# Atypical mycobacterial flexor tenosynovitis presenting as carpal tunnel syndrome: Presentation of three cases and review

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Three patients with carpal tunnel syndrome secondary to atypical mycobacteria flexor tenosynovitis are presented. Aggressive surgical debridement combined with long term antitubercular pharmacotherapy resulted in a good outcome, but the lag time to diagnosis and course of disease were long. Diagnosis of these infections requires a high suspicion index, adequate surgical biopsy and appropriate cultures. Atypical mycobacteria infections must be considered in the differential diagnosis in any patient with evolving chronic tenosynovitis, even if the patient has no history of immunosuppression, and especially if environmental risk factors are present.

**Key Words:** *Atypical mycobacterium; Carpal tunnel syndrome; Tenosynovitis*

## Ténosynovite mycobactérienne atypique du fléchisseur prenant la forme d'un syndrome du tunnel carpien : Présentation de trois cas et revue

**RÉSUMÉ :** On présente ici trois patients atteints d'un syndrome du tunnel carpien secondaire à une ténosynovite mycobactérienne atypique du fléchisseur. Un débridement chirurgical énergique allié à une pharmacothérapie antituberculeuse prolongée ont donné de bons résultats, mais les délais entourant le diagnostic et l'évolution de la maladie ont été longs. Le diagnostic de ces infections requiert un fort indice de suspicion, une biopsie adéquate et des cultures en bonne et due forme. Les infections mycobactériennes atypiques doivent être envisagées lors du diagnostic différentiel chez tout patient dont la ténosynovite se chronicise, même en l'absence d'immunosuppression, et surtout en présence de facteurs de risque dans l'environnement.

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Carpal tunnel syndrome (CTS) may be caused by any space-occupying lesion in the carpal tunnel that compresses the median nerve under the unyielding transverse carpal ligament. It is usually secondary to nonspecific chronic tenosynovitis, but systemic diseases, trauma, tumours, endocrine disorders and infectious diseases have been reported to manifest as CTS. Fungi, bacteria, viruses and parasites have been implicated as causative agents. *Mycobacterium* species are no exception, whether typical or nontuberculous. However, synovitis due to atypical mycobacteria are reported with increasing frequency, whereas tuberculosis is becoming less frequent in developed countries (1).

A delay in diagnosis is common with atypical mycobacterium infections, attributed frequently to insufficient clinical suspicion or awareness, which may result consequently in increased morbidity for the patient.

The present report describes three patients with CTS secondary to different strains of atypical mycobacteria.

## CASE 1 PRESENTATION

An otherwise healthy 70-year-old woman was referred to the Clinique du Parc Leopold, Belgium for swelling and pain in the right index finger, thumb and wrist, associated with numbness of the first three digits. She had undergone median nerve decompression surgery five months earlier in another institution for electrodiagnostically proven CTS. Earlier corticosteroid injections failed to alleviate the symptoms. The postoperative course was complicated by the early recurrence of pain and the appearance of swelling in the above mentioned areas. She denied any medical history or trauma, but reported being an occasional gardener.

The scar was tender at palpation. Hypesthesia was present in the territory of the median nerve. Tinel and Phalen signs were positive at the wrist. There was no visible drainage, lymphangitis, adenopathy or fever. Surgical exploration demonstrated a severe flexor synovitis with rice bodies. A palmar flexor tenosynovectomy was performed and the scar from the earlier surgery was excised. Cultures for *Mycobacterium* species, bacteria and fungi were ordered. Tuberculin test results were negative. Histological examination demonstrated noncaseating granulomas surrounded by a lymphocytic and plasmocytic infiltrate (Figure 1). Two months later, the patient presented with a palmar abscess, localized at the base of the third finger. This collection, containing turbid fluid, was drained surgically. At that time, cultures from the first operation identified *Mycobacterium nonchromogenicum* as the offending agent. Antituberculous therapy was initiated (ethambutol hydrochloride and rifampicin).

Three weeks later, the antibiogram demonstrated in vitro resistance to rifampicin, but because the evolution was favourable, the regimen was not changed. The antibiotics were discontinued after six months. Clinical evaluation at 11 months of follow-up demonstrated the patient to be free of disease.

