

# Nontuberculous Mycobacterial Tenosynovitis of the Hand: A 10-Year Experience at Two Centers in South Korea

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**Background**: The aim of this study was to investigate the clinical characteristics of nontuberculous mycobacterial tenosynovitis and to report the process of diagnosis and the outcomes of surgical debridement and drug administration in South Korea. **Methods**: Between 2010 and 2019, 23 patients (10 men and 13 women) with nontuberculous tenosynovitis of the hand were treated at two centers. Their average age was 64 years, and the average duration of symptoms was 8 months (range, 1–36 months). Eight patients had a history of trauma or surgery. The average number of corticosteroid injections before diagnosis was 2.6 for 7 patients. All 23 patients were treated with a combination of extensive tenosynovectomy and antibiotics.

**Results:** Of the 23 patients, 20 were available for the final follow-up (1, lost to follow-up; 1, transferred to another hospital; and 1, died from a comorbidity). The most common species was *Mycobacterium intracellulare* (70%), followed by *Mycobacterium abscessus* (10%). The frequency of involvement of the extensor/flexor tendon was similar to that of the wrist/finger. The mean number of surgical debridement operations was 2.2. The average duration of antibiotic administration was 9.8 months. At the last follow-up, 3 patients were symptom-free with full range of motion at the involved site, 1 patient complained of localized swelling or pain with full range of motion, 1 patient was found to have a recurrence of infection in a finger, and 15 complained of restricted joint motion. **Conclusions:** The most common species noted in patients with nontuberculous mycobacterial tenosynovitis was *M. intracellulare*. Patients with only 1 finger involved showed good range of motion at the final follow-up. Most patients experienced delayed wound healing and adverse effects from drug therapy during treatment and limited joint motion at the final follow-up. **Keywords:** *Tenosynovitis, Non-tuberculous, Infection, Hand* 

Tenosynovitis of the hand caused by nontuberculous mycobacteria (NTM) is a relatively rare chronic disease with slow progression.<sup>1,2)</sup> Its clinical manifestations are variable, ranging from painful swelling to carpal tunnel syndrome. Therefore, tenosynovitis caused by NTM can be difficult

Received July 27, 2022; Revised December 15, 2022; Accepted December 15, 2022 Correspondence to: Jin Sung Park, MD Department of Orthopedic Surgery, Yeson Hospital, 206 Bucheon-ro, Bucheon 14555, Korea Tel: +82-32-717-1638, Fax: +82-32-656-8274 E-mail: jsparkler1@gmail.com to distinguish from rheumatoid arthritis or other more common diseases, resulting in delayed diagnosis.<sup>3-5)</sup> Diagnosis of NTM tenosynovitis is achieved through a tissue culture of the affected site.<sup>6,7)</sup> Treatments include medication alone or combined with surgery. Unfortunately, the clinical prognosis of the disease is poor. For these reasons, it is important to recognize and treat NTM tenosynovitis as early as possible.<sup>6,8)</sup> The culture process for NTM is complicated, and the time required to confirm the specific bacterium depends on the hospital and its processes.<sup>9)</sup> Even after surgery, patients often have ongoing pain, problems with wound healing, swelling, and activity limitations that can interfere with their continued compliance with

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treatment.<sup>7)</sup>

NTM tenosynovitis of the hand takes time to satisfactorily respond to treatment, and much depends on the clinician's experience. Because bacterial strains vary by region, drug selection also differs by location. In this study, we retrospectively reviewed patients diagnosed with NTM tenosynovitis of the hand at two centers in South Korea to discuss their characteristics, treatment process, and outcomes of atypical mycobacterial infections that manifested as tenosynovitis of the hand.

