CASE REPORT / OLGU SUNUMU

DOI: 10.4274/mjima.galenos.2025.25495.22
Mediterr J Infect Microb Antimicrob 2025;14:25495.22
Erişim: http://dx.doi.org/10.4274/mjima.galenos.2025.25495.22

Unexpected Threat: Cutaneous *Mycobacterium marinum* from a Chestnut Thorn

Beklenmedik Tehdit: Kestane Dikeninden Bulaşan Kutanöz *Mycobacterium marinum*

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Abstract

Nontuberculous mycobacterial infections are typically seen in immunocompromised individuals; however, *Mycobacterium marinum* is a rare pathogen that can also affect immunocompetent hosts. It generally presents as a non-disseminated cutaneous infection limited to the skin and soft tissues, showing manifestations like papules, plaques, or single/multiple lesions. Water and fish exposures are well-known risk factors. However, our case shows no history of aquatic exposure; instead, the patient reports a chestnut thorn injury at the affected site. The differential diagnosis should include other granulomatous infections and autoimmune diseases. Species-level identification is essential for the disease diagnosis, but it is not feasible in every center. *M. marinum* is generally susceptible to ethambutol, rifampicin, sulfonamides, and macrolides. By contrast, our case reveals an unexpected resistance pattern. The species-level identification and the antibiotic susceptibility testing are of paramount importance for establishing accurate diagnosis and ensuring effective treatment.
Keywords: *Mycobacterium marinum*, chestnut thorn, soft tissue infections, nontuberculous mycobacteria, resistance

Öz

Tüberküloz dışı mikobakteriyel enfeksiyonlar genellikle immün sistemi baskılanmış bireylerde görülmektedir. Ancak, Mycobacterium marinum immünkompetan konakları da etkileyebilen ve nadir görülen bir patojendir. Genellikle sadece deri ve yumuşak doku ile sınırlı, sistemik yayılım göstermeyen kutanöz bir enfeksiyon şeklinde ortaya çıkar; papül, plak veya tekil/çoklu lezyonlar gibi belirtilerle kendini gösterebilir. Su ve balıkla temas, iyi bilinen risk faktörleri arasında yer almaktadır. Ancak, sunduğumuz olguda bu tarz bir riskli teması öyküsü bulunmamasına karşın lezyonların olduğu bölgeden kestane ağacı dikeniyle yaralanma hikayesi mevcuttu. Ayırıcı tanıda diğer granülomatöz enfeksiyonlar ve otoimmün hastalıklar göz önünde bulundurulmalıdır. Hastalığın tanısı için tür düzeyinde tanımlama şarttır ancak her merkezde bunu yapabilmek mümkün değildir. M. marinum genellikle etambutol, rifampisin, sülfonamid ve makrolidlere duyarlıdır. Oysa olgumuzda beklenmedik bir direnç profiliyle karşılaşılmıştır. Doğru tanı ve etkili tedavi için tür düzeyinde tanımlama ve antibiyotik duyarlılık testleri büyük önem taşımaktadır.
Anahtar Kelimeler: Mycobacterium marinum, kestane dikeni, yumuşak doku enfeksiyonları, tüberküloz dışı mikobakteri, direnç

Cite this article as: Özdemir E, Adım ŞB, Özakın C, Önal U. Unexpected threat: Cutaneous Mycobacterium marinum from a chestnut thorn. Mediterr J Infect Microb Antimicrob.

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Received/Geliş Tarihi: 14.05.2025 **Accepted/Kabul Tarihi:** 24.09.2025

Epub: 24.11.2025

Introduction

Mycobacterium marinum is an aerobic and Gram-positive, acid-fast bacterium that is classified as nontuberculous mycobacteria (NTM). In nature, *M. marinum* is found in soil, water sources, aquatic organisms (e.g., fish), and various plants. It appears as pink-colored bacilli on Ziehl–Neelsen staining. It is photochromogenic, producing a lemon-yellow pigment during light exposure, and is categorized in the first group of the Runyon classification. Phylogenetically, it is closely related to *M. tuberculosis*. *M. marinum* grows slowly on the Löwenstein–Jensen medium, depicting an optimal growth temperature of 32 °C, which is lower than that of *M. tuberculosis*[1]. It is an intracellular pathogen that may result in a positive tuberculin skin test similar to *M. tuberculosis*[2].

