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Delayed Diagnosis of *Mycobacterium marinum* Infection: A Case Series of Deep-Tissue and Extensive Disease Following Aquatic Exposure

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Case series

Patients: Male, 62-year-old • Female, 60-year-old • Male, 62-year-old

Final Diagnosis: *Mycobacterium marinum* infection

Symptoms: Cutaneous eruption • skin rash • cutaneous lesions • hand swelling • nodular skin lesion

Clinical Procedure: —

Specialty: Public Health

Objective: Unusual clinical course

Background: The slow-growing nontuberculous mycobacterium *Mycobacterium marinum* inhabits aquatic environments and causes cutaneous infections following minor trauma sustained during aquatic activities. It causes skin and soft-tissue infections with nonspecific clinical manifestations, frequently resulting in delayed diagnosis due to slow growth that requires specialized laboratory conditions. Diagnostic delay often leads to inappropriate antimicrobial therapy and unnecessary surgical interventions.

Case Reports: We describe 3 patients, 1 of whom had received immunosuppressive biologic therapy prior to diagnosis, with *M. marinum* infection, in whom prolonged diagnostic delays led to advanced disease involving soft tissue, tendon, and bone. Initial presentations mimicked common conditions such as cellulitis or inflammatory dermatoses, and all patients failed standard empiric therapy. Progressive disease included tenosynovitis, sporotrichoid spread, and osteomyelitis. Imaging, particularly magnetic resonance imaging, was instrumental in identifying deep-tissue involvement and guiding biopsy. Diagnosis was established through histopathology, mycobacterial culture under specialized conditions, and polymerase chain reaction testing, including culture-negative cases. All patients required prolonged multidrug therapy with macrolide- and rifampin-based regimens; 1 patient required repeated surgical debridement.

Conclusions: These cases illustrate that delayed recognition of *M. marinum* infection, regardless of baseline immune status, may coincide with progression to deep-tissue disease and prolonged morbidity. Failure of conventional antibiotics, history of aquatic exposure, and chronic or progressive symptoms should prompt early biopsy, targeted cultures, and molecular diagnostics. Early imaging and structured diagnostic evaluation are critical to prevent progression to deep infection, reduce morbidity, and avoid unnecessary interventions. Heightened clinical suspicion is particularly important in regions with frequent aquatic exposure.

Keywords: Osteomyelitis • Mycobacterium Infections, Nontuberculous • *Mycobacterium marinum* • Aquatic Organisms • Waterborne Diseases

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/953582>

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Introduction

Mycobacterium marinum is a slow-growing nontuberculous mycobacterium found in freshwater and marine environments that causes cutaneous and soft-tissue infections following minor skin trauma during aquatic exposure [1,2]. Clinical presentation is often nonspecific and may mimic bacterial cellulitis, inflammatory dermatoses, or other atypical infections leading to delayed diagnosis [1,3]. Standard laboratory cultures may fail to detect the organism unless specific growth conditions are requested, contributing to delayed diagnosis [2,4]. Delayed recognition can allow progression from superficial cutaneous lesions to deeper involvement, including tenosynovitis, osteomyelitis, and disseminated disease, resulting in significant morbidity [5,6]. We present a descriptive case series of 3 patients with *Mycobacterium marinum* infection, 1 of whom had received immunosuppressive biologic therapy prior to diagnosis, to illustrate how delayed recognition may coincide with progression to deep-tissue disease, diagnostic misclassification, and prolonged morbidity. The aim of this report is to highlight clinical patterns associated with delayed diagnosis and emphasize the importance of early suspicion, targeted cultures, and molecular diagnostics in refractory aquatic exposure-associated infections.

Case Reports

Case 1: Delayed Diagnosis of *Mycobacterium marinum* Tenosynovitis Following Recreational Water Exposure

A 62-year-old lineman from Alabama with previously treated latent tuberculosis developed a 2-year history of right-hand swelling, nodules, and a nonhealing rash after a minor hand injury sustained during a fishing trip (Figure 1). Symptoms began in October of 2021 with swelling of the right index finger. Then, over the following 2 years, he developed progressive wrist nodules and was treated for presumed rheumatoid arthritis, including biologic therapy, without response. The patient received multiple empiric treatments for presumed bacterial or inflammatory disease without improvement. Surgical exploration in February 2023 revealed rice bodies, but initial routine cultures were negative. HIV testing was negative; however, the patient had been receiving biologic therapy for presumed rheumatoid arthritis since before *M. marinum* was diagnosed, resulting in pharmacologic immunosuppression during much of his disease course. He was referred to a tertiary referral center in January of 2024, where magnetic resonance imaging (MRI) demonstrated tenosynovitis with erosive changes, prompting biopsy which revealed granulomatous inflammation.



