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## Tenosynovitis with Rice Body Formation Due to *Mycobacterium Intracellulare* Infection After Initiation of Infliximab Therapy

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Female, 74  
**Final Diagnosis:** Tenosynovitis  
**Symptoms:** Arthralgia • pain  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Infectious Diseases

**Objective:** Rare disease  
**Background:** Rheumatoid arthritis tenosynovitis is difficult to discriminate from non-tuberculous tenosynovitis on the basis of radiological and pathological findings.


**Case Report:** A 74-year-old woman with a 4-year history of rheumatoid arthritis was referred to our hospital to undergo treatment for uncontrollable tenderness and swelling in her right third metacarpophalangeal joint, right wrist, and left knee joint. In the previous year, she underwent surgery at a local hospital for the swelling in her right metacarpophalangeal joint, the information of which was not known precisely, but the swelling subsided in due course after an operation. We treated the patient with infliximab (monthly intravenous infusions of 150 mg), but 2 months later, she complained of exacerbation of the swelling in her right third metacarpophalangeal joint and right wrist, and fluid discharge that contained *Mycobacterium intracellulare*. After synovectomy and aggressive debridement in the palmar side of the right wrist, she was diagnosed as having granulomatous tenosynovitis caused by the *M. intracellulare* infection and abundant rice body formation in the right carpal tunnel area. We considered the rice bodies inside and outside the bursa, along with a history of tenosynovitis exacerbation after initiation of infliximab therapy (tumor necrosis factor alpha inhibitor [TNFi]), to be related to the *M. intracellulare* infection.

**Conclusions:** Tenosynovitis caused by atypical mycobacteria is uncommon and usually affects the hand or wrist. Therefore, for early diagnosis, mycobacterial infection should be considered in cases of indolent chronic granulomatous tenosynovitis, especially in RA cases that recur after TNFi therapy is started.

**MeSH Keywords:** Arthritis, Rheumatoid • Granulomatous Disease, Chronic • Nontuberculous Mycobacteria • Tumor Necrosis Factor-alpha

**Abbreviations:** TNFi – tumor necrosis factor alpha inhibitor; RA – rheumatoid arthritis

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/908785>

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## Background

Tumor necrosis factor alpha inhibitors (TNFi) can increase the risk of both tuberculosis and non-tuberculous *Mycobacterium* (NTM) infections. Winthrop et al. reported that cases of NTM disease associated with TNFi therapy occur twice as frequently as cases of TB associated with TNFi therapy in the United States [1]. Another report by Winthrop et al. reported that the incidences of TNFi-associated NTM and tuberculosis were 74 (95% confidence interval [CI]: 37–111) and 49 (95% CI: 18–79) per 100 000 person-years, respectively, and most of the enrolled patients (73.7%) had rheumatoid arthritis [2]. Furthermore, the sites of infection of TNFi therapy-associated cases of NTM disease were the pulmonary region, skin or soft tissue, bone or soft joint, disseminated, and eye, in that order [2].

Patients with early- and late-phase RA often exhibit rounded rice bodies that are mainly composed of fibrin, which correspond to a history of symptomatic joint involvement [3]. However, abundant rice body formation is rarely reported in cases of tuberculosis and non-tuberculous tenosynovitis, and the most common site is inside the bursa. We report a unique case of RA with abundant rice bodies inside and outside the bursa (in the carpal tunnel area and tendon sheaths) and tenosynovitis exacerbation after the initiation of TNFi therapy, which were likely caused by *Mycobacterium intracellulare* infection. This case exhibited peculiar radiological and pathological characteristics that may be useful for diagnosing similar cases.



