

Knee Synovitis Mimicking a Septic Arthritis

Jeong-Eun Park¹, Hyun-Sik Kim¹, Jae-Ho Seong¹, Sung-Sam Ha¹, Seoung-Wan Nam¹, Hyang-Sun Lee³,
Jae-Seok Kim², Jae-Won Yang², Taeyoung Kang³

Divisions of ²Nephrology and ³Rheumatology, ¹Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

Synovitis is the inflammation of the synovial membrane with unknown etiology which occurs in association with auto-immune inflammatory arthritis, mainly in rheumatoid arthritis. Synovitis manifesting as rapidly progressing monoarticular or pauciarticular symptoms could make early diagnosis difficult, thus it could be misdiagnosed as other forms of arthritic diseases. We experienced a rare case of knee joint synovitis which initially manifested as mimicking a septic arthritis. A 58-year-old-male patient underwent renovascular embolization due to retroperitoneal hemorrhage which was developed after renal biopsy. Suddenly, the patient's left knee joint became swollen rapidly with redness and tenderness. Moreover, his right knee also became inflamed. Surgical irrigation and intravenous antibiotics had never worked on his knee joint inflammation, however administration of intermediate dose of steroid could decrease inflammatory signs dramatically. Synovitis in a large joint could be mistaken as a septic arthritis, delaying the right diagnosis. Thus, we report this case with literature review. (*J Rheum Dis* 2015;22:39-44)

Key Words. Synovitis, Rheumatoid arthritis, Septic arthritis

INTRODUCTION

Synovitis is the inflammation of the synovial membrane that surrounds the synovial joint. The primary synovitis refers to synovitis of unknown etiology caused by auto-immune pathogenesis [1], and it is usually simply called as synovitis. The synovitis usually manifest. The primary synovitis usually manifest as chronic symmetric, inflammatory, peripheral polyarthritis. The affected joint become swollen and tendered. The longer these joint symptoms persist, the more likely diagnose of rheumatoid arthritis (RA) becomes. RA leads to deformity of affected joint through persistent inflammation, bone and cartilage erosion. There has been a growing evidences showing the importance of very early treatment of RA in order to reverse morbidity. However, the absence of typical symptoms usually suggests an alternative diagnosis. Synovitis manifesting as an acutely inflamed joint could be mistaken for other forms of arthritic diseases. We ex-

perienced a case of knee joint synovitis, mimicking a septic arthritis. No previous report has been published in rheumatology, thus we describe this case with literature review.

CASE REPORT

A 58-year-old male visited our hospital to undergo renal biopsy for incidentally found hematuria and proteinuria. An acute retroperitoneal hemorrhage was developed following the biopsy. Angiography was performed to locate the bleeding site and embolization was done. Three days later, the patient abruptly developed fever, pain and swelling of the left knee joint. Physical examination revealed body temperature 39°C, systolic/diastolic blood pressure 130/81 mmHg, pulse 100 times/min, respiratory rate 20 times/min. There was no audible wheezing or crackle on auscultation of the chest, and examination of the abdomen found no particular abnormality. The left

Received : January 6, 2014, **Revised :** (1st) March 6, 2014, (2nd) April 8, 2014, **Accepted :** April 16, 2014

Corresponding to : Taeyoung Kang, Division of Rheumatology, Department of Internal Medicine, Yonsei University Wonju College of Medicine, 20 Il-san-ro, Wonju 220-701, Korea. E-mail : taeyoung@yonsei.ac.kr

pISSN: 2093-940X, eISSN: 2233-4718

Copyright © 2015 by The Korean College of Rheumatology. All rights reserved.