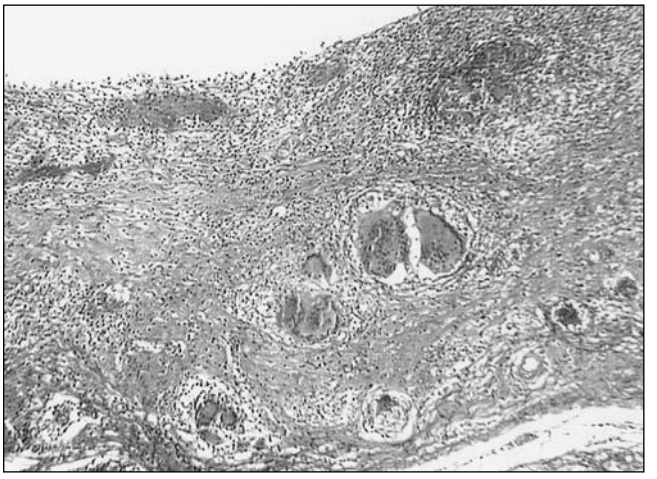

**Figure 1)** *Granulomatous synovium with lymphocytic infiltrate (Hematoxylin-eosin-safran stain, original magnification × 90)*

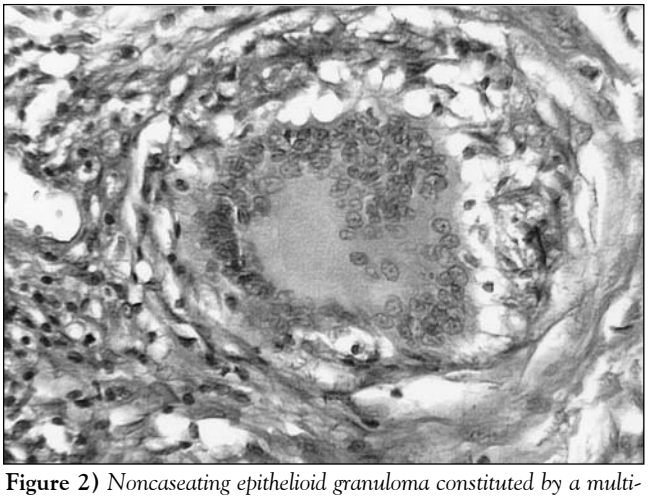

**Figure 2)** *Noncaseating epithelioid granuloma constituted by a multinucleated giant cell surrounded by lymphocytic infiltrate (Hematoxylin-eosin-safran stain, original magnification × 360)*

## CASE 2 PRESENTATION

A 60-year-old man with no known immunosuppressing disease or medication was operated on for left-sided CTS in another hospital. Surgery improved the symptoms only temporarily. Recurrent paresthesias in the second, third and fourth fingers and swelling of the volar forearm, proximal to the wrist flexion crease, mandated surgery. Exploration revealed aggressive synovitis involving the flexor tendons and the median nerve, as well as the presence of a yellow-tinged fluid. Extensive synovectomy was performed. Histological examination revealed the presence of granulomas with giant cells (Figure 2) surrounded by lymphocytes. No caseation was seen. Acid-fast stain was negative. Sarcoidosis was suspected and corticotherapy was initiated. An x-ray of the hand and wrist showed soft tissue swelling but no bone destruction. A gallium lung scan suspected hilar adenopathies but the chest x-ray and the angiotensin-converting enzyme rate were normal. In the postoperative period, the patient developed two collections of fluid around the incision site, causing neurological symptoms

and necessitating incision and drainage (52cm$^3$ and 25cm$^3$ of blood-tinged fluid). Two months after surgery, the results of the intraoperative cultures demonstrated the presence of *Mycobacterium kansasii*.

Corticosteroids were then withdrawn and an antibiotic regimen including rifampicin, ethambutol hydrochloride and isoniazid was started for a period of six months. The patient's course following completion of the regimen was uneventful.

## CASE 3 PRESENTATION

A 42-year-old woman underwent a computed tomography release for right-sided CTS. Four months following the intervention, she developed a draining sinus at the incision site. She was urgently reoperated on for drainage and synovectomy. Intraoperative cultures following the second intervention demonstrated the presence of *Mycobacterium chelonae*. The patient underwent treatment with a course of quinolones immediately after the drainage procedure, based on clinical suspicion. The patient's previously elevated erythrocyte sedimentation rate normalized after surgery. The patient was discharged from the hospital with an uncomplicated postoperative course. Antibiotics were discontinued after three months. Four months later, she presented for recurring swelling of the volar distal forearm and a painful widened scar. A radical synovectomy, median nerve neurolysis and scar excision were performed. Yellow rice bodies were present in the synovium. A distally-based radial forearm flap was used to cover the carpal tunnel area. On the first postoperative day, signs of vascular compromise to the flap were identified and an arterial thrombosis was diagnosed intraoperatively. It was treated with catheterization and heparinization. Despite these manoeuvres, the flap was lost a few days later. The area was covered eventually with a submammary pedicle flap that healed uneventfully. Histological examination revealed noncaseating granulomas, giant cells and a lymphocytic infiltrate. Acid-fast stain was negative. Clarithromycin was initiated after surgery. Two months later, alcohol-acid-resistant bacilli and *M chelonae* were cultured. A quinolone was then added to the antibiotic regimen. Antibiotics were administered for a total period of nine months. The patient healed eventually, following completion of the medical regimen.