### **METHODS**

Data for 23 patients who were treated at two centers (Gyeongsang National University Hospital and Samsung Changwon Hospital) for tenosynovitis of the hand caused by culture-proven NTM infection between March 2010 and March 2019 were analyzed retrospectively. This study was approved by the Institutional Review Board Committees of the Medical Research Institute of Gyeongsang National University Hospital (No. GNUH 2020-07-007) and Samsung Changwon Hospital, Sungkyunkwan University School of Medicine (No. SCMC 2020-12-001). The requirement for informed consent was waived owing to the retrospective nature of the study. The study population contained 10 men and 13 women, who had a mean age of 64 years (range, 30–84 years) at the time of their initial visits. The mean duration of the disease at the time of the first visit was 8.5 months. The patients were interviewed for their history of trauma, corticosteroid injections, or any occupation or hobbies associated with water exposure (including the sea, aquariums, or soil), according to the defined risk factors of NTM infection.<sup>4,7,9)</sup> Radiographs were obtained for all patients. Some patients also underwent preoperative ultrasound or magnetic resonance imaging (MRI). We evaluated the following laboratory findings obtained during their initial visits to our hospitals: white blood cell count, serum erythrocyte sedimentation rate, C-reactive protein, and rheumatoid factor concentrations. The detailed demographic characteristics of the patients are summarized in Table 1.

The treatment protocol comprised extensive debridement, including removal of the synovial membrane, and the administration of antimycobacterial drugs. Proliferative tendon synovitis was excised, and tenolysis was performed. Carpal tunnel decompression was performed simultaneously when there was extensive infection of the flexor tendon from the hand to the wrist. Tissue samples showing signs of inflammation or infection during surgery were examined microbiologically and histologically. Hematoxylin and eosin staining and fungal staining were performed to identify the microbial strain. Auramine-rhodamine fluorochrome (AFB) staining was performed for fluorescence microscopy to detect *Mycobacterium tuberculosis*. For the histopathological examinations, formalinfixed tissue was embedded in paraffin and stained with hematoxylin and eosin for the initial diagnosis.

For the microbiological assessment, aerobic, anaerobic, bacterial, and fungal cultures were prepared using surgically excised tissue. Mycobacteria were cultured in Mycobacteria Growth Indicator Tube medium (Becton Dickinson) and 3% Ogawa medium (Asan Pharmaceutical) at 36 °C. In hospital A, 19 types of mycobacteria, including *M. tuberculosis*, were detected using the Reverse Blot Hybridization Assay with MolecuTech REBA Myco-ID (Youngdong Pharmaceutical) in media. In hospital B, data were obtained from the Korean Institute of Tuberculosis (Osong) because no internal mycobacteria identification test was available until 2018. Both centers hired an external institution to conduct drug susceptibility tests. Once the pathogen was confirmed to be NTM, we initiated antimycobacterial drug administration in consultation with the department of infectious diseases. However, for 13 patients clinically suspected of NTM by a physician based on their medical history, physical examination, biopsy, AFB staining, or a polymerase chain reaction (PCR) test, empirical anti-tuberculosis drug combination therapy was initiated (in consultation with the department of infectious diseases) before the results of the NTM culture were obtained. For those patients, empirical administration was initiated by selecting anti-tuberculosis drugs, such as HREZ (isoniazid, ethambutol, rifampin, pyrazinamide), clarithromycin, and amikacin before confirming the species of NTM.

Antituberculosis drug therapy for NTM was maintained until 3 months after clinical symptoms disappeared. For patients whose clinical symptoms did not disappear over 3 months or complained of severe adverse effects, we considered a change of drug regimen. In some cases, we took an MRI in the middle of treatment and compared the size of the lesion with that in previous MRI. If the drug regimen was changed, the drug treatment was prolonged beyond 3 months. After combination therapy, patients were followed for at least 6 months to check for recurrences. The clinical results, such as range of motion, recurrence of infection, and complications, were recorded at the final follow-up. If patients had no restrictions in the movement of the affected joints, range of motion was classified as excellent; if the total range of motion was more than 50%, it was classified as good, and if it was less than 50%, it was classified as poor.

