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Undifferentiated Inflammatory Arthropathy as Knee Pain and Swelling - Case Series

Ratul Das

Medical Officer, MD-Physical Medicine and Rehabilitation, Fellowship Musculoskeletal Ultrasound in Pain Medicine, District Hospital South Tripura, Santirbazar, India

Corresponding Author: Dr. Ratul Das

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ABSTRACT

Introduction: Undifferentiated inflammatory arthropathy (UIA) characterized by inflammatory joint pain that does not meet the classification criteria for a specific rheumatic disease which is a diagnostic challenge in rheumatology. The diagnosis relies on combination of clinical evaluation, laboratory tests, and imaging studies to rule out other established arthropathies. It is essential to differentiate this condition from other causes of knee pain to avoid unnecessary treatments. This case series consists of three cases with atypical presentations of UIA highlighting the complexities in distinguishing the condition from more definitively classified rheumatic diseases and management.

Case Description: The case series represents three patients suffering from knee pain with swelling for more than 3 months duration, having great difficulty in bending knee, walking, climbing stairs etc. On clinical examination, patellar tap test was positive suggestive of effusion in knee joint. Rheumatoid factor, total Leukocyte count, C-reactive protein, uric acid, anti-cyclic citrullinated peptide was normal but erythrocyte sedimentation rate (ESR) was markedly high which was an indication of nonspecific inflammation. Ultrasonography of knee joint showed the presence of joint effusion and power doppler was indicating increase in blood flow within synovium suggestive of inflammatory type of arthropathy. They didn't meet any standard diagnostic criteria and diagnosed as undifferentiated inflammatory arthropathy. These patients were treated with DMARDS like Methotrexate, Sulfasalazine and intra-articular knee joint injection procedure using Triamcinolone acetonide. All three cases were reviewed after three months of treatment initiation and had excellent improvement in pain and functional parameters without knee joint effusion. Visual Analogue Scale score and Western Ontario and McMaster Universities Osteoarthritis Index score were markedly improved. All three cases were found to sustain their improvement at sixth month of follow-up.

Conclusions: Clinical picture, inflammatory marker like ESR and power doppler study is helpful in diagnosis of undifferentiated inflammatory arthritis and early management with DMARDS and intra-articular steroid is key to treat these patients to minimize disability.

Keywords: UIA, ESR, DMARDS

INTRODUCTION

Undifferentiated inflammatory arthropathy (UIA) characterized by inflammatory joint pain that does not meet the classification criteria for a specific rheumatic disease. It can manifest as knee pain and swelling, yet it may not always fit neatly into established diagnostic categories[1]. It is a rheumatology diagnostic challenge. Some patients with synovitis experience spontaneous resolution,

while others develop chronic progressive arthritis or continue with undifferentiated arthritis[2].

This condition is often marked by an asymmetrical disease pattern, often affecting the lower extremities. [3]. The diagnosis relies on a combination of clinical evaluation, laboratory tests, and imaging studies to rule out other established arthropathies[4]. Understanding the nuances of UIA is crucial to accurately diagnose and manage patients presenting with knee pain and swelling. The ambiguity inherent in undifferentiated arthritis necessitates a comprehensive approach, considering both the potential for spontaneous remission and the risk of progression to chronic arthritis. It is essential to differentiate this condition from other causes of knee pain to avoid unnecessary treatments[5,6].

This case series represents three cases with knee pain and swelling diagnosed as undifferentiated inflammatory arthropathy, highlighting the complexities in distinguishing this condition from more definitively classified rheumatic diseases.