M. marinum was first isolated from tubercles in 1926 during the autopsy of a dead saltwater fish inside an aquarium[3]. It primarily causes a tuberculosis-like systemic infection in fish and other aquatic animals. In humans, however, it typically presents as a non-disseminated cutaneous infection limited to the skin and soft tissues. Rare cases of disseminated *M. marinum* infection had been reported, particularly in patients with human immunodeficiency virus/acquired immunodeficiency syndrome[4].

This report presents a rare case of *M. marinum* infection in an immunocompetent patient without a typical exposure history. This work also documents an unexpected antibiotic resistance pattern.

Case Report

A 57-year-old woman presented with a 3-month history of swelling, erythematous raised lesions, and pain on the dorsal aspect of her right hand and forearm. She showed no known immunocompromised conditions. Her physical examination results revealed a painful nodule on the dorsum of the right hand, multiple impetigo-like plaques on the back of the right hand, and an erythematous plaque in the antecubital area, as displayed in Figure 1. An ultrasound of the superficial tissue over the dorsal aspect of the second metacarpal of the right hand showed a 2 × 1 cm irregular, hypoechoic, mostly solid mass. A purified protein derivative test resulted in a 16 mm induration. The skin punch biopsy of the erythematous plaque revealed a chronic granulomatous inflammation that was rich in neutrophils (Figure 2). The Ziehl–Neelsen staining of the biopsy sample exhibited pink bacilli (Figure 3). The cultures in the Lowenstein–Jensen and blood agar media grew NTM identified by a mycobacteria growth indicator tube and using rapid kit tests. Samples were sent to the National Tuberculosis Reference Laboratory because our center cannot perform species-level typing and antibiotic susceptibility testing. Pending results, the patient was empirically treated with oral ciprofloxacin at a dose of 500 mg twice daily and oral clarithromycin at a dose of 500 mg twice daily. A partial clinical response was observed by the fourth week of the empiric therapy, with reduced nodules becoming evident from the sixth week onward. *M. marinum* was identified after 13 weeks of treatment. The susceptibility testing results showed resistance to ethambutol, trimethoprim-

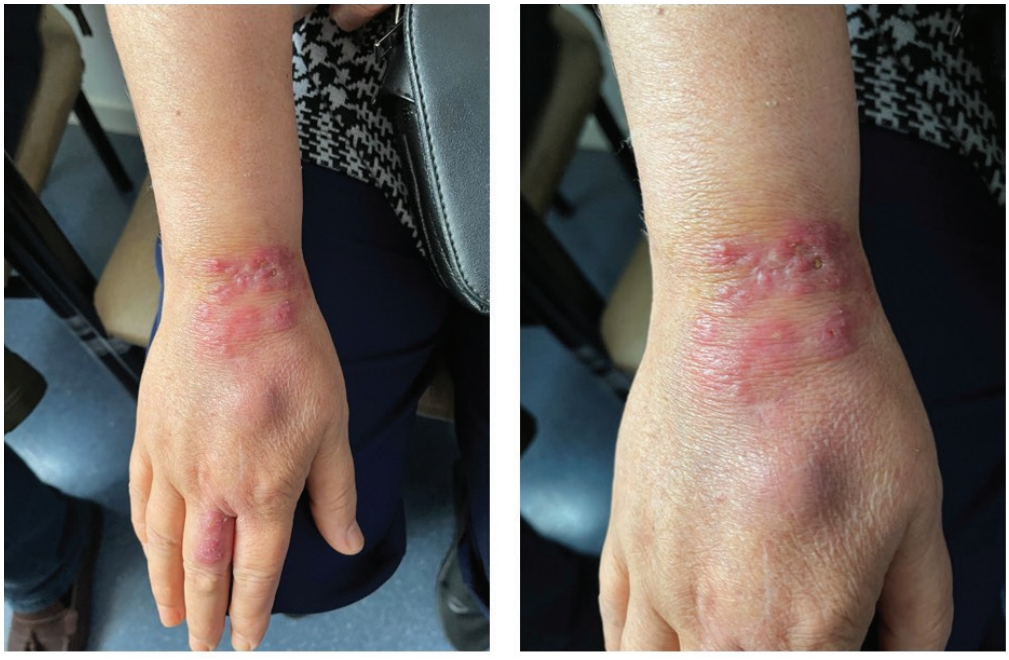

Figure 1. Nodules and multiple impetiginous plaques on the dorsum of the right hand, with the erythematous plaque extending to the antecubital area