	Period of follow- up (mo)	7	23.3	12.8	39.1		17.8	31.8	27.6	
	Out- come*	Excellent	Poor	Excellent	Good	Death: sepsis	Excellent	Poor	Finger: good, good	Transfer
	Compli- cations of medication	G-l trouble, optic neuritis	Urticaria, retino- pathy	None	Itching	None	Hepatitis	Amikacin induced hearing loss, cytopenia	None	None
	Period of anti- tuberculosis medication	ത	J	9	J	2	æ	24	3	9
	Confirmative medication	CRE + SM	CAM + RFP + SM	CRE	Cipro + CAM + EMB + SM/A	CRE	CRE	$\begin{array}{l} CRE \to Az + \\ RFP + EMB \\ + MOxi \to A \\ + Az + EMB \\ + MOxi + \\ CAM \to Az \\ CAM \to Az \\ + MOxi + \\ CAM \to CR \\ + Moxi \end{array}$	$Az + EMB + RFP + A \rightarrow -A \rightarrow +$ clofazimine + Linezolid $\rightarrow CRE$	CAM + EMB
	Empirical medication (before NTM identi- fication)		HERZ		HER + Levo				Az + EMB + RFP	RFP ± CAM ± RFP ± Moxi ± EMB ± A
	Duration of wound closure (wk)	4	24	2	en	т	16	5	m	5
	Number of operation	2	2	-	2	-	<del>~</del>	4	-	<del>~</del>
۲۵ ۲۵ ۲۵	NTM AFB PCR stain					+ 2+	+ 2+	+	+	
	NTM Identifi- cation period (wk)	ດ. ເ	3.3	3.3	3.9	2.7	3.9	2.3	2.9	9
synovitis	Species of tuber- culosis	Mycobac- terium intra- cellulare /MRSA	M. intra- cellulare /MRCNS	M. intra- cellulare	M. intra- cellulare	M. kansasii	Mycobact- erium massi- liense	M. intra- cellulare	M. intra- cellulare	M. intra- cellulare
terial Tenc	Involved tendon	Extensor	Flexor	Flexor	Flexor	Flexor	Extensor	Flexor	Flexor	Extensor
cobaci	uration of ymptom (mo)	-	~	с	വ	-	7	Q	~	2
ulous Mu	D Involved site s	Lt finger	Lt finger	Lt finger	Lt finger	Rt finger	Rt wrist	Lt finger	Rt finger (& wrist joint)	Rt wrist
ntubero	Steroid njection (time)	<b>က</b>	0	0	0	0	က	ى ا	0	0
nts with No	Trauma Hx/ operation Hx (within 6 mo)	Laceration	1 & D	Acupuncture	,				0 8 D	
the Patie	Occu- pation	House- wife	Tailor	House- wife	None	None	Fisher related	House- wife	Driver	Farmer
ography of	Underlying disease	HTN, DM, MI, CKD, hypothy- roidism, CHF	Thyroid Ca	,	MQ	HTN, DM, CKD, glomerulo- sclerosis	NTH		NTM flexor tenosyno- vitis wrist Rt (3 yr ago)	Aneurysm
Derm	Age (yr)	64	61	60	75	69	64	12	65	72
le 1.	Sex	ш	LL.	ш	Σ	Σ	Σ	щ	Σ	ш
Tab	Case	<del>-</del>	2	ę	4	ъ	9	~	ω	ത

