

Recognition of gout in rheumatoid arthritis

A case report

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Abstract

Rationale: Rheumatoid arthritis (RA) and gout are common rheumatic diseases. However, their coexistence has been rarely reported. Here in, we describe a case of a middle aged Chinese woman having RA complicated with atypical gout on both the knee joints.

Patient concerns: A 44-year-old Chinese woman complained of swelling and tenderness of multiple joints since 10 months. She had a positive rheumatoid factor and high titers of anti-CCP antibody. She was diagnosed with RA, and commenced on methotrexate, leflunomide, and methylprednisolone. Her symptoms of pain and swelling over interphalangeal and wrists joints subsided except the knee joints. She was started with treat to target treatment (TTT) for RA and rest of her medications was adjusted accordingly. Surprisingly, her symptoms did not improve ever after the addition of a biologic agent, tumor necrosis factor (TNF)- α receptor antagonist.

Diagnosis: Presence of urate crystals in the synovium was viewed under polarization microscope which was extracted from one of the knee joint. Hence, we established the diagnosis of RA complicated with gout.

Interventions: We commenced her on TNF- α receptor antagonist, colchicines, and febuxostat.

Outcomes: Her symptoms of pain and swelling improved significantly on both the knees and no longer recurred.

Lessons: Coexistence of RA and gout has been rarely reported as it is not frequently seen in clinical practice. Hence, when patients with RA with oligoarthritis repeatedly do not respond to TTT, a standard antirheumatism treatment, the possibility of RA complicating with gout should be rule out.

Abbreviations: CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, GCs = glucocorticoids, LEF = leflunomide, MP = methylprednisolone, MTX = methotrexate, NSAIDs = nonsteroidal antiinflammatory drugs, RA = rheumatoid arthritis, RF = rheumatoid factor.

Keywords: gout, rheumatoid arthritis, treatment

1. Introduction

Rheumatoid arthritis (RA) is one of the most common symmetric, peripheral polyarthritis, chronic inflammatory rheumatic diseases of an unknown etiology. The general prevalence of RA is about 0.5% to 1% in the adult population with a male and female

prevalence ratio of 1:3.^[1,2] Meanwhile, gout is a deposition of monosodium urate crystals which is present in about 1% to 4% of the general population; where males develop gout in 2:6 ratio compared to females.^[3,4] Although both RA and gout are commonly seen in clinical scenario, their coexistence has been rarely reported. There is a popular belief that RA and gout do not, or rarely, coexist with each other. However, it has been reported quite frequently in elderly males.^[5] This case report describes a 44-year-old Chinese woman with RA complicated with gout in both the knee joints.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

An informed consent was obtained from the individual included in this study.

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2. Case report

A 44-year-old Chinese woman in 2002 was admitted to our hospital's ward for swelling and tenderness of multiple joints since 10 months. On local examination there was fusiform swelling in proximal and distal interphalangeal joints of right hand, bilateral wrists, and knee joints. In addition, she complained of morning stiffness lasting for about 30 minutes. Her X-ray revealed of joint space narrowing of bilateral wrist and interphalangeal joints (Fig. 1).

Her laboratory tests performed at our hospital revealed of normal serum uric acid level, positive rheumatoid factor (RF), and an elevated RF-immunoglobulin A (IgA) 288.69 IU/mL (normal range, <20 IU/mL). In addition, she had a positive anti-CCP antibody and an elevated CCP-immunoglobulin G (CCP-IgG) 229.78 IU/mL (normal range, <25 IU/mL). There was a strong positivity for antinuclear antibody with the titer of 1:1000,

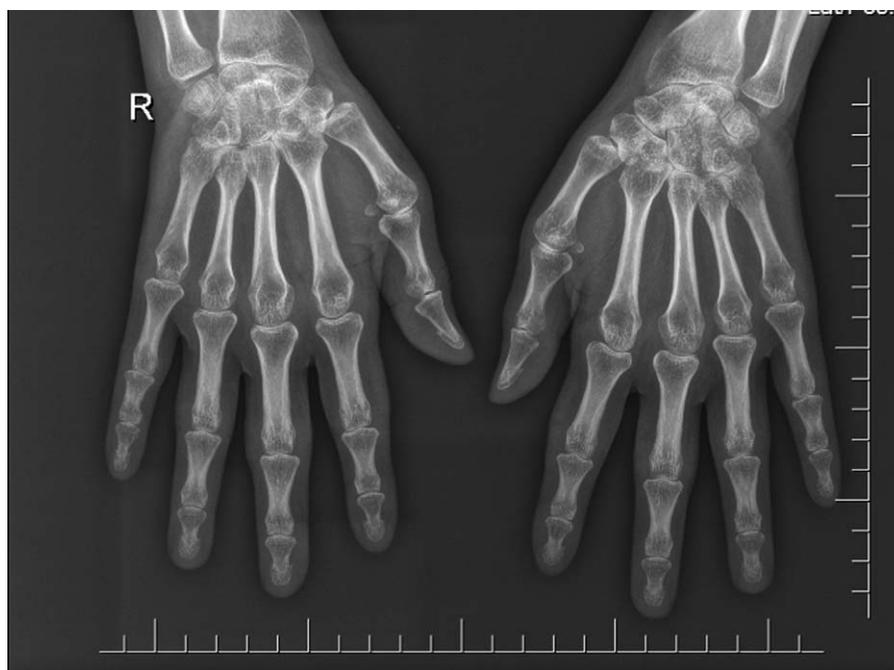


Figure 1. X-ray imaging of both hands. Joint space narrowing of the bilateral wrist and the interphalangeal joints.

