by kidney disease, gastritis, or cardiovascular disease. Selective COX-2 inhibitors (eg, celecoxib) have the advantage of a lower risk of gastrointestinal bleeding. Topical formulations (eg, diclofenac) may also come with a lower adverse effect profile. Corticosteroids are also an option but come with their own adverse effect profile. This patient does not have any of these comorbidities. Adjuvant therapies such as lidocaine patches or capsaicin cream can also provide relief. Gabapentin or pregabalin are indicated for any component of neuropathic pain. Opioids can be helpful for acute musculoskeletal pain, but there is no long-term benefit in chronic musculoskeletal pain.² The experience of pain is also multifactorial so ensuring that anxiety and insomnia are addressed is key.

► **Dr. Merz:** On hospital day 1, the patient asked to leave to consume alcohol to ease unremitting pain. He also expressed suicidal ideation and discharge was therefore felt to be unsafe. He was reluctant to engage with psychiatry and became physically combative while attempting to leave the hospital, necessitating the use of sedating medications and physical restraints.

Dr. Shahal, what factors led to the decision to place an involuntary hold, and how do you balance patient autonomy and patient safety?

► **Dr. Talya Shahal, MD, Consult-Liaison Psychiatry Service, VABHS, Instructor in Psychiatry, Harvard Medical School:** This is a delicate balance that requires constant reassessment. The patient initially presented to the emergency department with suicidal ideation, stating he was not able to tolerate the pain and thus resumed alcohol consumption after a period of nonuse. He had multiple risk factors for suicide, including 9 prior suicide attempts with the latest less than a year before presentation, active substance use with alcohol and other recreational drugs, PTSD, pain, veteran status, male sex, single status, and a history of trauma.^{3,4} He was also displaying impulsivity and limited insight, did not engage in his psychiatric assessment, and attempted to assault staff. As such, his suicide risk was

assessed to be high at the time of the evaluation, which led to the decision to place an involuntary hold. However, we reevaluate this decision at least daily in order to reassess the risk and ensure that the balance between patient safety and autonomy are maintained.

► **Dr. Merz:** The involuntary hold was removed within 48 hours as the patient remained calm and engaged with the primary and consulting teams. He requested escalating doses of opioids as he felt the short-acting IV medications were not providing sustained relief. However, he was also noted to be walking outside of the hospital without assistance, and he repeatedly declined nonopioid pain modalities as well as buprenorphine/naloxone. The chronic pain service was consulted but was unable to see the patient as he was frequently outside of his room.

Dr. Shahal, how do you address OUD, pain, and stigma in the hospital?

► **Dr. Shahal:** It is important to remember that patients with substance use disorder (SUD) and mental illness frequently have physical causes for pain and are often undertreated.⁵ Patients with SUD may also have higher tolerance for opioids and may need higher doses to treat the pain.⁵ Modalities like buprenorphine/naloxone can be effective to treat OUD and pain, but these usually cannot be initiated while the patient is on short-acting opioids as this would precipitate withdrawal.⁶ However, withdrawal can be managed while inpatient, and this can be a good time to start these medications as practitioners can aggressively help with symptom control. Proactively addressing mental health concerns, particularly anxiety, AUD, insomnia, PTSD, and depression, can also have a direct impact on the perception of pain and assist with better control.² In addition, nonpharmacologic options, such as meditation, deep breathing, and even acupuncture and Reiki can be helpful and of course less harmful to treat pain.²

► **Dr. Merz:** An X-ray of the knee showed no acute fracture or joint space narrowing. Magnetic resonance imaging confirmed a large knee effusion with no evidence of ligament

injury. Synovial fluid showed turbid, yellow fluid with 14,110 nucleated cells (84% segmented cells and 4000 RBCs). Gram stain was negative, culture had no growth, and there were no crystals. Anticyclic citrullinated peptide (anti-CCP), rheumatoid factor, HIV testing, and HLA-B27 were negative.

Dr. Serrao, what do these studies tell us about the joint effusion and the possible diagnoses?

