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### **Authors**

Wieczorek, Isabela

Taylor, Mihaela

Ben-Artzi, Ami

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## CLINICAL VIGNETTE

# Episodic Oligoarthritis: Differential Diagnosis and Review of Available Diagnostic Tools

Isabela Wieczorek, M.D., Mihaela Taylor, M.D. and Ami Ben-Artzi, M.D.

### Case Report

A 51-year-old Caucasian male presented to UCLA Rheumatology with episodes of joint pain. He initially noted acute-onset of sharp pain and tenderness in his right ankle after running a marathon 3 years ago. The initial pain lasted 3 days but has recurred for 3-5 day episodes, which has prevented him from running further marathons. He also notes episodic pain and swelling in his right knee and right wrist. His review of symptoms was negative for fatigue, fever, chills, dysuria, rash, or eye pain and redness. He is monogamous, and lives with his wife of 26 years. He has no other pertinent medical, social, or family history.

Physical exam was significant for a moderate effusion of the right knee and tenderness around the joint. The right wrist and left first MTP were also swollen and tender with no erythema. Despite some pain, he had full range of motion of all joints examined, and had only a mild limp when walking. Outside labs two months prior to his visit included normal CBC and metabolic panel, negative rheumatoid factor, and negative ANA. He also had a prior radiograph of his right knee, showing chondrocalcinosis of the hyaline cartilage (Figure 1).

Episodic oligoarthritis presents a broad differential diagnosis. In a 51-year-old male with episodic arthritis, gout would be the first diagnosis to consider. Gout can cause episodic joint pains, but most cases are monoarticular. This patient had no history of podagra, and while gout often causes extreme pain and inflammation, his physical exam suggests a less aggressive disease. The asymmetry of joint involvement, absence of stiffness, and negative rheumatoid factor argued against a diagnosis of rheumatoid arthritis. Arthritis can also be a component of systemic lupus erythematosus, scleroderma, and vasculitides, but our patient did not have other symptoms characteristic of these diseases.

Another diagnosis to consider is palindromic rheumatism, which can present as self-limiting, recurrent episodes of arthritis in 2 to 3 joints<sup>1</sup>. This is a diagnosis of exclusion, so other causes of arthritis must be ruled out. Although our patient did not have involvement of the cartilage of the nose and ear, relapsing polychondritis is also included in the differential of migratory polyarthritis.

The seronegative spondyloarthropathies, including reactive arthritis, psoriatic arthritis, and enteropathic arthritis, were also considered. Reactive arthritis occurs 1-3 weeks after a urethritis or enteritis from certain organisms including Chlamydia, Shigella, Salmonella, Campylobacter, and Yersinia<sup>2</sup>. The patient denied high-risk sexual activity, and did not exhibit signs or symptoms of a sexually transmitted disease. The absence of psoriasis, inflammatory bowel disease, and axial involvement with sacroiliitis made this group of arthritides less likely.

Infections can cause migratory arthritis. Viruses, including parvovirus B19, alphavirus, and rubella virus can cause arthralgias and arthritis, but the chronicity of our patient's disease and absence of other symptoms, including rash and fever, argue against a virally-induced arthritis<sup>3</sup>. Lyme disease, another consideration, was unlikely in a patient with no history of tick bites, erythema migrans, or neurologic and cardiac manifestations<sup>4</sup>. Disseminated gonococcal infection is another cause of arthritis, but is often accompanied by fever and dermatologic lesions ranging from macules and papules to pustules and bullae<sup>5</sup>. Rheumatic fever may also present as a migratory arthritis, but our patient did not have a history of pharyngitis or other symptoms of rheumatic fever.

Finally, polyarthritis can be a feature of a paraneoplastic syndrome, known as carcinomatous polyarthritis. The arthritis can precede the cancer diagnosis, but our patient had no symptoms suggestive of malignancy since the onset of his symptoms 3 years prior<sup>6</sup>.

Office ultrasound of his right wrist and right knee showed hyperechoic material within the femoral hyaline cartilage (Figure 2). Ten cc of cloudy, low viscosity synovial fluid was aspirated from his right knee. Microscopic examination of the synovial fluid revealed intra- and extra-cellular rhomboid-shaped crystals (Figure 3). Synovial fluid analysis revealed few RBCs, rare WBCs, and negative bacterial culture.

### Discussion

Based on the radiographic findings of calcium deposition in the cartilage as well as synovial fluid microscopy showing rhomboid-shaped crystals, we diagnosed this patient with

Calcium Pyrophosphate Deposition Disease (CPDD), also called pseudogout. CPDD is a disease of calcium pyrophosphate crystal deposition in the cartilage<sup>7</sup>. The main risk factor is age, as 7-10% of patients over 60 have CPDD<sup>8</sup>. Symptoms of pseudogout are due to the host inflammatory response to calcium pyrophosphate crystals released into the synovial fluid from cartilage.