This is a Free Access article, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

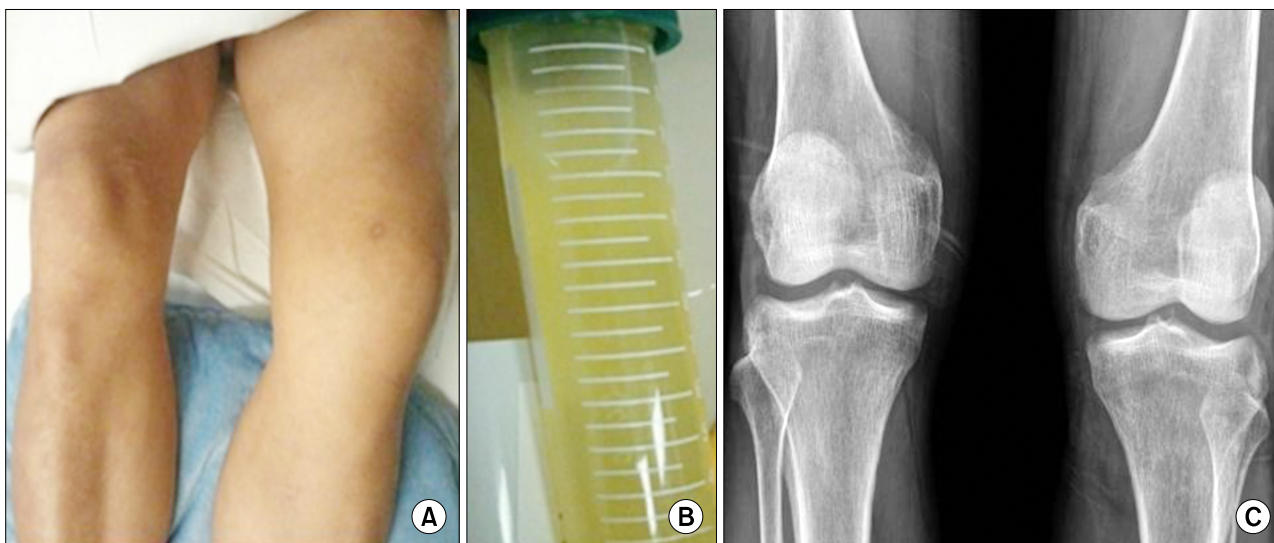


Figure 1. (A) The patient's left knee joint was swollen with local heat. His right knee joint was also swollen, but less obvious compared to the left side. (B) Total 60 mL of yellow, turbid synovial fluid was aspirated from the left knee joint. (C) The knee x-ray showed only soft tissue swelling around the knee joint.

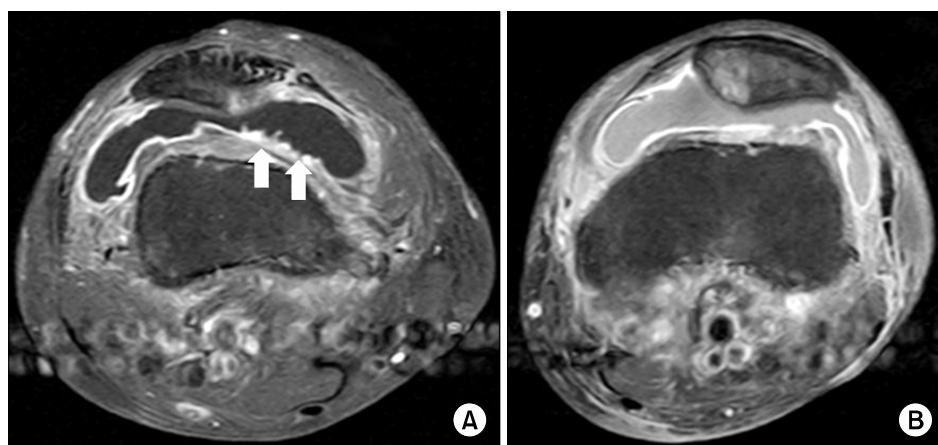


Figure 2. Knee magnetic resonance imaging showed large amount of joint effusion with synovial enhancement (arrows) on T1-weighted image in both right (A) and left (B) knee joint.

knee joint showed local heat, erythema, swelling and tenderness (Figure 1A). Flexion and extension of the knee joints were extremely restricted due to pain of the knee joints.