Figure 1. Right hand showing *Mycobacterium marinum* tenosynovitis and edema.

Table 1. Timeline summarizing clinical presentation, diagnostic milestones, and treatment progression in Case 1, highlighting delays in diagnosis and recovery trajectory.

Timeline of clinical events: Case 1	
Month/Year	Event
Oct 2021	Onset of right index finger swelling after minor trauma while fishing
2022-2023	Progressive swelling, wrist nodules, treated as RA; no response to biologics
Feb 2023	Exploratory hand surgery reveals rice bodies; cultures negative
Jan 2024	Referred to Mayo Clinic; MRI shows tenosynovitis and erosions
Feb 2024	Dermatology notes sporotrichoid rash; biopsies taken
Early Mar 2024	Pre-operative plastic surgery evaluation; no systemic symptoms
Mid-Mar 2024	Surgical debridement of wrist, metacarpophalangeal joint, and upper-arm nodules performed
Apr 2024	<i>Mycobacterium marinum</i> confirmed from biopsy; triple antibiotic therapy initiated
May-Aug 2024	Marked clinical improvement; return to work and recreation
Feb 2025	Patient reported 85%-90% resolution; continued treatment, no recurrence

RA, rheumatoid arthritis; MRI, magnetic resonance imaging.

Dermatologic evaluation in February of 2024 noted a sporotrichoid-pattern rash, and additional skin biopsies were obtained; pre-operative plastic surgery evaluation in early March of 2024 confirmed no systemic symptoms. Subsequent mycobacterial culture confirmed *M. marinum* infection.

In mid-March of 2024, the patient underwent surgical debridement of the wrist, metacarpophalangeal joint, and upper-arm nodules; *M. marinum* was confirmed on biopsy in April of 2024, and triple antimicrobial therapy with clarithromycin, rifampin, and ethambutol resulted in significant clinical improvement over several months. This case demonstrates how delayed diagnosis allowed progression to deep structures, resulting in prolonged hand dysfunction and occupational impairment. By May of 2024, he had returned to work and recreational activities. At follow-up in February of 2025 he reported 85% to 90% symptomatic resolution with no recurrence while continuing treatment. Antimicrobial therapy was continued for more than 10 months from initiation in April of 2024 (Table 1). The interval between symptom onset in October of 2021 and microbiologic confirmation of *M. marinum* in April of 2024 was approximately 30 months.

Case 2: Chronic Cutaneous and Osseous *Mycobacterium marinum* Infection in an Immunocompetent Host

A 60-year-old woman developed progressive nodular lesions on her right ring finger following minor trauma during saltwater aquarium maintenance (Figure 2). HIV testing was negative, confirming her immunocompetent status. The injury occurred during saltwater tank cleaning between December 2022 and August 2023, and the diagnosis was ultimately established from a wound swab obtained during hospitalization. MRI in



Figure 2. Chronic cutaneous and osseous *Mycobacterium marinum* infection of the right ring finger.

September 2023 revealed fourth-digit osteomyelitis, prompting initiation of a 5-drug antimicrobial regimen (rifampin 300 mg orally twice daily, levofloxacin 500 mg orally daily, ethambutol 400 mg orally daily, clarithromycin 500 mg orally twice daily, and doxycycline 100 mg orally twice daily). Despite prolonged treatment with this 5-drug regimen, delayed diagnosis led to progression to osteomyelitis. Definitive diagnosis was established through biopsy and mycobacterial culture. Histopathology from a finger biopsy obtained by her initial treating physician in 2023 reportedly showed granulomatous inflammation; the original pathology report was not available for review, and this finding is based on documentation in her outside medical records. Levofloxacin, 1 component of the regimen, was paused between April and June 2024 due to peripheral neuropathy (levofloxacin was discontinued and ethambutol was continued). However, it was then restarted in June of 2024 after a new elbow lesion developed. Then, MRI of the elbow in July of 2024 showed cellulitis without abscess (with a

Table 2. Timeline summarizing key clinical events in Case 2, from exposure to diagnostic confirmation and treatment course.

