Is it easy to clinically distinguish inflammatory arthritis of bacterial origin from monoarthritis attacks of gout disease?

Bakteriyel kaynaklı enflamatuvar artriti gut hastalığının monoartrit ataklarından klinik olarak ayırt etmek kolay mıdır?

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ABSTRACT
Acute monoarthritis is a common situation in orthopedic emergency where the patient presents with typical inflamed joint. It is hard to clinically distinguish inflammatory arthritis of bacterial origin from monoarthritis attacks of gout disease. If these two situations, which are the most common causes of acute monoarthritis, are misdiagnosed, outcomes might be catastrophic and costly. Synovial fluid analysis is the most reliable method for confirming the diagnosis although it might not always lead to definitive diagnosis. If there is clinical suspicion for crystal arthropathy, repeated examinations may provide benefits for confirming the diagnosis.

Keywords: Crystal arthropathy; gout arthritis; monoarthritis; septic arthritis

ÖZ

Anahtar sözcükler: Kristal artropati, gut artriti; monoartrit; septic artrit.
arthropathy, is crucial and poses a challenge to the clinician as septic arthritis may develop irreversible damage to the joint. Synovial fluid (SF) analysis is the most reliable method for confirming the diagnosis. Care should be taken, as these arthritides can coexist and presence of crystal does not always exclude bacterial arthritis.[9]

**CASE REPORT**

A 44-year-old male patient presented to our outpatient clinic for the first time with the chief complaint of ongoing pain on the left knee for the last two months. He described five attacks of monoarthritis in the same joint during 2010 to 2014, with six to twelve months in between. During the monoarthritis periods, he had pain, limited range of motion, swelling, and localized warmth. Upon his hospital admissions, this inflammatory condition had been thought to be of bacterial origin and he received antibiotic treatment. The latest attack, which started two months before his presentation to our clinic, had shown no sign of regression despite the use of antibiotics.

On physical examination, there was swelling, localized warmth, tenderness, and limited range of motion on the left knee. Blood chemistry screen resulted all within reference limits including the serum uric acid levels. Leukocytosis was recorded on cell count and acute phase reactant levels were high. Arthrocentesis showed a cloudy yellow SF which was then analyzed. Gram staining showed increased leukocytes but no bacteria and culture result was also negative. Synovial fluid cell count showed increased leukocytes and in SF chemistry analysis, a glucose level slightly lower than in blood was observed. Synovial fluid microscopy performed by pathologists showed no sign of crystals.

Conventional radiography showed no pathologies other than chronic findings of chondromalacia patella. Magnetic resonance imaging (MRI) showed apparent effusion, synovial hypertrophy, and high contrast accumulation suggesting septic arthritis.

Culture with negative results was associated with empiric antibiotic treatment that had been going on for the last two months and reason for the clinical situation was thought to be of bacterial origin. A second arthrocentesis was made and SF culture did not grow any bacteria. Deoxyribonucleic acid strain analysis was preformed and it was positive for *Leptothrix* spp. and *Schlegelella aquatica* spp. although these results were thought to be related with contamination. Patient received empiric antibiotic treatment. The patient was observed to be responding well to the treatment and symptoms started to fade.

However, 20 days after the empiric antibiotic treatment, the patient was admitted to our clinic once again with the same symptoms he had at his first presentation. Arthrocentesis was performed and joint fluid was analyzed. The fluid was macroscopically cloudy and yellow. Microscopic analysis was performed by rheumatologists and pathologists. Rheumatology department reported thin, needle-shaped crystals at direct microscopic view (Figure 1).

Pathology analyzed cytopinned and Diff Quik (DQ; Dade Behring-Switzerland) stained preparation under polarized light and also reported narrow, needle-shaped, mostly extracellular, negative birefringent monosodium urate (MSU) crystals which were very bright against the dark background (Figure 2, 3), and gout arthritis was diagnosed. There were structures which were thought to be bacteria with coccoid morphology and many leukocytes on the sample but blood and SF cultures did not grow any bacteria.

The patient responded well to the colchicine and indomethacin treatment he received and was discharged. A written informed consent was obtained from the patient.