**Figure 1.** Right wrist swelling (A) with erosion of the radius (B, arrow).



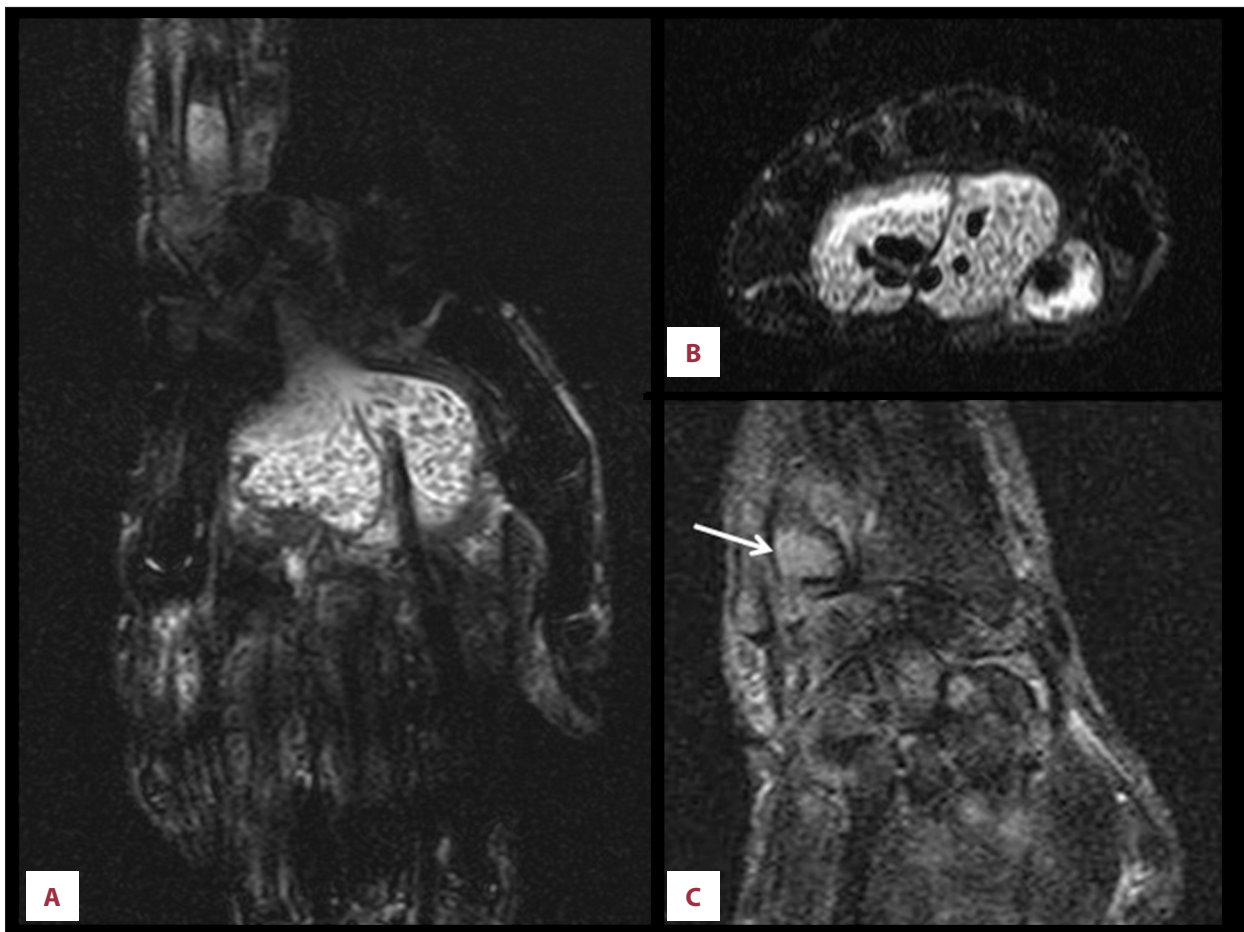
**Figure 2.** Swelling of the right middle finger (A) and right wrist (B) with an induration in the flexor side of the right wrist and palm. Serous fluid discharge from the right wrist is also visible (B, arrow). The right wrist swelling and protruding induration recurred after 5 years (C) and subsided again after 1.5 years of treatment (D).