Timeline of clinical events: Case 2	
Month/Year	Event
Dec 2022	Sustained injury while cleaning saltwater fish tank
Aug 2023	<i>Mycobacterium marinum</i> identified on wound swab during hospital admission
Sept 2023	MRI showed fourth-digit osteomyelitis; started 5-drug antibiotic regimen
Apr-Jun 2024	Temporarily stopped levofloxacin due to adverse effects
Mid-Jun 2024	Restarted levofloxacin due to new elbow lesion
Jul 2024	MRI of the elbow: cellulitis without abscess; QuantIFERON-TB Gold falsely positive
Aug 2024	MRI of the hand: resolving osteomyelitis
Aug 2024, 6 days later	Transitioned from levofloxacin to TMP-SMX due to intolerance
Nov 2024	Antibiotics discontinued after ~ 15 months of treatment
Dec 2024	Patient reports mild sensitivity in finger; no signs of recurrence
Jan 2025	Pain persists in finger; MRI with contrast ordered

MRI, magnetic resonance imaging; TMP-SMX, trimethoprim-sulfamethoxazole.

false-positive QuantiFERON result the same day), and imaging of the hand the following day showed resolving osteomyelitis, prompting a switch to trimethoprim-sulfamethoxazole later that week. The patient required prolonged multidrug antimicrobial therapy for approximately 15 months, with multiple regimen adjustments due to adverse effects. Antibiotics were discontinued in November of 2024. Follow-up imaging confirmed resolution of infection, allowing discontinuation of therapy. Although major functional recovery was achieved, mild residual sensory deficits persisted. At follow-up in December of 2024, she reported only mild finger sensitivity with no recurrence; however, persistent pain prompted a repeat MRI with contrast, ordered in late January of 2025 and obtained in mid-March of 2025. The MRI showed no evidence of osteomyelitis but did show apposing subchondral edema with enhancement and likely marginal osteophytosis that was most conspicuous at the 4th distal interphalangeal joint, without joint effusion. (Differential diagnoses included septic arthritis, erosive osteoarthritis, and, less likely, inflammatory arthritis.) In addition, a small amount of fluid was seen along the flexor pollicis longus tendon at the level of the first metacarpophalangeal joint to the proximal first phalanx, for which tenosynovitis treatment was recommended. Cellulitis of the distal thumb and the fourth and fifth digits was also suspected. There was no drainable fluid collection.

This case highlights the morbidity associated with delayed diagnosis and the challenges of treating osseous *M. marinum* infection, which requires extended antimicrobial therapy (Table 2). The interval between the patient's earliest documented aquatic exposure in December 2022 and identification of *M. marinum* from a wound swab in August 2023 was approximately 8 months.

Case 3: Extensive *Mycobacterium marinum* Infection Following Pond Water Exposure

A 62-year-old man developed progressive abscesses of the right upper extremity following a skin injury sustained during occupational pond water exposure (Figure 3). HIV testing was negative, and he was immunocompetent at initial presentation. Methotrexate was later initiated in April 2024, during antimycobacterial therapy, for a concurrent rheumatoid arthritis flare. Initial arm cultures obtained in January 2024 showed no growth, but he was admitted locally and underwent incision and drainage of 22 abscesses, with cultures remaining negative. He was readmitted in February 2024 for worsening purulence, requiring incision and drainage of 16 additional abscesses (more than 30 procedures in total), broadened empiric antibiotics (intravenous vancomycin and piperacillin-tazobactam), and surgical debridement before transfer to a tertiary referral center for biopsy. The patient underwent more than 30 drainage procedures over several months while



Figure 3. Extensive *Mycobacterium marinum* infection of the right upper arm.

receiving treatment for presumed bacterial, fungal, or autoimmune etiologies.