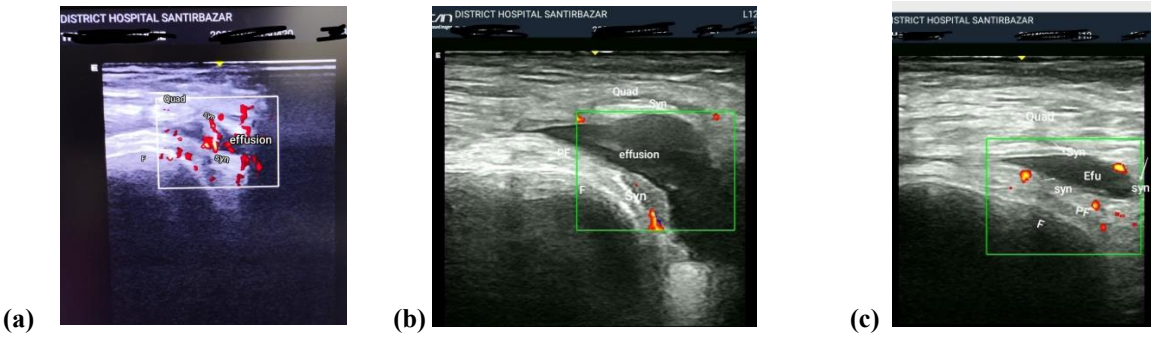
CASE PRESENTATION

Cases were presented as knee pain and swelling in Physical Medicine and Rehabilitation OPD in District Hospital South Tripura, Santirbazar, India. They were clinically examined and relevant blood tests, X-ray, ultrasonography (USG) with power doppler study of knee joint were done (Figure 1).

Figure 1: Patient with left knee joint swelling

Ultrasound (USG) is a highly valuable, first-line imaging tool for the assessment of knee effusion. It's rapid, dynamic, bedside, cost-effective, and involves no ionizing radiation. It can detect very small amounts of joint fluid and enables accurate and safe diagnostic aspiration and therapeutic injection procedure.

Power Doppler measures the amplitude (power) of the Doppler signal that represents the volume of moving blood cells which is more sensitive to low-velocity, low-volume flow in detecting subclinical inflammation. In a power doppler ultrasound study, the "red dots" or areas of colour are computer-generated colour overlay that represents the presence and intensity of blood flow. In the context of inflammatory arthropathies these red signals indicate active synovitis which is inflammation within the joint's lining accompanied by the growth of new, small blood vessels known as angiogenesis[7].



(a) **(b)** **(c)**

Figure 2 (a), (b), (c): USG of knee as transducer placed transversely through suprapatellar recess. Fluid is seen as an anechoic (black) or hypoechoic area between the quadriceps tendon (superficially) and the prefemoral fat pad/ femur (deeply) and power doppler study as red dots indicating increase vascularity within synovium. Quadriceps (quad), femur (F), prefemoral fat pad (PF), synovium (syn), effusion (efu)

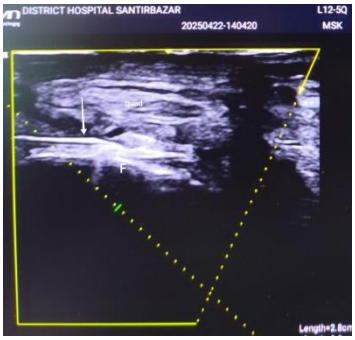


Figure 3: USG guided intra-articular knee joint aspiration with needle visualisation marked as white arrow into suprapatellar recess

Case 1:

A 70-year-old female presented (figure-1) with left sided knee pain with swelling which was gradual in onset for 3 months. She had great difficulty in bending knees, walking, climbing stairs and other day to day activities. On clinical examination, patellar tap test was positive suggestive of effusion in knee. She did not have history of recent viral fever, genito-urinary tract infection or skin lesion.

Rheumatoid factor (RA factor), total leukocyte count (TLC), C- reactive protein (CRP), uric acid, anti-cyclic citrullinated peptide (ACCP) was normal but erythrocyte sedimentation rate (ESR) was markedly high which was 65 mm/ 1st hr. An X-ray of left knee showed grade- 1 osteoarthritis changes.

Patient was further investigated by USG of left knee with power doppler which showed the presence of joint effusion with increase in blood flow (figure-2, a). She was diagnosed as UIA. Her pre-treatment Visual Analogue Scale (VAS) score was 8/10 and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC index) score was 85/96.