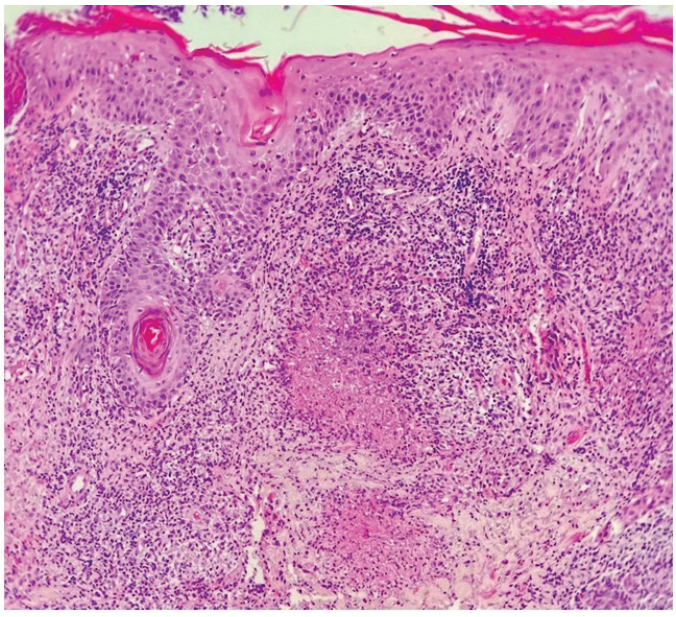

Figure 2. Skin punch biopsy of the erythematous plaque revealing a neutrophil-rich chronic granulomatous inflammation

sulfamethoxazole, and rifampicin. Meanwhile, the strain was sensitive to linezolid, moxifloxacin, and clarithromycin (Table 1). Considering the insufficient response, as depicted in Figure 4, linezolid at a dose of 600 mg twice daily was added on the 14th week, consequently leading to a significant improvement by the third week of its addition. The total duration of the antibiotic therapy was 24 weeks, including 6 weeks following clinical regression (Figure 5). No drug-related adverse effects were observed, except for mild gastrointestinal symptoms.

Discussion

M. marinum infections are classically associated with aquatic environments and occur in both immunocompetent and immunocompromised individuals; however, our case underscores that this pathogen can also affect immunocompetent hosts and may arise in the absence of a typical exposure history, consequently posing diagnostic challenges. It was first identified in humans in 1951 as the "swimming pool granuloma," a skin infection observed in swimmers exposed to polluted pools[5]. The infection can be transmitted through inoculation following skin trauma, which can range from minor abrasions to more significant injuries. The infection can spread along the lymphatics, leading to the formation of granulomatous nodules that may have a crusted or verrucous surface and contain pus. Lesions may appear as single or multiple papules, plaques, abscesses, or ulcers typically on the distal extremities[6].

The diagnosis can be established through the histopathologic and microbiologic examinations of a biopsy specimen taken from a suspicious nodule or plaque. The presence of granulomatous inflammation on histopathology supports the diagnosis, but it is not specific and may be confused with noninfectious granulomatous conditions, most commonly sarcoidosis[7]. The Ziehl–Neelsen staining or detection of the photochromogenic pigment is often challenging because of the typically low bacterial load. Cultures must be incubated at lower temperatures for at least 6 weeks. Polymerase chain reaction plays a critical role in species differentiation. A significantly positive tuberculin skin test was reported in more than two-thirds of the documented cases[8].