Definitive diagnosis was established using polymerase chain reaction and mycobacterial culture (biopsy sent late February 2024, with confirmation by early March 2024, via 16S rRNA gene PCR and sequencing), confirming *M. marinum*. Histopathology from a punch biopsy of the right arm skin performed in March of 2024 showed dermal suppurative granulomatous inflammation, with findings characteristic of an underlying soft-tissue infection. Acid-Fast Stain, Wade-Fite, Grocott's methenamine silver stain, and Periodic Acid Schiff-Fungal special stains were negative, and correlation with tissue culture was recommended. Combination antimicrobial therapy (rifampin, ethambutol, azithromycin, and moxifloxacin) led to clinical resolution of infection. Therapy was restarted by the local infectious disease team in March of 2024 (the patient was initially unreachable and was contacted through his wife). At follow-up later in March of 2024, he was doing well on the regimen, although a new lesion was noted, and a concurrent rheumatoid arthritis flare in April 2024 required restarting methotrexate. He showed clinical improvement with no new lesions and good adherence from May to June 2024, aside from minor blister lancing by his local physician. At last follow-up in June 2024, he had completed approximately 3 months of combination antimycobacterial therapy with no evidence of relapse. This case highlights how delayed diagnosis and insufficient initial testing allowed widespread disease progression, demonstrating the value of early molecular diagnostics in refractory or extensive infections (Table 3). The interval between the

Table 3. Timeline outlining the complex clinical course in Case 3, including abscess drainage, diagnostic delays, and response to multidrug therapy after PCR confirmation.

Timeline of clinical events: Case 3	
Month/Year	Event
Mid-Jan 2024	First arm culture obtained - no growth
Late Jan 2024	Admitted locally; 22 abscesses incised and drained; cultures remained negative
Feb 2024	Readmitted with worsening purulence and lymphadenitis; 16 more abscesses drained; empiric coverage expanded
Feb 2024, 3 days later	Underwent additional surgical debridement
Feb 2024, 2 days later	Admitted to Mayo Clinic Florida; Dermatology performed biopsy for histopathology and broad-range PCR
Feb 2024, 4 days later	Biopsy tissue collected; sent for bacterial broad-range PCR testing
Mar 2024	PCR confirmed <i>Mycobacterium marinum</i> ; attempts made to contact patient
Mar 2024, 1 day later	Patient's local infectious disease specialist restarted antibiotics; patient unreachable by phone
Mar 2024, 3 days later	Spoke with wife; patient started on rifampin, ethambutol, azithromycin, and moxifloxacin
Apr 2024	Spoke with patient; RA flaring since stopping immunosuppressants; started methotrexate
May 2024	Patient reported clinical improvement with no new lesions
Jun 2024	Continued clinical improvement; antibiotic regimen followed without missed doses; minor lancing of blisters by local infectious disease specialist
Dec 19, 2024	Patient evaluated in infectious disease clinic; doing well on new regimen; new lesion noted

PCR, polymerase chain reaction; RA, rheumatoid arthritis.

first documented culture on January 18, 2024 and polymerase chain reaction confirmation on March 7, 2024 was approximately 2 months, during which more than 30 drainage procedures were performed; the exact date of symptom onset following pond water exposure was not documented.

Discussion

This case series highlights the potential association between delayed diagnosis of *Mycobacterium marinum* infection and progression to advanced disease, regardless of baseline immune status. All 3 patients tested negative for HIV; however, Case 1 was receiving immunosuppressive therapy at the time of diagnosis and Case 3 was later immunosuppressed with methotrexate during treatment. Despite these differences in immune status, all 3 patients developed deep or extensive infection following prolonged diagnostic uncertainty. We present delayed recognition as an observed, illustrative contributor to this progression rather than as the dominant driver; host immune factors, pathogen virulence, and anatomic site of inoculation likely also shaped the course of disease in each patient, and a 3-case descriptive series cannot separate these contributions from one another. Early clinical manifestations in all 3 patients closely resembled common conditions such as bacterial cellulitis or inflammatory dermatoses, leading to

initial treatment with standard empiric therapies. The lack of response to conventional antibiotics was a key but underrecognized indicator of an atypical infectious process. These cases are intended to illustrate practical diagnostic challenges and emphasize a structured evaluation strategy for selected high-suspicion presentations.