CPDD can be sporadic, hereditary, associated with trauma, or secondary to metabolic diseases such as hyperparathyroidism, hemochromatosis, hypothyroidism, amyloidosis, hypomagnesemia, and hypophosphatemia<sup>7</sup>. The familial form has been associated with mutations in the membrane pyrophosphate channel gene (*ANKH*)<sup>9</sup>, which increase the elaboration and extracellular transport of pyrophosphate. If CPDD occurs before age 55 or is florid and polyarticular, a primary metabolic disorder or familial predisposition should be considered. After the age of 55, hyperparathyroidism should be ruled out<sup>8</sup>.

In acute pseudogout, patients present with several days to two weeks of joint pain and swelling<sup>10</sup>. Attacks occur spontaneously or after physical trauma. In most cases the presentation is monoarticular. The knee is involved in 50% of cases, but any joint can be affected including the first metatarsophalangeal and wrist. In almost half of patients the disease will progress to involve multiple joints, particularly the knees, wrists, metacarpophalangeal joints, hips, shoulders, elbows, and ankles<sup>10</sup>. Patients are generally asymptomatic between episodes<sup>10</sup>.

CPDD is definitively diagnosed by the presence of weakly positively birefringent, rod-shaped and rhomboid crystals in the inflammatory range synovial fluid<sup>10,11</sup>. Infection should be excluded<sup>10</sup>. Chondrocalcinosis (cartilage calcification) on radiographs is also suggestive of CPDD, although is neither sensitive or specific<sup>11</sup>. Recent evidence suggests that ultrasonography may be more sensitive and specific than x-rays<sup>12</sup>.

For acute attacks, the joint should be elevated and immobilized. Joint aspiration can help improve symptoms in large joints<sup>11</sup>. NSAIDs are the drugs of choice, however, intraarticular glucocorticoids may also be used<sup>13</sup>. Severe attacks involving multiple joints usually require short courses of systemic glucocorticoids<sup>11</sup>. Patients with recurrent attacks of pseudogout may benefit from daily low dose colchicine to reduce the number and duration of attacks<sup>12</sup>.

Our patient presented with recurrent episodes of acute joint pain and swelling, first involving only the right ankle, but then progressing to affect the right knee and wrist. The acuity of his symptoms as well as intensity of pain suggested crystal-induced arthropathies, including gout and pseudogout. The findings of rhomboid shaped crystals in the synovial fluid and chondrocalcinosis of the right knee are consistent with a diagnosis of CPDD. We prescribed colchicine as he has had

multiple recurrences over the past 3 years. Additionally, we excluded secondary causes of CPDD including hyperparathyroidism, hemochromatosis, thyroid disorders, and gout.

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**FIGURE LEGEND:**



Figure 1: X-Ray of right knee showing chondrocalcinosis of hyaline cartilage (arrow)

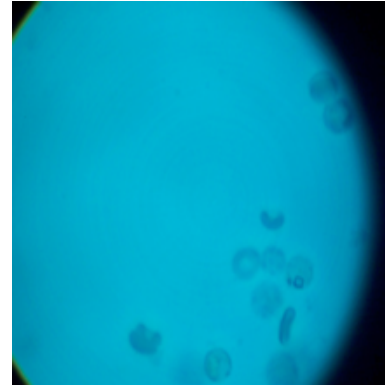


Figure 3: Microscopic view of right knee synovial fluid with intracellular rhomboid-shaped crystal (arrow)

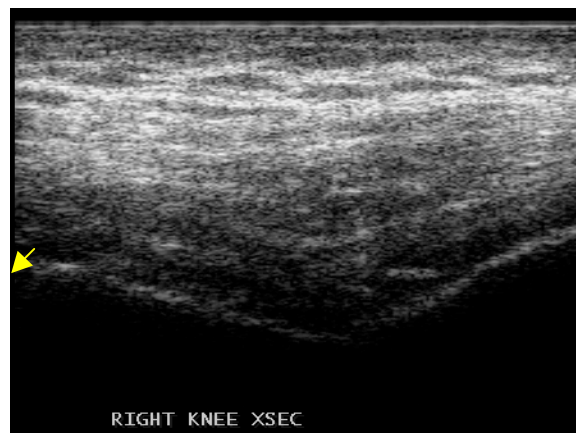


Figure 2: Ultrasound of right knee with hyperechoic area in femoral hyaline cartilage (arrow)