► **Dr. Richard Serrao, MD, Infectious Disease, VABHS, Clinical Associate Professor in Medicine, BUSM:** I would expect the white blood cell (WBC) count to be > 50,000 cells with > 75% polymorphonuclear cells and a positive Gram stain if this was a bacterial infection resulting in septic arthritis.⁷ This patient's studies are not consistent with this diagnosis nor is the chronicity of his presentation. There are 2 important bacteria that can present with inflammatory arthritis and less pronounced findings on arthrocentesis: *Borrelia burgdorferi* (the bacteria causing Lyme arthritis) and *Neisseria gonorrhoea*. Lyme arthritis could be consistent with this relapsing remitting presentation as you expect a WBC count between 3000 and 100,000 cells with a mean value between 10,000 and 25,000 cells, > 50% polymorphonuclear leukocytes, and negative Gram stains.⁸ Gonococcal infections often do not have marked elevations in the WBC count and the Gram stain can be variable, but you still expect the WBC count to be > 30,000 cells.⁷ Inflammatory causes such as gout or autoimmune conditions such as lupus often have a WBC count between 2000 and 100,000 with a negative Gram stain, which could be consistent with this patient's presentation.⁷ However, the lack of crystals rules out gout and the negative anti-CCP, rheumatoid factor, and HLA-B27 make rheumatologic diseases less likely.

► **Dr. Merz:** The patient received a phone call from another hospital where an arthrocentesis had been performed 3 weeks before. The results included a positive polymerase chain reaction (PCR) test for Lyme disease in the synovial fluid. A subsequent serum Lyme screen was positive for 1 of 3 immunoglobulin (Ig) M bands and 10 of 10 IgG bands.

Dr. Serrao, how does Lyme arthritis typically present, and are there aspects of this

case that make you suspect the diagnosis? Does the serum Lyme test give us any additional information?

► **Dr. Serrao:** Lyme arthritis is a late manifestation of Lyme disease. Patients typically have persistent or intermittent arthritis, and large joints are more commonly impacted than small joints. Monoarthritis of the knee is the most common, but oligoarthritis is possible as well. The swelling usually begins abruptly, lasts for weeks to months, and effusions typically recur quickly after aspiration. These findings are consistent with the patient's clinical history.

For diagnostics, the IgG Western blot is positive if 5 of the 10 bands are positive.⁹ This patient far exceeds the IgG band number to diagnose Lyme disease. All patients with Lyme arthritis will have positive IgG serologies since Lyme arthritis is a late manifestation of the infection. IgM reactivity may be present, but are not necessary to diagnose Lyme arthritis.¹⁰ Synovial fluid is often not analyzed for antibody responses as they are susceptible to false positive results, but synovial PCR testing like this patient had detects approximately 70% of patients with untreated Lyme arthritis.¹¹ However, PCR positivity does not necessarily equate with active infection. Serologic testing for Lyme disease by enzyme-linked immunosorbent assay and Western blot as well as careful history and the exclusion of other diagnoses are usually sufficient to make the diagnosis.

► **Dr. Merz:** On further history the patient reported that 5 years prior he found a tick on his skin with a bull's-eye rash. He was treated with 28 days of doxycycline at that time. He did not recall any tick bites or rashes in the years since.

Dr. Serrao, is it surprising that he developed Lyme arthritis 5 years after exposure and after being treated appropriately? What is the typical treatment approach for a patient like this?

► **Dr. Serrao:** It is atypical to develop Lyme arthritis 5 years after reported treatment of what appeared to be early localized disease, namely, erythema migrans. This stage is usually cured with 10 days of treatment alone (he received 28 days) and is generally abortive of subsequent stages, including Lyme

Clinical Takeaways

- Hospital-based assessment of a painful joint with effusion should begin with careful history and physical examination specifically focused on infectious exposures, review of systems, and chronicity as well as vital sign and laboratory analysis to rule out septic joint.
- Pain management should be tailored to the patient as well as the type of pain they are experiencing with a focus on multimodal analgesia and alleviating exacerbating factors like insomnia, anxiety, and substance use disorder, which is not a contraindication for opioids or aggressive pain management.
- Synovial fluid analysis is key to diagnosing joint effusions; white blood cell count of 3000 to 100,000 with a mean between 10,000 and 25,000 cells, > 50% polymorphonuclear leukocytes, and negative Gram stains could be consistent with Lyme arthritis.
- Lyme arthritis is a late manifestation of Lyme disease that most often presents with persistent arthritis of the large joints (monoarthritis of the knee most commonly) with effusions that quickly return after arthrocentesis.
- Balancing beneficence, nonmaleficence, and patient autonomy in medicine is a continuous challenge, but maintaining optimal communication between the patient and the health care practitioner, understanding the patient's goals of care, setting expectations and limits, and attempting to address the patient's needs while attempting to minimize stigma can help strike this balance.