A complete blood count revealed 47,540 cells/mm³ of white blood cells (polymorphic neutrophils 75.5%), while hemoglobin and platelet count were normal at 10.3 g/dL and 350,000 cells/mm³, respectively. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) was elevated at 8.29 mg/dL and 29 mm/h, respectively. Other notable laboratory studies included blood urea nitrogen of 59 mg/dL, serum creatinine of 1.76 mg/dL, total protein of 5.4 g/dL, albumin of 2.8 g/dL, and uric acid of 8.0 mg/dL. Liver enzymes were within normal range (aspartate transaminase 26 IU/L, alanine transaminase

11 IU/L). On urinalysis, urine protein and red blood cell returned as 2+ and 3+, respectively.

Immediate knee arthrocentesis was performed in his left knee joint, and a total of 60 mL of synovial fluid with turbid color was aspirated (Figure 1B). The cell differentiation of the aspirated fluid showed white blood cell count of 16,875 cells/ μ L (polymorphic neutrophil 97%, lymphocyte 3%) and red blood cell count of 162 cells/ μ L. Repeated polarizing microscopy showed no evidence of crystal associated arthropathies. A simple knee radiograph showed soft tissue swelling only (Figure 1C). Due to the high suspicion of septic arthritis, antibiotic treatment with 3rd generation cephalosporin and vancomycin was started. However, three days later, his right knee joint also developed rapid swelling and erythema. His body

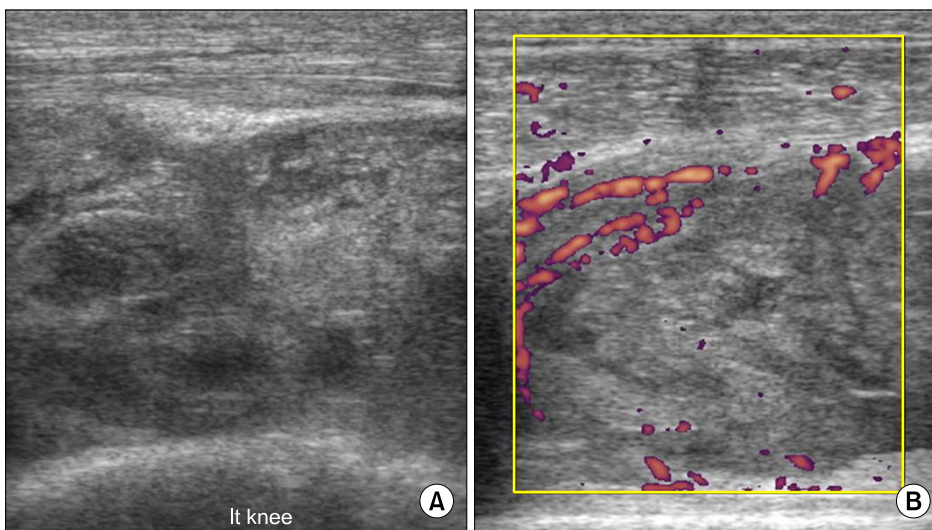


Figure 3. Left knee joint gray scale ultrasound showed highly proliferated synovium filling the suprapatellar bursa (A). Power Doppler signals were detected along the marginal areas of highly proliferated synovium (B).

temperature was also high up to 39°C. The patient underwent magnetic resonance imaging (MRI), showed large amount of joint exudates and thickened, enhanced synovial membrane on T1-weighted images (Figure 2). With high suspicion of spreading of septic arthritis, both knee joints were surgically irrigated. In the operating room, pus-like synovial fluid was noted. However, cultures of both aspirated synovial fluid and joint tissues obtained in the operating room did not show any organism.

The patient was referred to rheumatology for persisting fever and knee joint swelling after surgical irrigation. He denied any previous history of arthritis and gastrointestinal and urogenital infection before admission. We performed ultrasonographic examination of both knee joints, which showed highly proliferated synovium (Figure 3A) with increased power Doppler flow. The power Doppler was noted mainly in marginal areas of proliferated synovium, but not in the joint cavity (Figure 3B), which is compatible findings with synovitis usually seen in the inflammatory arthritis, commonly in RA, rather than septic arthritis. Osteophyte and double contour sign were not observed.