anti-Sjögren's syndrome related antigen (SSA) (+++), Ro 52 (++) , RNP/Sm (+++), and ribosomal P protein (RNP) (+++). Meanwhile her acute phase reactants such as erythrocyte sedimentation rate (ESR) 47 mm/h (normal range, <15 mm/h) and C-reactive protein (CRP) 20.67 mg/L (normal range, <10 mg/L) were remarkably elevated.

Our patient fulfilled the 2010 ACR/EULAR Rheumatoid Arthritis Classification Criteria for the diagnosis of RA.^[6] She was put on methotrexate (MTX), leflunomide (LEF), and methylprednisolone (MP) 12 mg/d. In a few days of time her symptoms of swelling and tenderness in both the knees subsided. Unfortunately, MTX and LEF had to be stopped due to impaired hepatic functions. We commenced her instead on tumor necrosis factor (TNF)- α receptor antagonist which showed good therapeutic response but later on due to high cost price of TNF- α receptor antagonist, our patient could not afford regularly. She took it with iguratimod only when the symptoms relapsed.

In 2015, she suffered from interstitial lung disease. Hence, low dose of oral MP 4 to 8 mg/d and LEF 10 mg was commenced. Meanwhile, as she was planning to conceive we replaced LEF with iguratimod and TNF- α receptor antagonist 50 mg once a week. During a follow-up visit after about 6 months she complained of mild swelling and tenderness in both the knees, more frequently on right knee during warm temperatures. These symptoms aggravated more after taking MP 4 mg, then 8 mg for 2 to 3 days. An ultrasonography of her right knee showed effusion, synovial thickening, "double track sign" of articular cartilages and bilateral popliteal cysts (Fig. 2). Under polarization microscope, there was presence of birefringence needle-like crystals extracted from knee joint fluid (Fig. 3). Laboratory examination showed raised RF 47.50 IU/mL (normal range, <20 IU/mL), CRP 26.90 mg/L (normal range, <10 mg/L), and ESR 31 mm/h (normal range, <15 mm/h), but a raised uric acid 363 μ mol/L (normal range female, 178.4–297.4 μ mol/L). Hence, diagnosis of RA complicated with gouty arthritis of knee joints was established. She was commenced on colchicine, febuxostat

40 mg/d, and TNF- α receptor antagonist. In the next follow-up (about 3 years) visit, her symptoms had completely subsided and no longer recurred.

3. Discussion

The RA and gout rarely coexists in the same patient.^[7] It is considered urate crystals can block the activation of T and B cells and also possess antioxidant with antiphagocytosis properties which may contribute reducing the incidence of RA with gout. In addition, interleukin-6 in patients with RA may be able to decrease gout attack.^[8] Moreover, MTX and LEF are commonly taken by patients with RA that reduce uric acid levels also.^[9,10] A recent study has demonstrated coexistence of RA and gout are not uncommon.^[11–13] However, a study by Petsch et al claimed incidence of gout with patients with RA do exist but is lower than the general population.^[11] Meanwhile, Merdler-Rabinowicz et al. consider incidence of gout in patients with RA is not lower than the general population.^[14] Hence, both the studies differ from each other.

Uric acid deposition has been found in most patients with RA with the use of dual energy computer topography (DECT) in gout patient in recent years.^[13] RA complicated with gout have been rarely reported previously which may be attributed to following reasons: polyarthritis in patient with RA can dominate the symptoms of atypical gout; long-term use of medicine such as glucocorticoids (GCs), nonsteroidal antiinflammatory drugs (NSAIDs) can prevent gout attack; and diagnosis of atypical gout mainly relies on joint puncture to find out urate crystals in the synovium, but it is often difficult to implement in small joints. Patients with RA with gout mostly are elderly men who have high RF titer and significant level of uric acid levels in serum than those suffering for only RA.^[14,15] The patient presented in this case report is a middle aged woman with normal serum uric acid levels and lacks typical gout history. Hence, there was no proper evidence to diagnose her for having gout in the beginning.