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	Period of follow- up (mo)	10.1	14	16.9	31.9	69.8	12		17.1
	Out- come*	Swelling, excellent (finger: -)	Poor	Excellent (finger: good)	Wrist: -, 5th finger: good	1, 3, 5th finger: poor, 2, 4th finger: good	Wrist: good, finger: good	Follow-up loss	Wrist: -, 1st finger: poor
	Compli- cations of medication	None	Diarrhea, skin rash, multiple arthralgia	Leukopenia	Gl trouble, optic neuritis, leukopenia	None	Leukopenia	None	G-I trouble
	Period of anti- uberculosis medication	2	Q	12	12	Ð	Q	Q	2
	Confirmative medication	CRE	$\begin{array}{l} A + Mox + Az \\ \rightarrow A + CAM \end{array}$	$\begin{array}{l} CAM + Moxi \\ + RFP \to Az \\ + HOxi \to \\ Az + Moxi + \\ EMB \to Az \\ + EMB \end{array}$	$\begin{array}{l} \text{CRE} \rightarrow \text{RFP} + \\ \text{CAM} \rightarrow \text{RFP} \\ + \text{EMB} + \text{Az} \end{array}$	CRE	CAM + Moxi + RFP → CAM + EMB	CAM + RFP + Levo	$\begin{array}{l} SM + \text{RFP} \\ + \text{CAM} \rightarrow \\ SM + \text{CAM} \\ + \text{Cipro} \rightarrow \\ Az + \text{RFP} + \\ \text{EMB} \end{array}$
	Empirical medication (before NTM identi- fication)		HERZ + Az	HREZ	HREZ			HREZ	CAM + Moxi
	Duration of wound closure (wk)	ო	с С	4	ო	14	ო	2	44
	Number of operation	~	5	4	с С	~	<del>~</del>	2	с <b>л</b>
	AFB stain					<del>,+</del>		<del>,+</del>	<del>,+</del>
	PCR								
	NTM Identifi- cation period (wk)	ი	ω	ى ك	m	ი	4	2	6.5
	Species of tuber- culosis	M. intra- cellulare	Mycobac- terium absce- ssus	M. intra- cellulare	M. intra- cellulare	M. intra- cellulare	M. intra- cellulare/ MSSA	Mycobac- terium szulgai	Mycobac- terium marinum, Mycobac- terium ulcerans
	Involved tendon	Extensor	Extensor	Flexor	Flexor	Flexor	Flexor	Flexor	Extensor
	Juration of ymptom (mo)	~	-	24	ന	36	Q	2	<del>~</del>
	I Involved site s	Lt wrist	Rt finger, joint	Rt wrist	Lt wrist	Rt wrist	Rt finger	Lt finger	Lt wrist
	Steroid njection (time)	0	~	0	0	2	-	0	<del>~</del>
	Trauma Hx/ operation Hx (within 6 mo)	1				Penetrating injury (wood)		Fasciotomy	Superficial openwound
	Occu- pation	None	Chef	House- wife	Farmer	Farmer	Farmer	Industry worker	Farmer
unea	Underlying disease	HTN, old pulmonarty TB, asthma, AI, gouty arthritis	Lung Ca, stroke, pulmonary TB	HTN		1	N	·	DM, COPD, lung Ca
COUL	Age (yr)	84	48	20	74	66	75	30	70
е.	Sex	Σ	ш	ш	ш	ц	ш	Σ	Σ
9	Case	10	7	12	13	14	15	16	17