Autoantibody studies showed rheumatoid factor (RF) of 11 IU/mL (reference range <20 IU/mL), anti-cyclic citrullinated protein (CCP) antibody of 238 U/mL (reference range <25 U/mL). The other antibodies including antinuclear antibody, anticytoplasmic anti-neutrophilic cytoplasmic antibody were not detected. We highly suspected of synovitis of knee joints, which could be the initial manifestation of early autoimmune inflammatory arthritis, particularly in RA. We started oral steroid (prednisolone 20 mg/d). Then, the fever started

to be subside and three days later intra-articular steroid was given into the both knee joint. Then, his knee pain and swelling were rapidly improved dramatically. Methotrexate 10 mg once weekly and sulfasalazine 1.5 g daily were also started as disease modifying anti-rheumatic drugs (DMARDs). About 4 months later, his both knee joints as well as laboratory parameters (ESR, CRP, etc.) recovered near completely without any residual deformity. He is now currently being monitored as an outpatient.

DISCUSSION

Initially the patient was highly suspected of septic arthritis, since his acute joint symptom was developed after catheterization for angiography. Septic arthritis is caused by infection of the joint by bacteria, fungus, mycobacteria, and other microorganisms and hematogenous spread is the cause in approximately 72% of septic arthritis [2]. Gram staining of aspirated synovial fluid gives a positive result in only from 29% to 50%, but synovial fluid culture is positive in the majority of patients with bacterial arthritis. However, in this case Gram stain and synovial fluid and synovial tissue cultures showed no organism. Synovial fluid white cell count can be used to differentiate between septic and other causes of inflammation. Synovial fluid white cell count of less than 50,000 cells/mm³ reduce the likelihood of the diagnosis of sepsis, but other study suggested that the cut-off value of above 17,500/mm³ could yield reasonable sensitivity and specificity [3]. In this case, the white blood cell count of the affected knee joint showed 16,875 cells/μL, which was

not implicative of septic arthritis.

The differential diagnosis to consider in a patient who presents with acute monoarticular symptoms are trauma, infection, and crystalline diseases. However, several systemic disorders may present with an acute monoarthritis including seronegative spondyloarthropathies, sarcoid arthropathies, myelodysplastic, and leukemic disorders. RA also can rarely present as a monoarthritis in its early stages. Persistent single joint arthritis, frequently of a large joint such as knee, hip, wrist, or ankle, may herald or may be the sole manifestation of the onset of polyarticular disease. There may be a history of joint event such as trauma or procedures like in this case as an apparent initiating event.

The interval between monoarthritis and polyarthritis may extend from several days to several weeks in patients those who disease progresses. Typical classic RA is usually insidious with symptoms of pain, stiffness and swelling of many joint. Frequently, the relatively small joints the metacarpophalangeal and proximal interphalangeal joints of hands, wrist the metatarsophalangeal joints of foots are site of arthritis in early disease. However, relatively large joint such as knee, elbows, shoulders, and ankles are also commonly affected in the early course of disease.

The general principles and treatment strategies that are applied in the management of RA also should be applied in the management of mono- or pauci-articular synovitis. The general target of treatment of synovitis is directed toward the control of synovitis and the prevention of joint injury. The choice of therapies depends on the several factors, including severity of disease activity when therapy is initiated. The choice of therapeutic agents can be derived for an increasing understanding of the disease and from evidences of other studies. In patients with active RA, glucocorticoids is frequently added for a short period to dampen down disease activity rapidly while awaiting a clinical response to DMARD [4].

Several clinical trials have suggested benefits of high-dose prednisolone therapy in early RA. An initial 6-month intensive combination treatment that includes high-dose corticosteroid in combination with other conventional DMARDs resulted in sustained suppression of the rate of radiographic progression over many years [5]. Furthermore, short-term use of glucocorticoids in doses less than 15 mg of prednisolone per day is known to seldom associated with serious adverse effect and this may be effective for up to six months. In this case, initial use of oral

prednisolone 20 mg/d resulted in rapid clinical improvement.

