CASE REPORT

A rare cause of oligoarthritis with septic presentation

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SUMMARY

A 33-year-old man presented with new-onset, asymmetric, migratory oligoarthritis in the setting of several weeks of nausea and vomiting, diarrhoea, fevers and dysuria. He was initially treated in the inpatient setting with broad-spectrum antibiotics due to concern for an evolving sepsis presentation. Arthrocentesis of a large right knee effusion revealed inflammatory synovial fluid without findings suggestive of septic arthritis. Human leucocyte antigen B27 was positive and, taken together with the antecedent history of gastroenteritis, dysuria and inflammatory oligoarthritis, the clinical diagnosis was most consistent with reactive arthritis. Antibiotics were discontinued. His treatment course proved refractory to non-steroidal anti-inflammatory drugs and intra-articular and systemic glucocorticoid therapy with concurrent use of sulfasalazine and ultimately necessitated treatment with a tumour necrosis factor alpha inhibitor.

BACKGROUND

This case highlights many of the classical clinical features of a relatively rare cause of oligoarthritis. The diagnosis of reactive arthritis (ReA) relies heavily on clinical impression as there are no validated consensus criteria for diagnosis. Overall, ReA accounts for only a small proportion of patients presenting with oligoarthritis and the annual incidence of the disease is only 0.6–27/100 000.¹ That being said, a detailed history and physical examination in conjunction with supportive laboratory and imaging studies must be appropriately used to make the correct diagnosis. Most often, ReA is triggered by an antecedent bacterial gastrointestinal or genitourinary infection, with the onset of arthritis 1 to 28 days after initial symptom onset.² The cornerstone of therapy is non-steroidal anti-inflammatory drugs (NSAIDs) although systemic steroids and intra-articular steroid injections are also used when NSAID therapy is contraindicated or ineffective. Traditional disease modifying antirheumatic drugs are used when NSAIDs and steroids are ineffective or a chronic presentation requires use of a steroid-sparing agent. This case also illustrates the full spectrum of pharmacotherapy that can be used to treat ReA depending on the clinical course.

CASE PRESENTATION

A 33-year-old man presented to the emergency department with several weeks of nausea and vomiting, diarrhoea, fevers and new-onset right knee and left index finger joint pain and swelling. His medical history was otherwise notable for

obesity and hypertension. His symptoms including crampy abdominal pain, nausea with non-bloody and non-bilious emesis and watery diarrhoea acutely appeared after a restaurant meal while at a resort in Northern Minnesota a couple of weeks prior to presentation. He denied any known tick exposures. He presented at an urgent care clinic for these symptoms and was treated with oral antibiotics for presumed diverticulitis. The gastrointestinal symptoms persisted for a week before resolution. A week later, he developed dysuria and was treated with another course of antibiotics by his urgent care provider for presumed prostatitis. The dysuria persisted, and he subsequently developed left index finger and right knee pain, which prompted him to present to the emergency department.

On initial presentation, the patient was tachycardic to 150 bpm and febrile to 39.4°C. He was diaphoretic with active rigors. Other notable physical examination findings included warm effusion of the right knee and dactylitis of the left index finger. There was no evidence of hepatosplenomegaly, rashes or skin lesions, and the eye examination was unremarkable.

INVESTIGATIONS

Initial laboratory studies (reference ranges provided parenthetically) revealed leucocytosis (white cell count, $15.1 \times 10^9/L$ ($3.5\text{--}10.5 \times 10^9/L$)) with neutrophilic predominance, as well as an elevated sedimentation rate (66 mm/1 hour ($0\text{--}22$ mm/1 hour)) and C reactive protein (74.4 mg/dL ($0.8\text{--}1.3$ mg/dL)). Serum lactate was normal (1.1 mmol/L ($0.6\text{--}2.3$ mmol/L)). Serum creatinine was elevated (1.6 mg/dL ($0.8\text{--}1.3$ mg/dL)) from baseline 1.0 but he had no other major electrolyte derangements. Antinuclear antibody was only weakly positive (1.3 units (<1.0 units)). Cyclic citrullinated peptide antibodies and rheumatoid factor were negative. Human leucocyte antigen (HLA)-B27 was positive. X-ray of the right knee showed a moderate effusion without any major bony abnormalities (figure 1). X-ray of the left hand showed soft-tissue swelling over his index finger but no fractures or erosive changes (figure 1). Blood cultures revealed no microbiological growth. Urine testing for gonorrhoea and chlamydia was negative. Stool studies to identify specific types of bacterial enterocolitis were not performed out of concern for cost to the patient and low likelihood of affecting management. Lyme serologies were obtained and were not suggestive of acute infection.

Arthrocentesis and synovial fluid analysis of the right knee effusion were notable for 36 617 total nucleated cells with 80% neutrophils and no

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Figure 1 (A) X-ray of the left hand demonstrating soft-tissue swelling of proximal first finger. (B) X-ray demonstrating moderate right knee joint effusion.

crystals. Synovial gram stain and culture were negative. Ophthalmology evaluation with slit lamp exam did not demonstrate anterior chamber inflammation.

DIFFERENTIAL DIAGNOSIS

The initial differential diagnosis considered in our patient included disseminated gonococcal infection, Lyme's disease, crystalline arthropathy, inflammatory bowel disease-associated arthritis, septic arthritis and ReA. His initial presentation was concerning for systemic infection and septic arthritis given his high fever, tachycardia and elevated inflammatory markers. The synovial fluid analysis was less consistent with a septic arthritis; however, it was inflammatory appearing. Taking the antecedent gastrointestinal infection and presentation of dysuria, inflammatory arthritis and HLA-B27 positivity, ReA arose as the most likely diagnosis. The lack of crystals made crystalline arthropathy unlikely.

