

Atypical Keratotic Nodule on the Knuckle

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A 75-year-old man presented with a lesion on the knuckle of 5 months' duration. He reported that the lesion initially grew very quickly before shrinking down to its current size. He denied any bleeding or pain but thought he may have had a splinter in the area around the time the lesion appeared. He reported spending a lot of time outdoors and noted several recent insect and tick bites. He also owned a boat and frequently went fishing. He previously had been treated for actinic keratoses but had no history of skin cancer and no family history of melanoma. Physical examination revealed a 2-cm erythematous nodule with central hyperkeratosis overlying the metacarpophalangeal joint of the right index finger. A shave biopsy was performed.

WHAT'S YOUR DIAGNOSIS?

- atypical mycobacterial infection
- chromoblastomycosis
- leishmaniasis
- sporotrichosis
- squamous cell carcinoma

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THE DIAGNOSIS: Atypical Mycobacterial Infection

The history of rapid growth followed by shrinkage as well as the craterlike clinical appearance of our patient's lesion were suspicious for the keratoacanthoma variant of squamous cell carcinoma (SCC). Periodic acid–Schiff green staining was negative for fungal or bacterial organisms, and the biopsy findings of keratinocyte atypia and irregular epidermal proliferation seemed to confirm our suspicion for well-differentiated SCC (Figure 1). Our patient subsequently was scheduled for Mohs micrographic surgery. Fortunately, a sample of tissue had been sent for panculture—bacterial, fungal, and mycobacterial—to rule out infectious etiologies, given the history of possible traumatic inoculation, and returned positive for *Mycobacterium marinum* infection prior to the surgery. Mohs surgery was canceled, and he was referred to an infectious disease specialist who started antibiotic treatment with azithromycin, ethambutol, and rifabutin. After 1 month of treatment the lesion substantially improved (Figure 2), further supporting the diagnosis of *M marinum* infection over SCC.

The differential diagnosis also included sporotrichosis, leishmaniasis, and chromoblastomycosis. Sporotrichosis lesions typically develop as multiple nodules and ulcers along a path of lymphatic drainage and can exhibit asteroid bodies and cigar-shaped yeast forms on histology. Chromoblastomycosis may display pseudoepitheliomatous hyperplasia and granulomatous inflammation; however, pathognomonic pigmented Medlar bodies also likely would be present.¹ Leishmaniasis has a wide variety of presentations; however, it typically occurs in patients with exposure to endemic areas outside of the United States. Although leishmaniasis may demonstrate pseudoepitheliomatous hyperplasia, ulceration, and mixed inflammation on histology, it also likely would show amastigotes within dermal macrophages.²

Atypical mycobacterial infections initially may be misdiagnosed as SCC due to their tendency to induce irregular acanthosis in the form of pseudoepitheliomatous hyperplasia as well as mild keratinocyte atypia secondary to inflammation.^{3,4} Our case is unique because it occurred with *M marinum* infection specifically. The histopathologic findings of *M marinum* infections are variable and may additionally include granulomas, most commonly suppurative; intraepithelial abscesses; small vessel proliferation; dermal fibrosis; multinucleated giant cells; and transepidermal elimination.^{4,5} Periodic acid–Schiff, Ziehl–Neelsen (acid-fast bacilli), and Fite staining may be used to distinguish *M marinum* infection from SCC but have low sensitivities (approximately 30%). Culture remains the most reliable test, with a sensitivity of nearly 80%.^{5–7} In our patient, a Periodic acid–Schiff stain was