## Case Report

A 74-year-old woman presented with a 4-year history of RA (Steinbrocker classification: class I, 1987 American College of Rheumatology classification: stage I). She sought treatment because of uncontrollable tenderness and swelling in her right third metacarpophalangeal joint, right wrist on the palmar side, and left knee joint. For the last 4 years, she had been treated with salazosulfapyridine (1.0 g/day), prednisolone (10 mg/day), and methotrexate (MTX; 6 mg/week). A physical examination revealed swelling and erythema that extended from the right wrist to the palm. The right middle finger was also swollen and edematous and had a limited range of motion. Radiography of the hands and left knee joint revealed normal findings, with the exception of the soft tissue swelling (Figure 1A) and erosion of the radius (Figure 1B, arrow). Chest radiography revealed no pathological changes. Laboratory data revealed the following values (normal range): white blood cells, 9600/mL (4000–8000/mL); erythrocyte sedimentation rate, 35 mm/h (<25 mm/h); C-reactive protein, 1.7 mg/dL (<0.3 mg/dL); and matrix metalloproteinase 3, 335 ng/mL (17.3–59.7 ng/mL). The initial disease activity score 28 using C-reactive protein levels

was 4.47, which suggested moderate activity. Therefore, we treated the patient with infliximab (150 mg once per month via intravenous infusion), in accordance with the existing guidelines for our region.

After 2 months of infliximab treatment, the tenderness and swelling in the right middle finger and right wrist significantly worsened (Figure 2). In addition, we observed a new induration in the right wrist, although the condition of the left knee improved. Furthermore, we observed fluid discharge from the right middle finger (Figure 2A, arrow) and right wrist (Figure 2B, arrow). Culture of the discharge revealed growth of *M. intracellulare*, and this result was confirmed using polymerase chain reaction testing. Around the same time, sagittal (Figure 3A) and axial (Figure 3B) T2-weighted fat-suppression magnetic resonance imaging of the right hand revealed low-intensity debris (size: 3 mm), which were consistent with abundant rice bodies in the carpal tunnel area, and high-intensity subperiosteal cystic change or intraosseous edema (Figure 3C, arrow). We diagnosed the patient as having tenosynovitis caused by *M. intracellulare* infection and performed synovectomy with aggressive debridement of the palmar side of the right wrist. Macroscopic



**Figure 3.** The sagittal (A) and axial (B) T2-weighted fat-suppression magnetic resonance images of the right hand show low-intensity debris (size: 3 mm) in the carpal tunnel area and high-intensity subperiosteal cystic change or intraosseous edema (C).

examination revealed that the flexor tendon sheath was also surrounded by abundant tiny rounded and yellow structures, which suggested the presence of rice bodies. Histological analysis revealed synovial papillary proliferation (Figure 4A, arrow) that enclosed a large quantity of fibrin (Figure 4C), which corresponded to the rice bodies (Figure 4A, asterisk), and epithelioid granulomas (Figure 4B). Specimens from the resection provided a positive culture and polymerase chain reaction results for *M. intracellulare*. After the debridement, we treated the patient with rifabutin (450 mg/day), ethambutol (750 mg/day), and clarithromycin (800 mg/day) for 6 months, which improved her clinical condition. She was subsequently discharged. Regarding the RA treatments, 2 months after the operation, she had arthralgia due to exacerbation of RA activity; thus, she was treated again with prednisolone (5 mg/day), MTX (6 mg/week), and salazosulfapyridine (2000 mg/day). In addition, TNFi therapy was discontinued just before the operation and never used again throughout the clinical course. However, 5 years later, the tenosynovitis recurred with protruded swelling of the right wrist joint (Figure 2C) and fluid discharge that was positive for *M. intracellulare*. Therefore, we replaced the MTX with