TREATMENT

With ReA as the most likely diagnosis, antibiotics were discontinued, and the patient was started on oral prednisone therapy. NSAIDs were not initiated because of acute kidney injury (prerenal aetiology) on admission. With improvement in renal function, prednisone was discontinued and naproxen 550 mg twice daily was initiated. The patient was discharged home with the recommendation to continue naproxen therapy until outpatient rheumatology follow-up.

OUTCOME AND FOLLOW-UP

On outpatient rheumatology evaluation, he was still symptomatic and continued to have elevated inflammatory markers. In addition, he had developed new onset left ankle pain and swelling as well as left sacroiliac pain. In light of this lack of clinical response to NSAIDs, he was again started on prednisone and eventually required addition of sulfasalazine 1500 mg twice daily. Because of the sacroiliac pain as well as his HLA-B27 positivity, a pelvic X-ray was obtained but was negative for sacroiliitis. The patient's arthritic symptoms continued to be refractory, and he eventually was started on adalimumab.

Patient's perspective

Below are some of my thoughts on my experience with reactive arthritis. I contracted a severe gastrointestinal bacterial infection that kept me out of work with constant nausea, vomiting and diarrhoea in addition to fever, body aches and cramping. A few days after the gastrointestinal infection passed, I began having trouble with urination; it was difficult to begin the stream and finish voiding. I then began having neck and back pain, as well as pain in the index finger of my left hand.

Unfortunately, throughout the next few days, the pain in my neck, back and left hand continued to increase. In addition, pain rapidly developed in my left shoulder and right knee. My knee, shoulder and fingers became extremely swollen and hot to the touch and I was running a very high fever. It was an absolutely terrifying experience because I had no idea what was happening to my body or the cause.

On arriving at the hospital, I was checked in and the medical team had a fairly quick working diagnosis that I may be suffering from reactive arthritis. I ended up staying in the hospital for a week in total with many tests performed. On my release from the hospital, I was put on a steroid regimen (prednisone), sulfasalazine and medications to assist with pain relief. For the first month or two of being home, I still required assistance from family to move around the house or get out of bed. The disease also moved into my left ankle, big toe of my right foot and tailbone, causing new pain and swelling in those areas.

I am now 5 months after my initial diagnosis and still working on recovery from the initial flare up. I have been regularly attending both occupational and physical therapy and have experienced some relief, but still have regular pain in some joints and have not returned to full daily activities at this point. I use a cane to walk and cannot grip anything of weight with my left hand, but at this point, I am thankful to my medical team for their expertise in diagnosing this disease and with the education and continued treatment I receive. I am hopeful that I will make it through this flare up and not have any significant flare ups in the future, though I understand that is not a guarantee.

Learning points

- ▶ Reactive arthritis (ReA) classically has referred to the triad of conjunctivitis, urethritis and arthritis following infection and is a rare cause of oligoarthritis.
- ▶ Initial presentation of ReA can mimic sepsis and a systemic inflammatory response, which can lead to misdiagnosis and delay in appropriate treatment as well as unnecessary antibiotic administration.
- ▶ There is no specific test or diagnostic criteria to make a diagnosis of ReA, making it a true clinical diagnosis.
- ▶ One of the hallmarks of ReA is its occurrence in the postinfectious setting, although in up to half of the cases, no specific microbial pathogen is identified.
- ▶ The symptomatic sequelae of ReA are significant for patients, can be associated with significant morbidity and often greatly impair activities of daily living.

DISCUSSION

This patient's presentation was thought initially to be sepsis of active infection leading to tachycardia and fevers, and for this reason he was managed aggressively with broad-spectrum

antibiotics. As the clinical course progressed and additional medical, microbiological and laboratory data became available with strong evidence and findings of inflammatory synovial fluid as well as HLA-B27 positivity, the clinical diagnosis of ReA was made which had large implications for ongoing medical management of this patient.

ReA earlier known as Reiter's syndrome, may present with a triad of conjunctivitis, urethritis and arthritis following an antecedent infection.³ Common antecedent infections include *Chlamydia trachomatis*, *Salmonella*, *Shigella*, *Yersinia* and *Campylobacter*, with the most common being *Chlamydia*.⁴ However, it is important to recognise that in 50% of cases of ReA, no causative infectious organism is ever identified. As in our case, oftentimes this may be because investigations aimed at identifying a particular causative organism may not be in line with cost effective care if the causative organism would not be one treated with antimicrobials. This is well illustrated in our case, and the inability to isolate the infectious organism should not prevent or delay treatment of ReA if the remainder of the clinical scenario suggests this as the diagnosis.

ReA shares similar clinical characteristics to other HLA-B27-associated spondyloarthropathies with features of dactylitis, sacroiliitis and enthesitis.⁵ Approximately 50% of patients with acute ReA have HLA-B27 positivity, and if present, is often associated with greater symptom severity and greater risk for development of chronic symptoms.⁶ The patient in this case did have a positive HLA-B27 and had persistent, disabling symptoms following hospital discharge.

This case also illustrates the array of pharmacological treatment options for patients with ReA. NSAIDs as well as systemic and intra-articular steroids are first-line options. When cases become chronic and patients require steroid-sparing agents, Disease modifying agent antirheumatic drugs (DMARDs), such as

sulfasalazine, have proven to be effective in management as well. Antitumour necrosis factor alpha agents are typically reserved as a last-line agent in patients with chronic ReA and are needed in refractory cases such as this.^{7 8}

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