arthritis. Furthermore, the patient reported no symptoms of arthritis until recently since that time. Therefore, one can argue that the excessively long span of time from treatment to these first episodes of arthritis suggests the patient could have been reinfectured. When available, comparing the types and number of Western blot bands (eg, new and/or more bands on subsequent serologic testing) can support a reinfection diagnosis. A delayed postinfectious inflammatory process from excessive proinflammatory immune responses that block wound repair resulting in proliferative synovitis is also possible.¹² This is defined as the postinfectious Lyme arthritis, or antibiotic-refractory Lyme arthritis, a diagnosis of exclusion more apparent only after patients receive appropriate antibiotic courses for the possibility of untreated Lyme as an active infection.¹²

Given the inherent diagnostic uncertainty between an active infection and posttreatment Lyme arthritis syndromes, it is best to approach most cases of Lyme arthritis as an active infection first especially if not yet treated with antibiotics. Diagnosis of postinflammatory processes should be considered if symptoms persist after appropriate antibiotics, and then short-term use of disease-modifying antirheumatic drugs, rather than further courses of antibiotics, is recommended.

► **Dr. Merz:** The patient was initiated on doxycycline with the plan to transition to ceftriaxone if there was no response. One day after diagnosis and treatment initiation and in the setting of continued pain, the patient again asked to leave the hospital to drink alcohol. After eloping and becoming intoxicated with alcohol, he returned to his room. He remained concerned about his continued pain and lack of adequate pain control. At the time, he was receiving hydromorphone, ketorolac, lorazepam, gabapentin, and quetiapine.

Dr. Serrao, do you expect this degree of pain from Lyme arthritis?

► **Dr. Serrao:** Lyme arthritis is typically less painful than other forms of infectious or inflammatory arthritis. Pain is usually caused by the pressure from the acute accumulation and reaccumulation of fluid. In this case, the rapid accumulation of fluid that this patient experienced as well as relief with arthrocentesis suggests that the size and acuity of the effusion was causing great discomfort. Repeated arthrocentesis can prove to be a preventative strategy to minimize synovial herniation.

► **Dr. Merz:** Dr. Shahal, how do you balance the patient subjectively telling you that they are in pain with objective signs that they may be tolerating the pain like walking around unassisted? Is there anything else that could have been done to prevent this adverse outcome?

► **Dr. Shahal:** This is one of the hardest pieces of pain management. We want to practice beneficence by believing our patients and addressing their discomfort, but we also want to practice nonmaleficence by avoiding inappropriate long-term pain treatments like opioids that have significant harm as well as avoiding exacerbating this patient's underlying SUD. An agent like buprenorphine/naloxone could have been an excellent fit to treat pain and SUD, but the patient's lack of interest and the frequent use of short-acting opioids were major barriers. A chronic pain consult early on is helpful in cases like this as well, but they were unable to see him since he was often out of his room. Repeated arthrocentesis may

also have helped the pain. Treatment of anxiety and insomnia with medications like hydroxyzine, trazodone, melatonin, gabapentin, or buspirone as well as interventions like sleep hygiene protocols or spiritual care may have helped somewhat as well.

We know that there is a vicious cycle between pain and poorly controlled mood symptoms. Many of our veterans have PTSD, anxiety, and SUD that are exacerbated by hospitalization and pain. Maintaining optimal communication between the patient and the practitioners, using trauma-informed care, understanding the patient's goals of care, setting expectations and limits, and attempting to address the patient's needs while attempting to minimize stigma might be helpful. However, despite optimal care, sometimes these events cannot be avoided.

► **Dr. Merz:** The patient was ultimately transferred to an inpatient psychiatric unit where a taper plan for the short-acting opioids was implemented. He was psychiatrically stabilized and discharged a few days later off opioids and on doxycycline. On follow-up a few weeks later, his pain had markedly improved, and the effusion was significantly reduced in size. His mood and impulsivity had stabilized. He continues to follow-up in the infectious disease clinic.

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Ethics and consent

Informed consent was obtained from the patient reported in this case report.

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