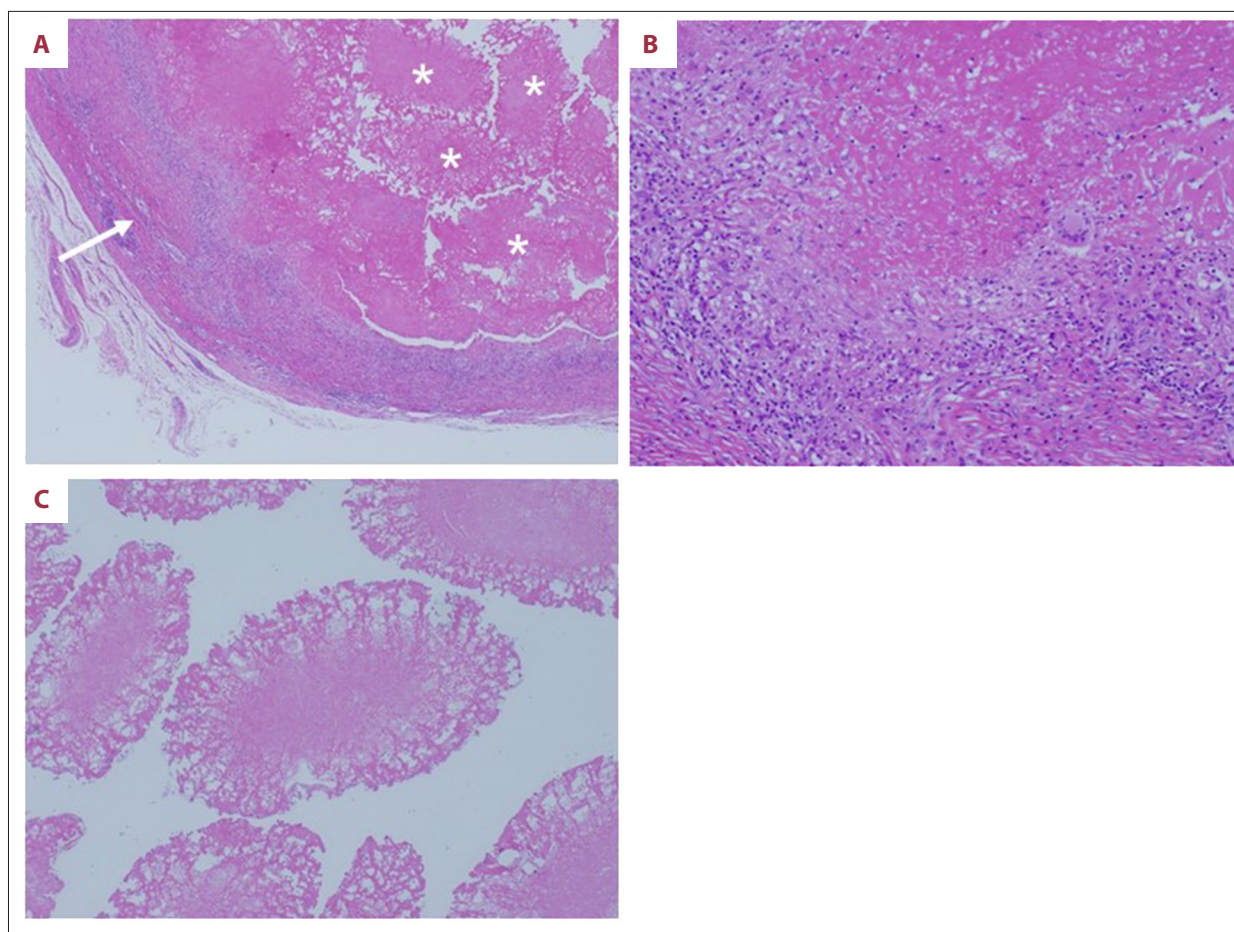
oral iguratimod (25 mg/day) and restarted the rifabutin, ethambutol, and clarithromycin therapy, which was continued for 1.5 years. We did not observe any microbiological and clinical signs of recurrence during follow-up (Figure 2D).

## Discussion

We present a rare case of granulomatous tenosynovitis caused by *M. intracellulare* infection in a patient with RA. The clinical features of atypical *Mycobacterium* tenosynovitis are pain and tendon sheath swelling, although the disease is initially indolent and insidiously destructive [4], as in the present case. In addition, this tenosynovitis has a predilection for the flexor tendons of the fingers, palm, wrist, and forearm, while atypical *Mycobacterium* infections of the hand are uncommon. Furthermore, >50% of the reported cases have involved *M. marinum*, followed by *M. kansasii* and *M. avium* complex [5].