## DISCUSSION

CTS is a very common disorder that rarely results from infection (2). Atypical mycobacteria, once thought to be harmless saprophytes or opportunistic pathogens, are recognized increasingly as being responsible for flexor tenosynovitis (3), even in healthy patients, as was seen in the three cases reported in the present article. Factors that should heighten suspicion for infection by *Mycobacterium terrae* complex include exposure to soils and a history of farm activity (4,5). This complex comprises three species – *M terrae*, *M nonchromogenicum* and *Mycobacterium triviale*. The first patient was an occasional gardener with recurrent exposure to soils.

*M kansasii* is, on rare occasions, cultured from tap water or milk (6), or from cows and pigs. *M chelonae* is a ubiquitous saprophyte organism. It was isolated first from a turtle in 1903 by Friedman, and later from soil. It is sometimes cultured from sputum and gastric washings of healthy people (7). It is often difficult to eradicate because it tends to be resistant to most antituberculous drugs (7,8), as was seen with the third patient.

Clinical signs of flexor tenosynovitis usually include swelling, a palpable mass or spontaneous drainage involving the wrist or fingers (5) in middle-aged nonimmunocompromised patients (9).

Delay to diagnosis is often long and can average up to one year (5). The erythrocyte sedimentation rate is usually normal. More importantly, tuberculin skin test results are often negative or weakly positive (9,10). It was performed only in our first patient, and the results were negative.

The anterior aspect of the forearm is often involved and, therefore, CTS is frequent (10-12). Most infections are reported to be secondary to direct inoculation or trauma. Rice bodies are fibrinous ovoid masses, 2 to 20 mm long, that have glistening surfaces that look similar to grains of polished white rice. They were long claimed to be pathognomonic for tuberculosis but, in fact, lack specificity because they can be associated with sporotrichosis, coccidioidomycosis, brucellosis and rheumatoid arthritis. Furthermore, they are not always present (13).

Diagnosis of infectious process relies mainly on culture, which is a long and tedious process. Lag time to diagnosis is often long, requiring empirical treatment without a laboratory diagnosis. Specimens should be inoculated into two specific media (Lowenstein-Jensen egg-based media and Middlebrook agar-based media) and should be incubated at 37°C and 31°C because *M chelonae* and *Mycobacterium marinum* may grow only at the lower temperature, for a minimum of three months.

Direct microscopic examination (Zielh's colouration) lacks sensitivity because a large number of organisms must be present to be detected. Thirty per cent of the patients with proven atypical mycobacteria infections have positive stains (5).

Histological analysis often demonstrates noncaseating granulomatous synovitis (4). In longstanding cases, sequential biopsies may sometimes show transformation from nonspecific inflammation to granuloma formation (14). Polymerase chain reaction (PCR) may, according to some authors (15-16), provide a highly sensitive and specific tool for detection and identification of these microorganisms. The use of nucleic acid sequence amplification, if clinically proven sensitive and specific, would constitute a major improvement in the diagnosis of these infections because detection and species identification would be provided in a matter of hours or days instead of weeks or months (15,16). Misdiagnosis may lead to unnecessary and potentially harmful steroid therapy (12,17,18).

Most authors believe that the combination of surgery

(extensive tenosynovectomy) and long term chemotherapy is the most reliable and safe therapeutic choice (12,17,18). Tenosynovectomy cannot remove all infected tissue, but will decrease the mycobacterial load, giving drug therapy a better chance to eradicate the disease (5).

Multiple surgical procedures, as seen with the three cases presented, are often required. After surgery, physiotherapy should be initiated promptly to minimize adhesion formation. Medication should be started empirically in the immediate postoperative period if history and physical examination are typical and if granulomas are identified despite negative fungi stains.

The recommended combination of drugs is rifampicin, isoniazid and ethambutol with clarithromycin (12) for a minimum of nine months. Because upper extremity atypical mycobacteria infections are uncommon, the accurate duration of the antibiotherapy is not known. Zenone et al (12) recommend the continuation of treatment for at least three months after resolution of symptoms and signs. Frequent consultation with an infectious disease specialist is recommended because these antituberculous drugs have significant toxicity.

## CONCLUSIONS

Atypical mycobacteria are an uncommon cause of CTS secondary to chronic flexor tenosynovitis. Diagnosis is often delayed because of low clinical suspicion, the slow and indolent course of the disease, and the delay in microbiological diagnosis.

Aquatic exposure or soil exposure are important anamnestic risk factors. A history of trauma is not commonly found. Most patients are immunocompetent. Steroid injections without precise diagnosis should be avoided because they can aggravate the condition. Surgical biopsy is mandatory. Direct microscopic examination, specific cultures and PCR should be ordered. The combination of extensive synovectomy and long term pharmacotherapy is recommended for managing these infections. Once clinical suspicion of the disease is present, treatment should be initiated if no contraindication to the treatment regimen is present.

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