As the disease progressed, involvement of deeper structures became evident, including tenosynovitis, osteomyelitis, and extensive cutaneous disease. In Case 1, MRI revealed extensive tenosynovitis and deep soft-tissue involvement, which prompted biopsy and targeted microbiologic evaluation [7]. Imaging played a critical role in recognizing atypical disease patterns and guiding appropriate tissue sampling. Case 2 demonstrated sporotrichoid spread with ascending nodular lesions along lymphatic channels, a pattern that can mimic sporotrichosis, nocardiosis, or inflammatory conditions, and further complicate early diagnosis. Case 3 illustrates the opposite extreme: repeated, extensive local disease. More than 30 abscesses were drained across 2 hospitalizations, with persistently negative routine cultures, which delayed recognition until broad-range PCR was pursued at a tertiary center. This underscores that a negative culture does not exclude *M. marinum* when clinical suspicion remains high. In all cases, failure of standard antimicrobial therapy should have prompted earlier diagnostic reconsideration and tissue-based evaluation [1,8].

Tables 1-3 summarize the clinical timelines for all 3 cases and illustrate several cross-case patterns. Exposure sources differed: a recreational fishing injury in Case 1, saltwater aquarium maintenance in Case 2, and occupational pond water contact in Case 3. Yet, each patient experienced a prolonged, multi-month interval between symptom onset and mycobacterial confirmation, marked by negative or unrequested mycobacterial cultures early in the diagnostic course. Quantified individually, the interval from symptom onset or earliest documented exposure to microbiologic confirmation was approximately 30 months in Case 1 and 8 months in Case 2, both exceeding the median diagnostic delays of 15 to 27 weeks (approximately 3.5 to 6 months) reported in previous series [4,5]. In Case 3, the documented interval was shorter, approximately 2 months, but confirmation was reached only after more than 30 drainage procedures and repeatedly negative routine cultures. Delayed recognition in this patient therefore reflected the intensity of unsuccessful intervention rather than elapsed time alone.

Deep-structure involvement also differed in character: tenosynovitis with joint erosion in Case 1, osteomyelitis in Case 2, and extensive multifocal abscess formation in Case 3. Diagnostic confirmation likewise relied on different modalities across cases: histopathology and mycobacterial culture in Case 1, wound-swab culture and biopsy in Case 2, and broad-range PCR after repeatedly negative cultures in Case 3, underscoring that no single diagnostic approach was uniformly effective. **Figures 1-3** capture this same spectrum, from tenosynovial swelling of the hand and wrist (**Figure 1**) to a chronic nodular lesion of the finger with underlying osseous involvement (**Figure 2**) to extensive multifocal abscess and sinus tract formation of the upper arm (**Figure 3**).

M. marinum is a slow-growing, photochromogenic nontuberculous mycobacterium that is a leading cause of extra-respiratory mycobacterial infection [1,2]. Because initial exposure often follows minor, easily overlooked trauma, patients may not recall a clear inciting event, further contributing to delayed recognition [1,3].

The estimated U.S. incidence is approximately 0.27 cases per 100 000 population, although this likely underestimates the true burden [9]. Risk is considerably higher in coastal and subtropical regions where human-water contact is frequent. This includes states with active commercial fishing, seafood processing, aquaculture, and aquarium industries, as well as areas with substantial recreational water exposure - particularly Florida, Georgia, the Carolinas, Gulf Coast states, coastal California, Hawaii, the Pacific Northwest, and the Atlantic seaboard. During a 2013-2014 outbreak in New York City, investigators identified 98 cases linked to fish handling, and hand injury during fish preparation was associated with an 8.3-fold

increased risk (95% CI 3.8-19.1) [5]. Although historically referred to as “swimming pool granuloma” or “fish tank granuloma”, infection now occurs predominantly in individuals with occupational or recreational aquatic exposure, including fishermen, aquarium enthusiasts, and outdoor workers [1,2]. Interestingly, military personnel may face similar exposure during water purification duties, tank cleaning, or working in aquatic training facilities without adequate protection [10,11].