Methotrexate 15 mg once weekly and Sulfasalazine 1gm twice daily was given. Etodolac 400 mg was given as on needed basis 12 hourly for pain initially. USG guided 28 ml of transparent pale-yellow synovial fluid was aspirated (figure-3) from the knee joint and injection Triamcinolone acetonide 40 mg intra-articular was given.

The patient was evaluated at 3rd month and was clinically far better and knee swelling subsided. Her VAS score was 2/10 and WOMAC score was 27/96 which shows marked improvement in both parameters. Patient was reviewed at 6th month and she sustained clinical improvement without knee joint swelling.

Case 2:

Patient was a 45-year-old female presented with right sided knee pain and swelling for 5 months. She was treated by general physician for her knee pain and took different non-steroidal anti-inflammatory drugs (NSAIDS) for many days. RA factor, TLC, CRP, uric acid, ACCP were normal while ESR was 115/1st hr which was quite high. There was no history of fever. X-ray of knee joint was grading 2 osteoarthritis changes. USG showed presence of joint effusion and power doppler study showed increase in signal around the joint fluid suggesting increased blood flow (figure 2, b).

Her initial VAS score was 10/10 and WOMAC score was 90/96. She was managed by Methotrexate 15 mg once weekly and sulfasalazine 1 gm twice daily. USG guided 52 ml of transparent pale yellow synovial was aspirated from knee joint and intra-articular injection Triamcinolone acetonide 40 mg was given. She was evaluated after 3 months which showed marked improvement in VAS score which was 3/10 and WOMAC score was 30/96. Patient sustained clinical improvement without knee joint swelling at 6th month follow-up.

Case 3:

Patient was 73-year-old male, presented with left sided knee pain with swelling for 3 years. ESR was 68 mm/1st hr. RA factor, TLC, CRP, uric acid, anti CCP was normal. There was no history of fever and X-ray knee joint showed grade 2 osteoarthritis changes. USG of knee joint showed joint effusion and increase in blood flow by power doppler study (figure-2, c). He was managed by Methotrexate 15 mg once weekly and Sulfasalazine 1gm twice daily.

USG guided 45 ml of transparent pale-yellow synovial fluid was aspirated from knee joint and injection Triamcinolone acetonide 40 mg intra-articular was given.
His initial VAS score was 10/10 and WOMAC score was 92/96. After 3 months of treatment, his VAS score came to 3/10 and WOMAC score was 27/96 which indicates marked improvement in clinical symptoms. Patient was reviewed at 6th month and he sustained the clinical improvement without knee joint swelling.

Table 1: Laboratory blood test

Parameters	Case 1	Case 2	Case 3
ESR (reference range up to 20 mm/ 1st hr)	65 mm /1st hr	115 mm /1st hr	68 mm /1st hr
CRP (reference range up to 6.0 mg / dl)	1.5 mg/dl	2.04 mg/dl	2.5 mg/dl
RA factor	Negative	Negative	Negative
ANTI CCP	Negative	Negative	Negative
Uric acid (reference range male: 2.5 to 7.0 mg /dl; Female:1.5 to 6.0 mg/dl)	5.0 mg/dl	4.2 mg/dl	5.5 mg/dl

DISCUSSION

In this case series, it was found that knee pain and swelling for more than 3 months duration and all these patients needed support to walk and daily care activities.
Among the laboratory blood tests, only ESR was elevated in all cases (table 1). An elevated ESR indicated the presence of inflammation but could not pinpoint its source or confirm a specific type of arthritis.
USG with power doppler study was indicating joint effusion and increase in blood flow into synovium. There was no history of fever. Joint aspiration had clear transparent synovial fluid. Acute Septic arthritis as differential diagnosis was excluded eventually.
To rule out gouty arthritis, serum uric acid was done which came out normal. There was no history of involvement of other joints, low back pain, genito-urinary tract infection, diarrhoea, dysentery, urinary tract infection in recent months. There was no history of skin disease or lesion over the body. X-ray of sacroiliac joint was normal. It helped to rule out spondyloarthropathy.
In this case series, nonspecific inflammatory marker i.e. ESR, knee joint effusion by USG study and inflammatory pattern into knee synovium by power doppler study were the findings. The cases were definitely having inflammatory pattern of arthropathy. Due to lack of any standard diagnostic criteria, they were diagnosed as UIA.