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lable	. Con	itinued																		
Case Se	x Age (yr)	u Underlying disease	Occu- pation	Trauma Hx/ operation Hx (within 6 mo)	Steroid injection (time)	l Involved site s	Duration of symptom (mo)	Involved tendon	Species of tuber- culosis	NTM Identifi- cation period (wk)	PCR st	.FB Nu ain ope	imber 0 of of sration 0	Juration f wound closure (wk)	Empirical nedication (before JTM identi- fication)	Confirmative medication t	Period of anti- uberculosis medication	Compli- cations of medication	Out- come*	Period of follow- up (mo)
18 F	54	1	Farmer	A1 pulley release	0	Rt finger	~	Flexor	M. intra- cellulare/ Candida parap- silosis	ω	+	<u>+</u>	ო	7	Levo + CAM + EMB + A	CRE→CAM + Moxi	2	Hepatitis	Good	58.5
19	55	MQ	Fisher	1 & D	0	Lt wrist (Mp joint)	18	Extensor	species	~	+	<u>+</u>	ω	2	HREZ → CRE	CRE	24	Optic neuritis	Wrist: -, 1st: poor, 2, 3, 4, 5th: good	32.6
20 F	64	1	House- wife		0	Rt wrist	വ	Extensor	M. absce- ssus	1.4		<u>+</u>	4	2	HR + CAM	A +Az	G	G-l trouble, skin rash	Wrist: -, 2nd: excellent, 3, 4, 5th: good	33.1
21 N	1 67	DM, HTN	Farmer		0	Rt finger	12	Extensor	Mycobac- terium gordonae	6.4			-	13.5	HREZ + CAM	CRE	ω	G-I trouble	Good, recur- rence	62.4
22 N	99	TB synovitis	Farmer	,	0	Rt wrist	24	Flexor	M. intra- cellulare	6.8			с	2		CRE	12	Itching	Stiffness	19.8
23 F	61	HTN	Oyster shu- cker	,	7	Rt finger, joint	12	Extensor	M. intracell- ulare	ω			-	2		CRE	11.5	G-I trouble	Poor	23.4
Hx: history failure, Lt: negative s azithromyc *Excellent:	, NTM: left, MI aphyloc in, Moxi full ran	nontuberculous RSA: Methicillin- coccus, HERZ: ist i: moxifloxacin, T ae of motion. Go	mycobacte -resistant 5 oniazid + e B: tubercul od: > 50%	ria, PCR: polym taphylococcus thambutol + ri osis, COPD: ch range of motio	nerase cha aureus, CF (ampin + p ronic obstr n. Poor: < 5	in reaction, RE: clarithro yrazinamide uctive pulmo 50% range o	AFB: aura mycin + ri , CAM: cl mary dise f motion.	amine-rhodar ifampin + etl larithromycin ease, Mp: me	mine fluoroch nambutol, SN , RFP: rifamp tacarpal phal	rome, HTN: I: streptomy in, HER: isoi angeal.	hyperter cin, -: no niazid +	nsion, DN o data: G ethambut	M: diabeti -I: gastroir tol + rifam	c mellitus,   ntestinal, C: npin, Levo:	MI: myocardia a: cancer, I&D levofloxacin, C	al infarction, CK 1: incision and d Cipro: ciprofloxa	D: chronic kidl rainage, MRCI cin, EMB: eth	ney disease, C NS: Methicilli ambutol, A: ar	HF: congesti 1-resistant co nikacin, Rt: r	ve heart bagulase ight, Az:

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### RESULTS

The most common symptoms were swelling and pain in the affected hand. The affected area was the flexor tendon in 14 patients and the extensor tendon in 9. A finger was affected in 13 cases, 9 of which showed tenosynovitis of the flexor tendon. The wrist was affected in 10 cases, 7 of which showed tenosynovitis of the extensor tendon (Table 2). Two patients experienced rupture of the extensor tendon before surgery. Three patients had a history of trauma to the affected area, 4 underwent surgery within 6 months before their initial hospital visit, and 1 underwent acupuncture treatment. Seven of the 21 patients received a mean of 2.6 local corticosteroid injections before visiting a study hospital.

Diagnosis of infection was confirmed by clinical examination and bacterial culture of tissue from the tendon sheath. In 2 cases, we had to perform a second histological examination because no bacterial growth was detected despite a high likelihood of NTM infection. Positive NTM results were obtained with AFB staining in 8 patients and with PCR in 6 patients. All patients underwent extensive tenosynovectomy and biopsy, though the results of 2 biop-

Table 2. Clinical and Laboratory Characteristic	s of 23 Patients
Factor	Value
Male: female (case)	10 : 13
Mean age (yr)	64
Infected site (right : left) (case)	13 : 10
Involved site	
Extensor : flexor	10 : 13
Finger : wrist	13 : 10
Average duration of symptom (mo)	8
Trauma history (case)	3
Operation history (case)	4
Steroid injection history (case)	7 (2.6 times)
Wound closure duration (wk)	7.02
Average number of surgical procedures	2.2
Laboratory finding (average)	
WBC count (× $10^3/\mu$ L)	7.4
CRP level (mg/L)	12.5
ESR (mm/hr)	30.4