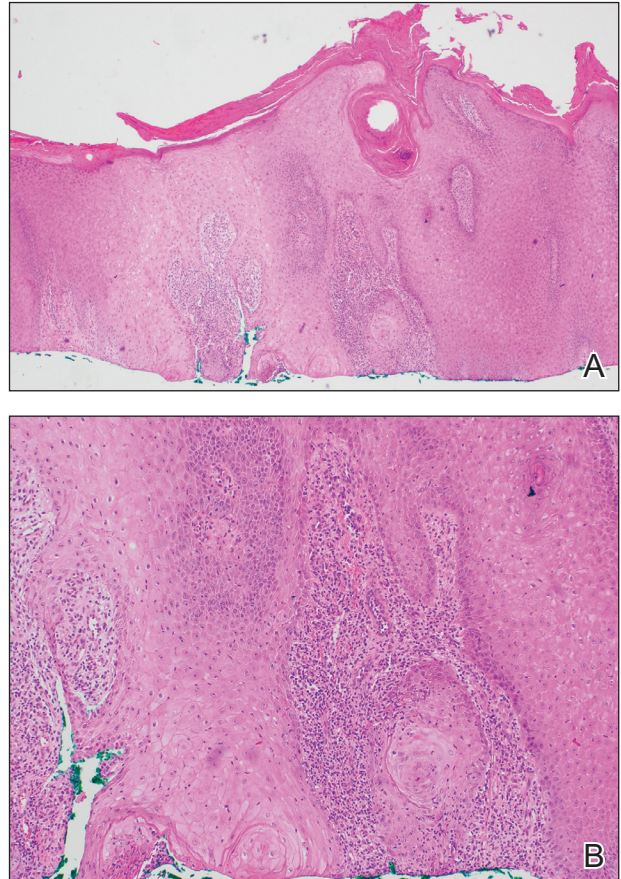


FIGURE 1. A and B, Shave biopsy sections demonstrated superficial portions of a squamous process with marked irregular acanthosis, cytologic atypia, and mixed inflammation involving the superficial dermis, suggestive of squamous cell carcinoma (H&E, original magnifications ×50 and ×100).

obtained prior to receiving culture results, and acid-fast bacilli and Fite staining were added after the culture returned positive; however, all 3 stains failed to highlight any mycobacteria.

The primary risk factor for infection with *M marinum* is contact with aquatic environments or marine animals, and most cases involve the fingers or the hand.⁶ After we reached the diagnosis and further discussed the patient's history, he recalled fishing for and cleaning raw shrimp around the time that he had a splinter. The Infectious Diseases Society of America recommends a treatment course extending 1 to 2 months after clinical symptoms resolve with ethambutol in addition to clarithromycin or azithromycin.⁸ If the infection is near a joint, rifampin should be empirically added to account for a potentially



FIGURE 2. After 1 month of antibiotic treatment, the *Mycobacterium marinum*-infected lesion showed resolution of hyperkeratosis and overall improvement and regression.

deeper infection. Imaging should be obtained to evaluate for joint space involvement, with magnetic resonance imaging being the preferred modality. If joint space involvement is confirmed, surgical debridement is indicated. Surgical debridement also is indicated for infections that fail to respond to antibiotic therapy.⁸

This case highlights *M marinum* infection as a potential mimicker of SCC, particularly if the biopsy is relatively superficial, as often occurs when obtained via the common shave technique. The distinction is critical, as *M marinum* infection is highly treatable and inappropriate

surgery on the typical hand and finger locations may subject patients to substantial morbidity, such as the need for a skin graft, reduced mobility from scarring, or risk for serious wound infection.⁹ For superficial biopsies of an atypical squamous process, pathologists also may consider routinely recommending tissue culture, especially for hand and finger locations or when a history of local trauma is reported, instead of recommending complete excision or repeat biopsy alone.

REFERENCES

1. Elewski BE, Hughey LC, Hunt KM, et al. Fungal diseases. In: Bologna J, Schaffer JV, Cerroni L, eds. *Dermatology*. 4th ed. Elsevier; 2018:1329-1363.
2. Bravo FG. Protozoa and worms. In: Bologna J, Schaffer JV, Cerroni L, eds. *Dermatology*. 4th ed. Elsevier; 2018:1470-1502.
3. Zayour M, Lazova R. Pseudoepitheliomatous hyperplasia: a review. *Am J Dermatopathol*. 2011;33:112-122; quiz 123-126. doi:10.1097/DAD.0b013e3181fcb47
4. Li JJ, Beresford R, Fyfe J, et al. Clinical and histopathological features of cutaneous nontuberculous mycobacterial infection: a review of 13 cases. *J Cutan Pathol*. 2017;44:433-443. doi:10.1111/cup.12903
5. Abbas O, Marrouch N, Kattar MM, et al. Cutaneous non-tuberculous mycobacterial infections: a clinical and histopathological study of 17 cases from Lebanon. *J Eur Acad Dermatol Venereol*. 2011;25:33-42. doi:10.1111/j.1468-3083.2010.03684.x
6. Johnson MG, Stout JE. Twenty-eight cases of *Mycobacterium marinum* infection: retrospective case series and literature review. *Infection*. 2015;43:655-662. doi:10.1007/s15010-015-0776-8
7. Aubry A, Mougari F, Reibel F, et al. *Mycobacterium marinum*. *Microbiol Spectr*. 2017;5. doi:10.1128/microbiolspec.TNMI7-0038-2016
8. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med*. 2007;175:367-416. doi:10.1164/rccm.200604-571ST
9. Alam M, Ibrahim O, Nodzinski M, et al. Adverse events associated with Mohs micrographic surgery: multicenter prospective cohort study of 20,821 cases at 23 centers. *JAMA Dermatol*. 2013;149:1378-1385. doi:10.1001/jamadermatol.2013.6255