Paskins, Kamath & Hassell found that the presentation of UIA can be particularly challenging in elderly patients, where atypical manifestations and co-morbidities often obscure the clinical picture, making differentiation from degenerative conditions[8]. Jacobson Girish, Jiang et al. stated that the meticulous diagnostic approach integrates clinical acumen with advanced imaging and serological markers to distinguish inflammatory arthropathy from other pathologies, such as osteoarthritis[9]. Carotti, Salaffi, Manganelli et al. found that power doppler study may be a valuable tool in distinguishing between inflammatory and non-inflammatory pannus of knee joints in rheumatoid arthritis[10]. Radu & Bungau et al. mentioned that rheumatoid arthritis, though often presenting with clear diagnostic criteria, can manifest atypically, particularly in its early stages or in specific patient populations, thereby overlapping with presentations of UIA[11].
These patients were treated with DMARDS like Methotrexate, Sulfasalazine and had excellent improvement in pain and functional parameters. Majorczyk, Mazurek-Mochol, Pawlik et al. found that Methotrexate, a folate antagonist remains a cornerstone in the management of rheumatoid arthritis and similar inflammatory conditions due to its ability to reduce disease activity and prevent joint damage[12]. Taylor, Alten, Gomez-Reino et

al. reported that the effective management strategies, including the early and optimal use of DMARDS like Methotrexate, can mitigate progressive structural joint damage for moderate to severe disease activity [13].

Clear knee joint synovial fluid was aspirated followed by intraarticular injection Triamcinolone acetonide steroid was done for each patient in this case series which resulted in fast pain relief and swelling reduction. Scherer, Rainsford, Kean et al. found that intra-articular injections of Triamcinolone acetonide are effective in reducing inflammation and pain in joint diseases with minimal to no mineralocorticoid adverse effects[14].

Ganapati, Gowri, Antonisamy et al. found that the combination of Methotrexate and Salfasalazine is particularly relevant for patients who may not fully meet the classification criteria for established inflammatory arthritis but exhibit persistent inflammatory features[15]. Song, Kim, Kim et al. stated that the timely initiation of DMARDS is crucial for improved clinical outcomes, as delayed treatment can lead to irreversible joint damage and increased disability[16]. Pavlov-Dolijanovic, Bogojevic, Nozica-Radulovic et al. found that the diagnostic complexity is further compounded by the fact that many inflammatory arthropathies, exhibit increased prevalence and incidence in the elderly, frequently presenting with an acute infection-like onset that can significantly delay accurate diagnosis and timely therapeutic intervention[17].

All three cases were reviewed at 3rd month of treatment initiation. There was marked improvement in VAS scale (table 2) and WOMAC index score (table 3) which was supported by reduction in knee pain and regained functionality to perform moderate daily care activities like walking, climbing stairs etc.

Table 2: Improvement of VAS scale score

Patients	VAS (initial)	VAS (post treatment)
Case 1	8/10	2/10
Case 2	10/10	3/10
Case 3	10/10	3/10

Table 3: Improvement of WOMAC index score

Patients	WOMAC (initial)	WOMAC (post treatment)
Case 1	85/96	27/96
Case 2	90/96	30/96
Case 3	92/96	27/96

All three cases were found to sustain their improvement without any further knee swelling at 6th month of follow up. The case series describes the complexity of making diagnosis and therapeutic challenges in patients presenting with UIA to achieve sustained remission and functional improvement.

CONCLUSION

- Clinical picture, inflammatory marker like ESR and power doppler study is helpful in diagnosis of UIA.
- Early management with DMARDS like Methotrexate and Sulfasalazine is essential to manage such inflammatory arthropathy.
- Knee intra-articular steroid injection like Triamcinolone acetonide followed by joint aspiration is helpful for providing fast pain relief.
- Diagnosing early and treating promptly is the approach to tackle such UIA to minimize disability.

Declaration by Authors

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