Rice bodies that were mainly composed of fibrin have been reported in cases of tuberculous infection, RA, and seronegative





**Figure 4.** The histological analysis result shows synovial papillary proliferation (A, arrow) that enclosed a large quantity of fibrin (A, asterisk) and epithelioid granulomas (B) with inflammatory cell infiltration. The abundant rice bodies from the debridement specimens exhibit a reticular structure that was mainly composed of fibrin (C).

inflammatory arthritis [6]. However, abundant rice body formation is rare in both tuberculous tenosynovitis [6] and non-tuberculous tenosynovitis [7,8]. RA tenosynovitis is difficult to discriminate from non-tuberculous tenosynovitis on the basis of radiological and pathological findings. Moreover, rice bodies in patients with RA are typically observed in the subacromial bursa and are rarely observed outside the bursa (e.g., in the tendon sheaths) [6]. In the present case, we observed abundant rice bodies inside and outside the bursa (i.e., in the tendon sheaths), which indicates that these findings were related to *M. intracellulare* infection rather than RA tenosynovitis.

The risk of infectious tenosynovitis is increased among patients with RA, mixed connective tissue disorders, diabetes mellitus, solid organ transplants, steroid medication, cancer, previous trauma, surgical procedure, and non-apparent inoculation (e.g., water contamination) [9,10]. To the best of our knowledge, only 4 reports/7 cases of infectious tenosynovitis after the initiation of TNFi have been described [11–14] (Table 1). In our review, we found that the time from onset to

diagnosis ranged from several months to >3 years, and most cases required multiple surgeries. Surgical debridement is essential for treating infectious tenosynovitis, although the importance and optimal duration of antimycobacterial chemotherapy for mycobacterial tenosynovitis are unclear, as some infections are cured using surgery alone [15].

Curtis et al. [14] reported that the risk of infection is similar for TNFi and prednisone doses of >10 mg/day. In this context, our patient had been receiving MTX and prednisolone (10 mg/day), although her disease onset had not been precisely defined. Curtis et al. also found that TNFi treatment was associated with a 1.9-fold higher risk of infection than with MTX alone and that the incidence of infection increased by 4-fold within 6 months after initiation of TNFi therapy [16].

In summary, our case exhibited infectious granulomatous tenosynovitis caused by *M. intracellulare* infection after TNFi therapy was started, which presented as characteristic abundant rice bodies in the carpal tunnel area. This case is important

**Table 1.** Infectious tenosynovitis after treatment for rheumatoid arthritis using tumor necrosis factor alpha inhibitors: a summary of the reported cases.

Year	M/F	Age	Underlying disease	Time from onset to diagnosis	Biologics	Other drugs	Pathogen	Operations (times)	Treatment
2010	F	82	Psoriatic arthritis	NA	Infliximab	MTX	<i>Enterobacter cloacae</i> $\alpha$ -hemolytic streptococci mycobacteria	3	ST, AZM
	F	59	RA	3 years	Etanercept	MTX corticosteroid injection	<i>Staphylococcus aureus</i> <i>Mycobacterium mucogenicum</i>	3	RFB, CAM, LVFX
	M	65	Seronegative RA	< Several months	Etanercept Infliximab	Prednisone MTX plaquenil	<i>Mycobacterium marinum</i>	3	AZM, EB, CAM
2010	F	47	RA, lupus, pulmonary <i>M. kansasii</i>	< Several months	Etanercept Infliximab	Prednisone	Unknown	2	CAM, linezolid, moxifloxacin
	F	77	RA	< Several years	Infliximab	Plaquenil, MTX	<i>Scedosporium apiospermum</i>	<3	Voriconazole
2008	F	48	Seronegative RA	<3 years	Leflunomide	MTX corticosteroid injection	<i>Mycobacterium kansasii</i>	3	RFP, CAM, EB
2002	M	61	RA	>4 months	Etanercept Infliximab	Corticosteroid injection	<i>Mycobacterium marinum</i>	1	CAM

NA – not available; RA – rheumatoid arthritis; MTX – methotrexate; ST – trimethoprim/sulfamethoxazole; AZM – azithromycin; RFB – rifabutin; CAM – clarithromycin; LVFX – levofloxacin.

because there are few previous reports of tenosynovitis caused by non-tuberculous mycobacteria infection [17].

## Conclusions

A mycobacterial origin should be considered for patients who present with indolent chronic granulomatous tenosynovitis,

especially in cases that recur after treatment with disease-modifying antirheumatic drugs and/or TNFis.

## Conflicts of interest

None.

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