Physicians practicing in regions with frequent aquatic exposure should maintain heightened suspicion for *M. marinum* in patients with persistent or atypical skin and soft-tissue infections following relevant environmental exposure. The incubation period ranges from 5 to 270 days (median 21 days), with more than a third of cases exceeding 30 days. This variability necessitates obtaining a detailed exposure history extending several months prior to symptom onset [3,12]. Even after symptom onset, diagnosis is frequently delayed, with reported median times ranging from 15 to 27 weeks [4,5]. The indolent course and nonspecific presentation contribute to frequent misdiagnosis, often as sporotrichosis, nocardiosis, or inflammatory arthritis [1,2,8]. As a result, patients commonly receive multiple courses of ineffective therapy or undergo unnecessary procedures before appropriate diagnostic testing is pursued [8,13]. These delays are observed, in this and other reports, alongside progression to deeper infection, including tenosynovitis, osteomyelitis, and disseminated disease, resulting in substantial functional and occupational morbidity [5,6]. Recent reports in BMJ Case Reports illustrate the same pattern in patients receiving immunosuppressive therapy: in 1 report, sporotrichoid lesions failed repeated empiric treatment until biopsy established the diagnosis; in another, localized cutaneous infection progressed over approximately 18 months to disseminated disease before *M. marinum* was recognized [14,15].

Although delayed diagnosis and deep-tissue involvement in *M. marinum* infection have been previously reported, this case series reinforces several clinically important themes within a contemporary diagnostic context. What distinguishes this series from prior reports is the co-occurrence, in all 3 patients, of substantial diagnostic delay, negative HIV status, and progression to deep-structure involvement, spanning tendon sheath, bone, and extensive multifocal cutaneous disease, along with a shared diagnostic pathway. Each case ultimately required imaging-guided biopsy, mycobacterial culture under specific low-temperature growth conditions, and molecular testing, including a culture-negative case resolved only by broad-range PCR, to reach a diagnosis that had eluded standard evaluation for months. First, all 3 patients, regardless of baseline immune status, experienced prolonged diagnostic uncertainty with progression to advanced soft tissue, tendon, or osseous involvement despite repeated healthcare encounters. Second, the cases illustrate how persistent treatment-refractory disease

following aquatic exposure may mimic more common bacterial, inflammatory, or autoimmune conditions, contributing to diagnostic misclassification. Finally, these cases highlight the practical value of integrating exposure history, early imaging when deep involvement is suspected, targeted mycobacterial cultures, and molecular diagnostics into a structured evaluation pathway for selected high-suspicion presentations [1,5].

Immunocompromised patients face considerably higher risk of disseminated disease, including multifocal cutaneous lesions, lymph node involvement, pulmonary infiltrates, and bacteremia, and often require more prolonged and intensive therapy because of increased risk of relapse and dissemination [1,16].

Diagnostic confirmation is often challenging due to limitations of routine culture methods. *M. marinum* requires incubation at approximately 30°C rather than the standard 37°C, and growth may take several weeks [2,4]. As a result, routine bacterial cultures frequently remain negative unless mycobacterial cultures are specifically requested. Similarly, in our Case 3, routine cultures yielded no growth, and broad-range bacterial PCR (16S rRNA gene PCR with sequencing) was ultimately required to establish the diagnosis [1,2,4]. Histopathology typically shows granulomatous inflammation, lacking specificity for *M. marinum* [1,5].

Molecular diagnostics have emerged as valuable tools, particularly in culture-negative cases. During the New York outbreak, PCR identified *M. marinum* in 60% of cases where culture had failed [8]. More recent data demonstrate that targeted next-generation sequencing achieves 77.8% sensitivity compared with 17.8% for acid-fast staining, 42.2% for culture, and 57.8% for Sanger sequencing, while maintaining 100% specificity [17]. Earlier implementation of molecular diagnostics may reduce unnecessary procedures, limit disease progression, and shorten time to effective therapy [13]. Such testing may be particularly valuable in chronic, refractory, atypical, or culture-negative infections where aquatic exposure history raises suspicion for nontuberculous mycobacterial disease [17,18].

These cases support a structured diagnostic approach for selected high-suspicion presentations, particularly infections that are persistent, progressive, treatment-refractory, associated with aquatic exposure, or concerning for deep-structure involvement. In such cases, early imaging, particularly MRI, may help to identify tenosynovitis, osteomyelitis, or other deep-tissue extension, and may help guide tissue sampling [7]. Failure of standard antimicrobial therapy, as occurred in all 3 of our cases, should prompt early biopsy with a specific request for mycobacterial culture at 30°C and molecular testing. PCR proves particularly useful when cultures remain negative, as demonstrated in our Case 3 [18].