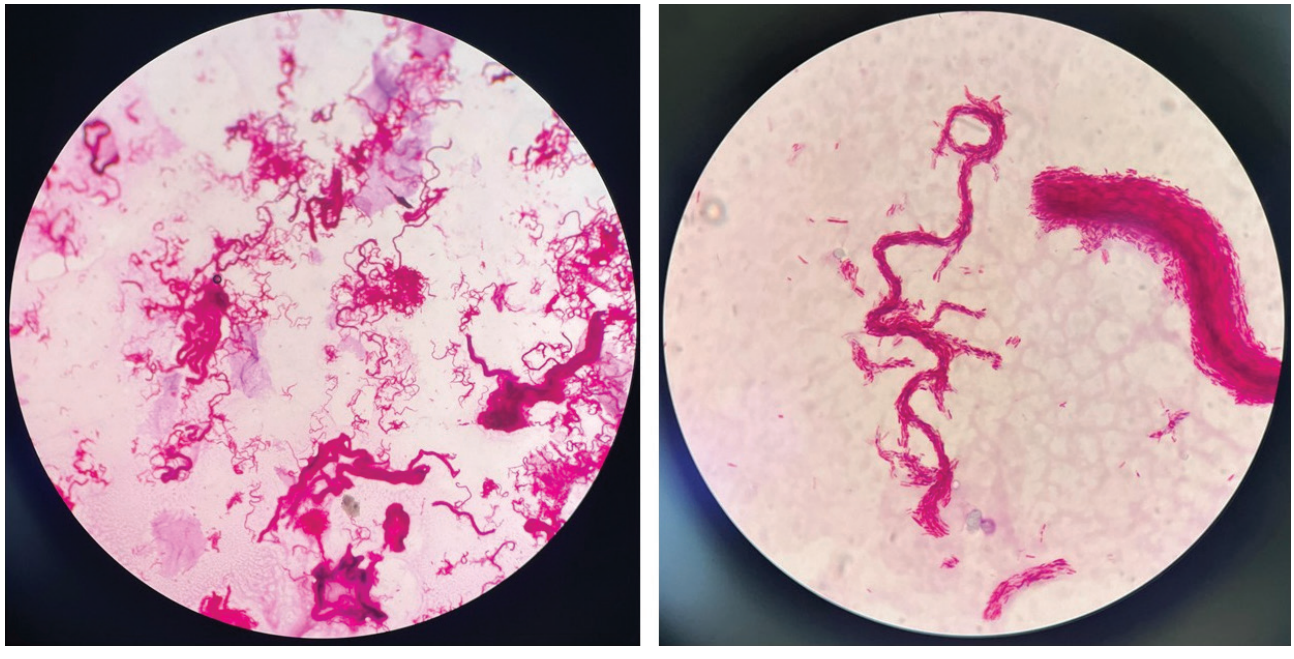

Figure 3. Ziehl–Neelsen staining of the biopsy sample showing pink bacilli: (a) image at a 10× objective; (b) image at a 100× objective

Table 1. Typing and antibiotic susceptibility results at the species level of the National Tuberculosis Reference Laboratory of the General Directorate of Public Health of the Ministry of Health

Microscopy and culture confirmation	**Positive**
Mycobacterium tuberculosis – other mycobacteria Differentiation test	*M. tuberculosis*-negative
Nontuberculous mycobacteria species identification	*M. marinum*
Antibiotic susceptibility results (minimum inhibitory concentration)	
Amikacin	Susceptible (2 µg/ml)
Clarithromycin	Susceptible (0.25 µg/ml)
Doxycycline	Resistant (16 µg/ml)
Ethambutol	Resistant (16 µg/ml)
Linezolid	Susceptible (4 µg/ml)
Moxifloxacin	Susceptible (0.25 µg/ml)
Rifabutin	Susceptible (0.5 µg/ml)
Rifampin	Resistant (4 µg/ml)
Trimethoprim-sulfamethoxazole	Resistant (8 µg/ml)