Synovitis presenting as a monoarticular disease can be mistaken as other monoarticular diseases, particularly as septic arthritis if accompanied by fever and short latency of the disease. Of important, MRI evidence of synovitis is highly sensitive in patients with suspected early RA [6]. In some patients, RA can be diagnosed using MRI before they meet the classification criteria of American College of Rheumatology (ACR) [7]. In this case, MRI showed joint effusion with synovial enhancement in T1-weighted images, which could be implicative of synovitis, but septic arthritis can also show similar findings. Furthermore, rapid development of knee swelling with acute inflammatory signs made it sufficient to be diagnosed clinically as septic arthritis. Power Doppler is reliable for assessing inflammatory activity in the synovial joints of RA patients and correlates well with MRI synovitis [8]. Musculoskeletal ultrasound in rheumatology has rapidly integrated into routine clinical practice as a powerful tool for diagnosis, treatment and prediction of recurrence of synovitis. However, so far, there are few published data regarding whether ultrasound can distinguish between synovitis and septic arthritis in rheumatology [9]. In this case, increased power Doppler signals seen along the marginal areas of highly proliferated synovium is indicative of synovitis.

Anti-CCP antibodies may be helpful in distinguishing RA from other forms of arthritis. Anti-CCP antibodies have a higher specificity for RA than does RF. The presence of anti-CCP antibodies in a population of patients with undifferentiated arthritis is associated with a high rate of the development of RA [10]. Studies have indicated that anti-CCP antibodies are a valuable adjunct to the diagnosis of RA [11]. In this case, although the patient have positivity for anti-CCP antibody, elevated CRP, and ultrasonographic evidences of synovitis, the lack of other clinical findings including number and site of affected joint had made insufficient to diagnose RA according to the 2010 American College of Rheumatology/ European League against Rheumatism (ACR/EULAR) or 1987 revised ACR criteria.

Despite of massive antibiotic treatment and surgical irrigation, sustained systemic fever, swelling and pain of knee joints had let us diagnose synovitis. Although a high level of serum uric acid possible due to high serum creatinine level was observed at the time of referral, gout or calcium pyrophosphate crystal arthropathy could be

ruled out because no crystal was found on repeated polarizing microscopy. Reactive arthritis could also be ruled out due to absence of history of urinary tract or gastrointestinal tract infection, as well as lack of other clinical findings such as uveitis. Arthritis related with renal disease should be considered; however, it was ruled out because renal biopsy was reported as diffuse proliferative glomerulonephritis suggestive of postinfectious glomerulonephritis, which is unlikely to be associated with arthritis and it is usually manifested along with Henoch-Schönlein purpura.

Synovitis occurring at large joints, such as the knee, may become difficult to distinguish from septic arthritis when accompanied by fever, arthralgia, swelling, and erythema, and past history suggesting septic arthritis such as trauma, surgery, and catheterization may further complicate the diagnosis. The patient in this case was also initially suspected of septic arthritis, and therefore, incision and drainage of the knee joint was performed, and he was later referred to rheumatology due to persisting condition.

Mortality rate due to septic arthritis ranges from 10% to 15% [12], and may reach up to 50% if occurred across multiple joints by *Staphylococcus aureus* [13]; therefore, its treatment should be prioritized when suspected. Nonetheless, if Gram stain or culture of the aspirated joint fluid obtained through arthrocentesis returns as negative, synovitis should be considered, and additional studies, including serum analysis, ultrasonography, and MRI should be performed. Ultrasonography and MRI can be helpful in discovering synovitis in patients with normal findings in simple radiography [14].

In pediatric rheumatology, very rare case of rapidly occurred pigmented villonodular synovitis of hip joint that was developed after fall down on her left side was reported [15]. In rheumatology, to the best of our knowledge, knee synovitis developed like a septic arthritis after catheterization for angiography has not been reported. It is unclear whether the catheterization might act as a triggering factor for the initiation of the abnormal immune responses. However, rapid response to the steroid treatment also supported the autoimmune pathogenesis of the inflamed knee joints.