WBC: white blood cell, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate. sies were misplaced. Histological examination confirmed chronic granulomatous inflammation with necrosis in 5 patients and chronic granulomatous inflammation with caseous necrosis in 12. The remaining patients showed nonspecific chronic granulomatous inflammation. The results of the cultures revealed that Mycobacterium intracellulare infection was the most common (15 patients), followed by Mycobacterium abscessus infection (2 patients) (Table 3). Mixed infections caused by several microbes were observed in 5 patients (19.5%). The organisms involved in these mixed infections included Candida, methicillin-resistant coagulase-negative staphylococci, methicillin-resistant Staphylococcus aureus, and methicillin-sensitive S. aureus (Table 3). After the NTM-positive culture and susceptibility results became available, triple combination therapy (rifampin, clarithromycin, and ethambutol or streptomycin) or another corresponding therapy (azithromycin or amikacin) was administered after consultation with the department of infectious diseases.

The mean number of surgeries performed per patient, including the initial surgery performed at the 2 centers, was 2.2 (range, 1–8). The mean duration of treatment was 9.8 months (range, 2–24 months). The most common side effect of the medication involved the gastrointestinal system in 6 patients, followed by ethambutol-induced

Table 3. Microbiological Characteristics of 21 Patients					
Characteristic	Number				
Mycobacterium species					
M. intracellulare	15				
M. abscessus	2				
M. marinum, M. ulcerans	1				
M. massiliense	1				
M. szulgai	1				
M. gordonae	1				
M. kansasii	1				
Unclassified	1				
Coinfection					
Candida	1				
MRCNS	1				
Staphylococcus aureus	1				
MRSA	2				

MRCNS: methicillin-resistant coagulase negative staphylococcus, MRSA: methicillin-resistant *Staphylococcus aureus*.

optic neuritis in 3, and retinopathy in 1. In 4 other patients, hematopoietic disorders, such as leukopenia, were observed. One patient complained of hearing loss induced by amikacin (Fig. 1). Two patients with extensor tendon rupture showed extension lag at the final follow-up and refused additional surgery. The condition of 1 patient (patient no. 19) progressed to septic arthritis of the second metacarpophalangeal joint, for which arthrodesis of the second metacarpophalangeal joint was performed (Fig. 2). One patient (patient no. 23) also progressed to septic arthritis and osteomyelitis of distal phalangeal joint, for which arthrodesis was performed. Patient no. 21 complained of pain and extension lag after 5 years and 5 months, which suggested a recurrence of NTM infection. He refused further evaluation and closed follow-up.

Of the 23 patients, 1 died of a comorbidity during treatment, 1 was lost to follow-up, and 1 was transferred to another hospital. The mean follow-up duration was 29.41 months (range, 10–81 months) for the remaining 20 patients. The mean follow-up period after the end of medication was 24.1 months. At the last follow-up, 3 patients were symptom-free with full range of motion at the involved site, 1 patient complained of localized swelling or pain with full range of motion, 1 patient was found to have a recurrence of infection in a finger, and 15 complained of restricted joint motion (Table 4). Excellent and good ranges of motion were maintained in more than 60% of the patients whose infections affected only a finger. In some patients infected at the wrist, the range of motion of the wrist

joint could not be confirmed due to insufficient charting. However, the range of motion of the fingers and wrists of patients with wrist infections varied as described in Table 5.



**Fig. 2.** A 55-year-old male patient with a history of repeat surgery (for tuberculosis infection) complained of swelling of the dorsal side of the wrist and deformity of the second metacarpophalangeal (MP) joint. We performed synovectomy of an infected extensor tendon and debridement of the MP joint. He was diagnosed with non-classified nontuberculous mycobacteria infection. (A) Initial radiologic image showing significant joint space narrowing and subluxation of the second MP joint. (C) Radiologic image showing union of the second MP joint.



Fig. 1. (A) A 71-year-old female patient with a history of repeated steroid injections complained of finger edema that began 1 month ago. (B) Ultrasonography showed synovial hypertrophy around the flexor tenon. (C) A synovectomy was performed initially. (D) During treatment, the drug was changed due to cytopenia and hearing loss, and a second synovectomy was performed due to relapse in the third finger and wrist. (E, F) At 18 months of relapse, tendon excision was performed, followed by 6 months of additional medication, total 24 months of medication. At final follow-up, there was no evidence of recurrence with limited range of motion.