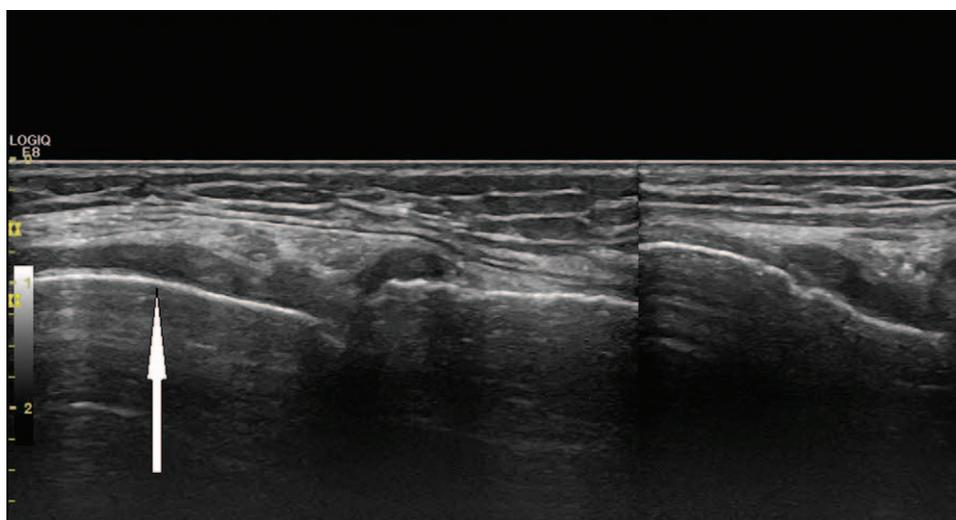


Figure 2. An ultrasonography of right knee joint. A “double track sign” of the articular cartilages (TIF).

After 6 months from discharge during a follow-up, she complained of swelling and tenderness in both the knee joints which aggravated more in warm temperatures. The symptoms relapsed even after the commencement of biologic agent. This manifestation in joints was not consistent with the features of RA. So we checked serum uric acid levels in blood which was slightly raised. Meanwhile, ultrasonography of her knees showed “double track sign,” a typical characteristic image seen in gout. Moreover, for confirmatory diagnosis of gout we extracted the synovial fluid from one of the knee joint and birefringent needle-like crystals were observed under polarization microscope. Meanwhile, the patient’s serum uric acid level was slightly raised. It may be due to: Female patients have estrogen and progesterone which can promote the elimination of uric acid such that it can maintain the normal uric acid levels; as our patient was on MTX and LEF for the treatment of RA, it is possible that MTX can inhibit synthesis of purine and increase the level of adenosine,^[9] and LEF can increase the elimination of uric acid by reducing the levels of uric acid through regulation of urate transporter in renal epithelial cells^[10]; and RF is likely to prevent the deposition of uric acid crystals. Hence, for these reasons, the

level of uric acid presents to be slightly higher, or even normal. In addition, there is usually at least one acute episode of attack that happens in majority of patients with RA with gout.^[15] However, as our patient initially denied any history of acute attack with the relapse of symptoms of swelling and tenderness over knees, we misdiagnosed for not reaching the target, clinical remission, or low disease activity.^[16] So the patient did not completely stop the treatment with GCs and other drugs. Perhaps, the reason for no attack of gout must have been associated with long term use of GCs, NSAIDs, and biologic agents.

Another interesting aspect seen in our case report is our patient complained of swelling and tenderness in both the knees especially in July, at night or in warm weather. A research has revealed increasing onset of acute gouty arthritis from March to July and highest in July. From July started to decrease till September which was recorded lowest. Moreover, autumn had a significant association with the onset of acute gouty arthritis. This physiochemical changes are associated with increased mean temperature between neighboring days may lead to the formation of monosodium urate crystals.^[17] In addition, the onset of gout in the early morning and evening is more common than daytime, possibly due to cortisol level falling to the lowest during midnight and at 4:00 AM.^[18] Furthermore, high temperature and high humid environment or a high temperature and low humid environment may cause physiologic changes or behavior associated with acute attack of gout and latter more relevant.^[19] Therefore, if joint pain is associated with season, weather, and night, we do need to rule out possibility of gout.

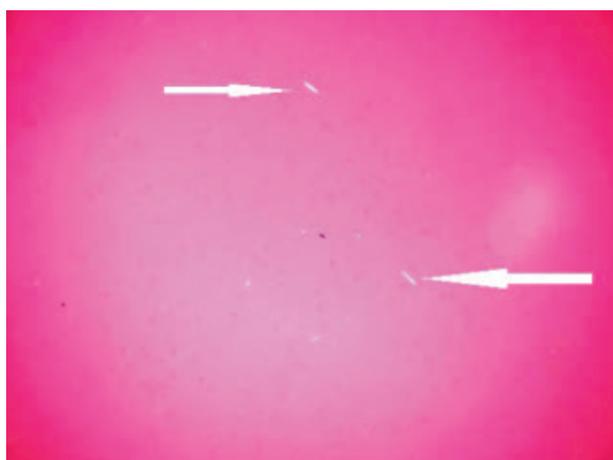


Figure 3. Positive birefringence needle-like crystals of extracted knee joint fluid.

4. Conclusion

Coexistence of RA and gout are rarely reported as it is not frequently seen in clinical scenario. We hold an opinion when patients with RA with oligoarthritis repeatedly attacked cannot meet the treat to target, a standard antirheumatism treatment, the possibility of RA complicated gout should be considered or rule out else wise. Hence, it is very important to examine the joint by DECT, and ultrasonography to detect uric acid deposition in tissue and joints and furthermore, it is wise to aspirate synovial fluid and analyze it under polarization microscope to detect urate crystals.

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Author contributions

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