SUMMARY

In summary, this case report describes a rare case of synovitis that initially present like a septic arthritis. Our experience shows that if the results of synovial fluid analysis

including cultures are not favor of septic arthritis, the possibility of acute mono- or pauci-articular manifestation of synovitis, especially as early manifestation of RA, must be considered. Short-term use of intermediated to high dose of glucocorticoid with subsequent DMARD can induce rapid clinical improvement.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Hitchon CA, El-Gabalawy HS. The synovium in rheumatoid arthritis. *Open Rheumatol J* 2011;5:107-14.
2. Morgan DS, Fisher D, Merianos A, Currie BJ. An 18 year clinical review of septic arthritis from tropical Australia. *Epidemiol Infect* 1996;117:423-8.
3. Li SF, Cassidy C, Chang C, Gharib S, Torres J. Diagnostic utility of laboratory tests in septic arthritis. *Emerg Med J* 2007;24:75-7.
4. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum* 2002;46:328-46.
5. Landewé RB, Boers M, Verhoeven AC, Westhovens R, van de Laar MA, Markusse HM, et al. COBRA combination therapy in patients with early rheumatoid arthritis: long-term structural benefits of a brief intervention. *Arthritis Rheum* 2002;46:347-56.
6. Narváez J, Sirvent E, Narváez JA, Bas J, Gómez-Vaquero C, Reina D, et al. Usefulness of magnetic resonance imaging of the hand versus anticyclic citrullinated peptide antibody testing to confirm the diagnosis of clinically suspected early rheumatoid arthritis in the absence of rheumatoid factor and radiographic erosions. *Semin Arthritis Rheum* 2008; 38:101-9.
7. Sugimoto H, Takeda A, Hyodoh K. Early-stage rheumatoid arthritis: prospective study of the effectiveness of MR imaging for diagnosis. *Radiology* 2000;216:569-75.
8. Szkudlarek M, Court-Payen M, Strandberg C, Klarlund M, Klausen T, Ostergaard M. Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dynamic magnetic resonance imaging. *Arthritis Rheum* 2001;44:2018-23.
9. Merino R, de Inocencio J, García-Consuegra J. Differentiation between transient synovitis and septic arthritis of the hip with clinical and ultrasound criteria. *An Pediatr (Barc)* 2010;73:189-93.
10. van Gaalen FA, Linn-Rasker SP, van Venrooij WJ, de Jong BA, Breedveld FC, Verweij CL, et al. Autoantibodies to cyclic citrullinated peptides predict progression to rheumatoid arthritis in patients with undifferentiated arthritis: a prospective cohort study. *Arthritis Rheum* 2004;50:709-15.
11. Laskari K, Ahmadi-Simab K, Lamken M, Csernok E, Gross

- WL, Hellmich B. Are anti-cyclic citrullinated peptide auto-antibodies seromarkers for rheumatoid vasculitis in a cohort of patients with systemic vasculitis? *Ann Rheum Dis* 2010;69:469-71.
12. Kaandorp CJ, Krijnen P, Moens HJ, Habbema JD, van Schaardenburg D. The outcome of bacterial arthritis: a prospective community-based study. *Arthritis Rheum* 1997; 40:884-92.
13. Dubost JJ, Fis I, Denis P, Lopitiaux R, Soubrier M, Ristori JM, et al. Polyarticular septic arthritis. *Medicine (Baltimore)* 1993;72:296-310.
14. Szkudlarek M, Narvestad E, Klarlund M, Court-Payen M, Thomsen HS, Østergaard M. Ultrasonography of the metatarsophalangeal joints in rheumatoid arthritis: comparison with magnetic resonance imaging, conventional radiography, and clinical examination. *Arthritis Rheum* 2004; 50:2103-12.
15. Rantapää-Dahlqvist S, de Jong BA, Berglin E, Hallmans G, Wadell G, Stenlund H, et al. Antibodies against cyclic citrullinated peptide and IgA rheumatoid factor predict the development of rheumatoid arthritis. *Arthritis Rheum* 2003;48:2741-9.