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# Table 4. Duration of Anti-tuberculosis Medication and Final Outcomes

Variable	Valua
Vallable	value
Mean duration of antibiotic treatment (mo) (n = $18$ )	9.75
≤ 6 mo (case)	6
7–12 mo (case)	11
> 12 mo (case)	3
Outcome (case)	
Follow-up loss	3
Symptom-free with full ROM	3
Localized swelling with good ROM	1
Limited ROM	15
Amputation	0
Recurrence of infection	1

ROM: range of motion.

### DISCUSSION

In this study, M. intracellulare-induced infection was observed in about 70% of patients. NTM are environmental microorganisms that can be found globally,<sup>10,11)</sup> with more than 200 species identified. The distribution of NTM species and incidence of NTM infection show regional differences.<sup>12)</sup> Among the cases of tenosynovitis reported, Mycobacterium marinum infections are the most common, followed by Mycobacterium kansasii and Mycobacterium avium infections.<sup>4,8,13,14)</sup> Unlike previous reports, the culture results in this study show that infection with M. intracellulare was most common, observed in 15 patients, followed by M. abscessus in 2 patients. M. intracellulare infection was also more common in two other studies of NTM tenosynovitis in South Korea.<sup>9,15)</sup> The centers in which this study was conducted are both located in cities within 1 hour of ports, farmlands, and factory sites and do not show a bias regarding the causative environmental factors associated with NTM infection. In a recently published paper, M. intracellulare accounted for about 50% of NTM infections in Korea.<sup>16)</sup> Therefore, we cautiously suspect that *M. intracellulare* is the most common species of NTM causing tenosynovitis in our country, based on previously reported literature and our findings.

Several important risk factors for NTM tenosynovitis are trauma, surgery, corticosteroid injections, and marine-related activities such as handling fish.<sup>4,7,17)</sup> In our

#### Table 5. Outcomes of Range of Motion at Final Follow-up Total range of motion Involved site Excellent Good Poor Insufficient No (50%-75%) (>75%) (< 50%) chart record 2 5 4 Finger Wrist 3 1 5

study, 3 patients had a history of trauma, and 4 had a history of surgical treatment before their diagnosis of NTM infection. Those surgeries were performed to treat symptoms such as triggering or swelling in the infected area. Repeated corticosteroid injections in patients with no history of trauma are also suspected as a cause of infection.<sup>4,18</sup> In the current study, 7 patients received corticosteroid injections for hand symptoms before their first visits to the study hospitals. Therefore, physicians should suspect NTM infection in patients who have a history of trauma or repeated steroid injections if their symptoms do not improve with conventional treatment.

The treatment of NTM tenosynovitis includes drugs, surgery, or a combination of the two.<sup>1,3,4)</sup> Chow et al.<sup>19)</sup> insisted on using only anti-tuberculosis drugs for NTM tenosynovitis because extensive tenosynovectomy forms a wide scar, after which wound recovery is very slow and often causes movement limitations. Most cases or papers published since then have reported using a combination of anti-microbial drugs and surgery because NTM tenosynovitis is a deep invasive infection.<sup>1,2,8,13,15,17,20-23)</sup> Synovectomy significantly reduces the volume of infected tissue, decreasing the residual infection that must be removed by the drug.<sup>1,3,5)</sup> Some authors have argued that extensive synovectomy will shorten the duration of drug treatment and help prevent adverse drug effects.<sup>1,19)</sup> Although the appropriate duration of drug therapy in NTM is unclear, a minimum of 3-6 months is recommended, depending on the clinical findings. Gunther and Levy<sup>5)</sup> argued that drug therapy should be maintained for 3-4 months after complete resolution of clinical symptoms.<sup>1,5)</sup> According to a review of the literature, combined antibiotic treatment should be continued for at least 6 months; however, more than 12 months is unnecessary because a longer treatment period does not appear to reduce the possibility of negative outcomes.<sup>8)</sup>