Treatment recommendations vary by disease extent and host immune status. For immunocompetent patients with localized disease, guidelines recommend 2-drug combination therapy continued for 1-2 months after complete lesion resolution, typically totaling 3-4 months [19]. Preferred regimens include clarithromycin combined with either ethambutol or rifampin. Deep infections require longer treatment courses and frequently necessitate surgical intervention. In this series, all patients required prolonged multidrug therapy, reflecting the advanced stage of disease at diagnosis, and the patient in Case 1 required multiple debridements in addition to prolonged antibiotic therapy [1,6,19].

Immunocompromised patients and those with deep or disseminated disease require more intensive treatment: 3 or more antimicrobials for 6 to 12 months or longer [16,17]. Susceptibility data show that all *M. marinum* isolates are susceptible to clarithromycin, amikacin, and linezolid. Most isolates (87%-97%) demonstrate susceptibility to rifampin and ethambutol. However, only 3% are susceptible to doxycycline, despite its frequent empiric use for water-associated infections [6].

Clinicians in regions with frequent aquatic exposure should maintain a high index of suspicion for *M. marinum* infection. Dermatologists and primary care physicians typically evaluate these patients initially, when clinical presentations closely resemble cellulitis, inflammatory arthritis, or autoimmune disease. Greater awareness of epidemiological risk factors, prolonged incubation periods, and potentially misleading clinical patterns can reduce diagnostic delay, prevent disease progression, and minimize long-term functional impairment.

Prevention is straightforward. Protective gloves should be worn when cleaning aquariums, handling fish or shellfish, and performing water-related work [1,2]. Alcohol-based hand disinfection after contact with fish tank water or marine environments provides additional protection.

Because this report describes a small descriptive case series without a comparator group, the findings should be interpreted as illustrative of a clinical pattern rather than evidence establishing the relative contribution of diagnostic delay, host immune status, or pathogen-specific factors to disease severity.

Conclusions

This case series illustrates a recurring diagnostic pattern in *M. marinum* infection: chronic or progressive soft-tissue disease following aquatic exposure, failure of standard empiric therapy, delayed recognition, and eventual progression to deep-tissue or extensive involvement regardless of baseline immune status. These cases emphasize the importance of maintaining clinical

suspicion for atypical mycobacterial infection in unresolved aquatic exposure-associated soft-tissue disease. Earlier biopsy, mycobacterial culture under appropriate growth conditions, imaging when deep involvement is suspected, and molecular diagnostics may facilitate earlier diagnosis of *M. marinum* infection.

This series also highlights 2 broader clinical lessons. First, autoimmune disease can complicate the diagnostic and therapeutic course in more than 1 way: it may represent the initial misdiagnosis that delays recognition of infection, or a genuine comorbidity that flares during antimycobacterial therapy and requires concurrent management. In either scenario, close coordination between infectious disease and rheumatology is warranted. Second, standard multidrug regimens achieved clinical improvement in all 3 patients, though treatment courses extended well beyond the 3 to 4 months typically recommended for localized disease. These observations are limited by the small number of cases, the absence of a comparator group, and exposure histories that are plausible but not microbiologically confirmed.

Dermatology, primary care, rheumatology, and occupational medicine are the specialties most likely to encounter these infections at initial presentation, given that all 3 cases in this series were initially misattributed to cellulitis, an inflammatory dermatosis, or autoimmune arthritis. Maintaining awareness of this presentation in these specialties, and ensuring access to mycobacterial-specific culture, molecular diagnostics, and infectious disease consultation, is warranted when such infections are suspected.

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Closer coordination between primary care, occupational health services, and infectious disease or dermatology referral centers is warranted for infections associated with occupational or recreational aquatic exposure, and incorporating these practices into clinical training and referral pathways is a reasonable consideration based on the diagnostic challenges observed in this series.

Department and Institution Where Work Was Done

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Data Availability Statement

No new data were created or generated in this case report. All information presented is derived from the patient's clinical course and existing medical records, and no publicly archived datasets were analyzed. Data sharing does not apply to this article.

Consent

Informed consent was obtained from the patients to write this case series.

Declaration of Figures' Authenticity

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