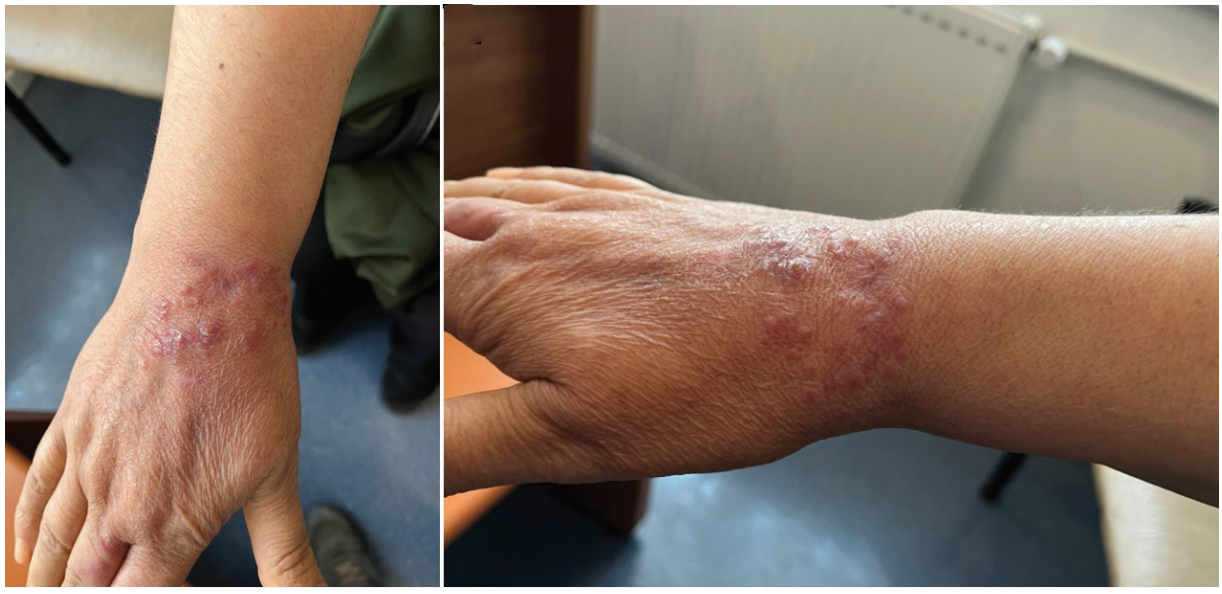

Figure 4. Nodule and plaque regression after empiric treatment prior to linezolid addition

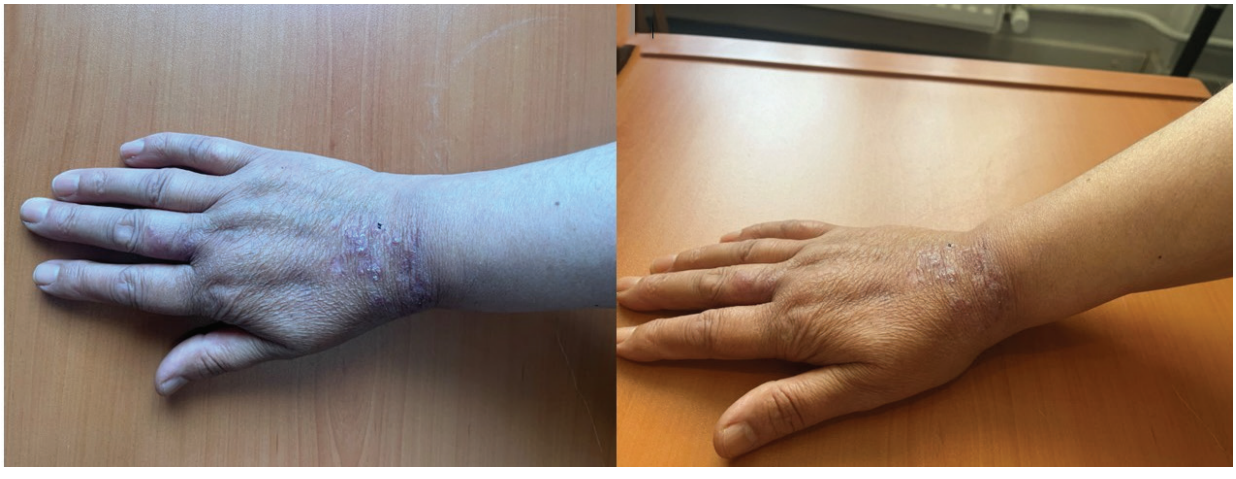

Figure 5. Final examination after 24 weeks of antibiotic treatment showing marked lesion improvement

The limited accessibility of the species-level identification and the antimicrobial susceptibility testing for NTM represents a major diagnosis and treatment selection challenge. Although matrix-assisted laser desorption/ionization time-of-flight mass spectrometry is routinely employed in our center, a reliable species-level identification cannot be achieved in our case. The isolates were referred to the national reference laboratory because a precise identification cannot be established. However, the process of transferring samples and obtaining results from the reference laboratory may take weeks or even months due to the workload and shortages of diagnostic test kits. At this stage, empirical therapy may be initiated, considering that patients frequently request prompt treatment without waiting for the test results.

Rifampicin, rifabutin, ethambutol, clarithromycin, sulfonamides, and trimethoprim sulfamethoxazole are effective against *M. marinum*. However, the organism is intrinsically resistant to isoniazid and pyrazinamide, which are critically important anti-tuberculosis agents[9]. Streptomycin, amikacin, linezolid, tetracyclines, and fluoroquinolones are also preferable alternative agents. Another limitation of empirical therapy is our country's restricted access to anti-tuberculosis agents, such as ethambutol and rifabutin, which are expected to be active against *M. marinum*, outside of a confirmed tuberculosis diagnosis. In our case, considering the most likely NTM species based on clinical presentation and the availability of effective agents, an empirical regimen comprising ciprofloxacin and clarithromycin was initiated.