**DISCUSSION**

Acute monoarthritis is a common situation in orthopedic emergency. There are difficulties in differentiating the two most common causes of acute monoarthritis; septic arthritis and crystal induced arthritis. It is extremely crucial to distinguish these because septic arthritis on one hand may lead to irreversible damage to the joint and gout arthritis on the other hand may receive inappropriate treatment which leads to increased cost and discomfort due to
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continuous admissions to hospital with no sign of recovery. Many reports show that misdiagnosis in these arthritides is costly.\textsuperscript{[10,11]}

Gout arthritis with no treatment usually goes into remission within few days. Many patients suffer a second attack most commonly within six months to two years after the initial attack.

Only two thirds of patients have abnormal levels of serum uric acid during an acute attack.\textsuperscript{[12,13]} There is evidence that other blood chemistry work is of little value for diagnosis.\textsuperscript{[14]} Urine uric acid is also usually observed within normal range during an arthritis attack.

According to the recommendations by European League Against Rheumatism and the American College of Rheumatology published in 2015, SF analysis is the main diagnostic method for gout arthritis.\textsuperscript{[15]} Observing monosodium urate (MSU) crystals in SF samples is solely enough for diagnosis. They appear as narrow, needle-shaped crystals which are very bright against a dark background and can be seen intracellular or extracellular under the microscope. Although they can be observed with standard microscope, their negative birefringent properties that could be seen under polarized microscope are characteristic, which enables their discrimination from other crystals. Pseudogout, which is calcium pyrophosphate crystal deposition, must be considered in differential diagnosis.\textsuperscript{[15]} These crystals are rod or rhomboid shaped polymorphic crystals which are mostly intracellular and smaller than MSU crystals. Most of them do not show birefringent properties but some can be birefringent with positive elongation. It should be kept in mind that crystals formation and resolution depend on the pH and temperature; after aspiration the fluid should be examined rapidly at room temperature.\textsuperscript{[16]} Cytospin and Diff-Quick (Dade Behring-Switzerland) stain technique has high sensitivity and specificity.

There is interobserver and intraobserver error in the assessment of cells and identification of crystals in SF.\textsuperscript{[17]} It is reported in several studies that some of the patients with gout were negative for MSU crystals on initial SF examination, and then were found to be positive if the microscopic examination was repeated with the same specimen.\textsuperscript{[18,19]} If there is clinical suspicion for crystal arthropathy, repeated examinations may provide benefits on diagnosis.

As the whole clinical picture of gout arthritis might mimic septic arthritis or there is possibility of coexistence, analysis for bacteria detection must be performed.

Radiography is not useful in diagnosis during an acute attack.\textsuperscript{[20]} Although findings such as soft tissue swelling and effusions might be present, they are not specific.\textsuperscript{[21]} Ultrasound lacks ionizing radiation and due to being relatively cheap, is easy to access. But its sensitivity is lower than MRI showing joint inflammation and structural changes.\textsuperscript{[22]} Its biggest limitation is its operator-dependent nature. On patients with gout arthritis, it may show an abnormal hyperechoic band over the superficial margin of the articular hyaline cartilage, defined as double contour sign.\textsuperscript{[23]} Although its use in rheumatoid arthritis has been studied thoroughly, there are limited number of studies specific to its use in gout arthritis. There are no internationally recognized descriptions and definitions of pathology seen in gout on US.\textsuperscript{[22]} The standardization and validation of US abnormalities

\textbf{Figure 2.} Diff Quik stained preparation under polarized light, 600x magnification.

\textbf{Figure 3.} Crystal showing negative birefringence under polarized light, 1000x magnification.
are necessary for advancing its use as a reference imaging method for diagnosis of gout arthritis.[24] Magnetic resonance imaging is an excellent method for viewing synovium, cartilage, soft tissue, and bone. Limitations are its high cost, poor accessibility and long scanning time. It may show bone marrow edema which is uncommon in gout and if seen, should raise the question of infection.[25]

Rest, local cold application to the affected joint, colchicine, non-steroidal anti-inflammatory drugs, or both is recommended for treatment of the acute attack. Urate lowering therapy is indicated for patients with recurrent gout attacks, chronic arthropathy, and tophi. Systemic or intra-articular steroids might be preferred for patients with impaired renal function. Patient education has an outstanding value for the management of gout. Slow weight reduction, avoidance of beer, meat, and sea food are recommended.

In conclusion, it is hard to clinically distinguish inflammatory arthritis of bacterial origin from monoarthritis attacks of gout disease. These two conditions are very common and easy to misdiagnose. In such a scenario of misdiagnosis, results might be catastrophic and costly.

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