The diagnosis and treatment of NTM infection depend on the following three factors: strong clinical suspicion of infection, medical drug treatment, and suitability of the patient for surgical treatment. The biggest problems

we encountered while treating NTM infections were difficulty in detecting bacteria and delay in drug treatment after surgery due to the nature of the bacteria and the low positivity rates in AFB and PCR testing. In our study, hospital A identified the strains within 1 week by performing an internal identification test. However, hospital B took an additional 4 weeks (beyond the minimal culture period) due to use of an external vendor for bacterial identification. For this reason, anti-microbial drugs were administered first in cases in which NTM infections were suspected clinically or chronic granulomatous necrosis was observed histologically in the presence of a positive NTM, PCR or AFB staining result. We support aggressive treatment because tuberculosis infection is endemic in our country, and cases of NTM infection are on the rise.<sup>24)</sup> It is preferable to initiate anti-tuberculosis treatment empirically, such as rifampin, ethambutol, or clarithromycin, if 2-3 months are required to obtain a microbiology test report. However, if the hospital can obtain such reports quickly and internally, it seems reasonable to wait for culture results to select a drug.

In addition, an in-depth consultation is required to increase patient compliance because patients might lose trust in their physician if swelling or symptoms persist postoperatively. In our study, it took an average of 7 weeks for the surgical wound to heal. For 3 patients, wound dehiscence occurred within 3 months or swelling persisted postoperatively. In many cases, patient compliance declined due to persistent swelling or incomplete healing of the surgical site during the first 2 to 3 months. Furthermore, most patients (15/18) complained of adverse effects from the accompanying drugs, which are thought to be the significant reasons for reduced drug therapy compliance. To improve compliance, periodic monitoring during treatment is essential. It is important to help patients understand through regular face-to-face consultations that slow healing does not indicate treatment failure. Patients should be educated about the gradual and prolonged process of recovering from NTM infection.

Most previous papers reported cures, but they did not report results showing patients' range of motion or pain and swelling in the affected area.<sup>2,8,18-20)</sup> In our study, patients with only finger involvement showed complete healing with a good range of motion (Fig. 3). NTM infection of the wrist joint, which involved more extensive tenosynovitis, tended to cause decreased range of motion in the fingers. However, the range of motion in the wrist itself was relatively preserved because the infection had not invaded the wrist joint itself.

A major limitation of our study is the small number of patients, which precludes statistical identification of factors influencing outcomes. Statistical significance could not be verified for the treatment period or prognosis depending on the frequency of surgery, disease duration, or location of infection. Second, treatment was performed by two surgeons and multiple infectious disease physicians across two different healthcare systems. Developing and following universally agreed treatment protocols for deal-



Fig. 3. (A) A 75-year-old male patient visited the hospital with resin edema in the left hand that began 5 months ago. (B) Ultrasonography showed synovial thickening and fluid collection of flexor tendon. (C) The first surgery was performed for biopsy and Mycobacterium intracellulare was identified. (D) Due to severe itching and skin rash, which are side effects of drug treatment, the patient himself stopped drug treatment for 6 weeks, and then the symptoms recurred and a second operation was performed. (E) Clinical resolution after anti-tuberculosis treatment for a total of 9 months was achieved and there was no recurrence at the last follow-up of 39 months, but range of motion of the finger was limited.

ing with these infections could be helpful, but we have not been able to do so. The rarity and nature of this disease limit improvements in diagnostic methods and treatments.

In this paper, we identified a predominant species of NTM infection in the hand in Korea, which will be helpful in selecting empirical antibiotics. We have discussed the challenges we faced during patient care, such as wounds and edema during the treatment process, drug adverse effects, the positive rate of actual tests, and specific treatment courses, such as sequelae after a cure. This work is important because the rarity and nature of NTM tenosynovitis pose many challenges for surgeons.

# **CONFLICT OF INTEREST**

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

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