Combination regimens containing clarithromycin, ethambutol, and rifampicin are the most commonly utilized and recommended therapeutic options[9,10]. However, alternative therapeutic strategies may be required because of atypical resistance profiles, treatment failures, limited drug accessibility, and adverse effects. Previous studies demonstrated the *in vitro* activity of linezolid and fluoroquinolones against *M. marinum*[11]. Among the fluoroquinolones, moxifloxacin shows higher susceptibility rates compared to ciprofloxacin[11,12]. In some reported cases, successful treatments were realized with linezolid-containing combination regimens[13,14]. In our case, linezolid may represent a suitable alternative when an adequate response cannot be achieved with a quinolone and clarithromycin combination or when drug substitution is required considering the adverse effects. Clarithromycin-based combination regimens are generally associated with the highest clinical success and antibiotic susceptibility rates[15-17]. In some reported cases as well, adjunctive thermotherapy in combination with antibiotic therapy was proven to be beneficial[18, 19]. The treatment duration may vary according to the depth and extent of infection. The involvement of the joints, tendons, or bone and the presence of an abscess formation particularly necessitates prolonged therapy courses. Surgical excision may be considered as an adjunct to medical therapy in certain cases. Although no consensus has yet been reached on the optimal treatment duration, therapy is generally recommended to continue for 4–8 weeks after the clinical resolution of symptoms[20].

Although routine antibiotic susceptibility testing is not recommended in managing *M. marinum* infections, susceptibility testing is advised in cases failing to respond to therapy[9,10]. In our case, the isolation of *M. marinum* that is resistant to doxycycline, ethambutol, rifampicin, and trimethoprim-sulfamethoxazole is unexpected and noteworthy. Several studies and case reports documented resistance to doxycycline, trimethoprim-sulfamethoxazole, rifampicin, and ethambutol[11,12,20-22], but our case is particularly rare and valuable because of the concomitant *in vitro* resistance to both rifampicin and ethambutol. Ideally, treatment must be guided by a species-level identification and an antibiotic susceptibility testing. Nevertheless, logistical limitations and the urgency of therapy initiation often render this approach difficult. In these circumstances, empiric treatment with clarithromycin-based combination regimens appears to be a safe and reasonable strategy.

The patient was carefully questioned about the possible risk factors for *M. marinum* infection, including contact with aquariums, fish, and other aquatic animals, swimming pools, or seawater; however, no such exposure was reported. Note that she sustained a chestnut thorn injury to the affected arm a few months before the lesions appeared. A literature review did not reveal any previous cases of the *M. marinum* infection linked to chestnut thorns or similar plants. In the reported case series, the majority of cases showed a history of exposure to an aquarium, a pool, or fish, although cases linked to procedures (e.g., trauma or injections) were also presented[14,20,23]. By contrast, our case showed no history of prior injection or similar interventions before the lesions. *M. marinum* was isolated from both aquatic environments and animals and from soil and plants in natural settings. These reservoirs were theoretically proposed as the potential transmission sources between organisms[24]. A risky exposure history cannot be found in some patients within the reported case series, and "source unknown" classifications were used, suggesting that there may be as yet unidentified sources and relationships underlying the *M. marinum* transmission. In this context, a recently published case report on *M. marinum* found no aquatic or water-associated exposure, as in our case. The proposed source was transmission from a pet reptile[25].

The literature has not yet identified cases of *M. marinum* arising after injuries from chestnut-tree thorns or other plant-related grazes. Conversely, given that the patient had a history of chestnut harvesting with injury from a chestnut thorn to the affected limb, and the bacterium was isolated from the soil and

plants, the most plausible hypothesis is transmission via this injury.

In summary, our case represents the first instance of *M. marinum* arising from a chestnut-tree or plant-related injury.

Conclusion

M. marinum must be considered in patients with chronic skin lesions resistant to treatment, even without typical aquatic exposure. In the case presented herein, a chestnut thorn injury was identified as a potential infection source, highlighting the importance of considering environmental trauma. Clarithromycin-based combination therapy is a reliable empirical treatment in the absence of definitive data. This case underscores the need to consider NTM infections in unusual clinical presentations.

Ethics

Informed Consent: Informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Ö., Ş.B.A., C.Ö., U.Ö., Concept: E.Ö., U.Ö., Design: E.Ö., U.Ö., Data Collection or Processing: E.Ö., Ş.B.A., C.Ö., Analysis or Interpretation: E.Ö., U.Ö., Literature Search: E.Ö., U.Ö., Writing: E.Ö.

Conflict of Interest: Uğur Önal, one of the authors of this article, is a member of the editorial board of the Mediterranean Journal of Infection, Microbes and Antimicrobials; however, he did not participate in any stage of the editorial evaluation process of this manuscript. The other authors declare no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

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