

Case report



ATYPICAL MYCOBACTERIAL INFECTION

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ABSTRACT:

We describe a 47-year-old healthy man who, after an injury to the third finger of the right hand, developed a reddened papule that did not disappear. Over a period of three months, edema developed on the finger and dorsum of the right hand, followed by several variegated nodules along the 3rd finger, dorsum of the right hand, and right forearm. There are no subjective complaints. The patient has an aquarium at home, and the complaints coincide with a period of growth of the fish in it. The diagnosis of *Mycobacterium marinum* infection is made on the basis of history, clinical picture, histology and molecular genetic testing for mycobacteria. Treatment with numerous antibacterial agents was carried out, and the long-term (9 months) therapy with clarithromycin, rifampicin and ethambutol, appointed after the diagnostic clarification, led to the cure of the infection. A brief review of the literature on the issue is made.

Keywords: atypical mycobacteria, *Mycobacterium marinum*, granulomatous inflammation, aquarium,

INTRODUCTION:

Skin infections caused by atypical mycobacteria are rare diseases, but in recent years, enough scientific publications have been accumulated to increase the number of infected individuals. *Mycobacterium marinum* is an acid-resistant microorganism from the group of atypical mycobacteria, which live in natural fresh and salt water, swimming pools, home aquariums. [1]

In freshwater and saltwater fish, *Mycobacterium marinum* causes a tuberculosis-like disease, but in humans, it leads to a granulomatous inflammation of the skin and soft tissues. [2, 3] A broken skin surface, even after minimal trauma, is the gateway to infection after direct contact with infected material, most often contaminated water. The disease is known as Swimming pool granuloma, Fish tank granuloma or aquarium granuloma. [4]

CASE PRESENTATION

A healthy 47-year-old Caucasian male consults about a 3-month-old skin infection on the back of the right palm.

In September 2021, he pricked the tip of the third finger of his right hand with dry herbs. A miliary erythematous papule remained at the site of the trauma, which did

not disappear. Three months later, swelling appeared on the back of the right palm, without subjective complaints, for which he also underwent systemic antibiotic treatment with beta-lactam agents, macrolides and tetracyclines, but with inconclusive effect. After the swelling subsided, erythematous nodules of various sizes were formed along the 3rd finger and the back of the right palm, imitating cutaneous sporotrichosis. After a month, a reddened nodule appeared on the back of the right forearm, measuring 2/2 cm. It suppurated spontaneously with the discharge of a yellowish discharge. There was no lymphadenopathy and any manifestations of toxoinfectious symptoms. (fig. 1)

Fig. 1. Erythema and edema of the third finger with nodules of various sizes over the right right hand and proximal forearm with sporotrichoid model of appearance.

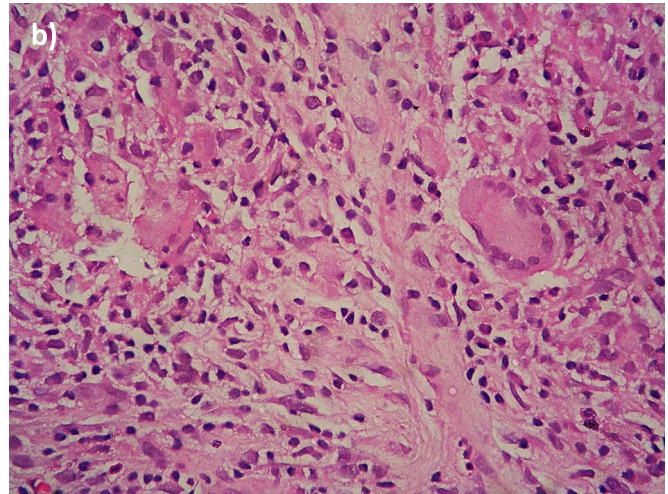
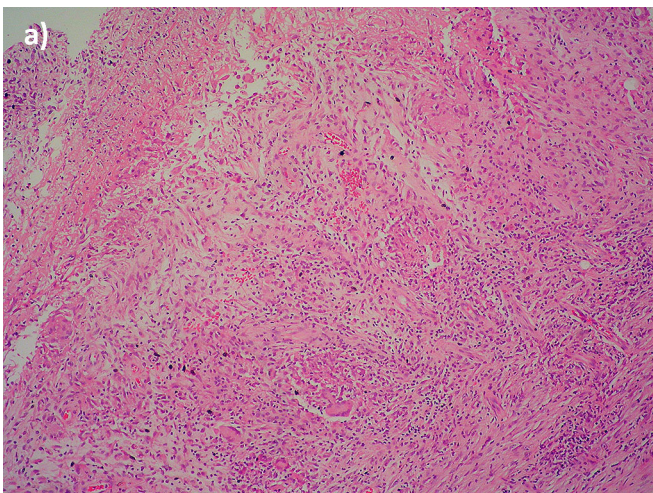




The patient has a home aquarium with tropical fish that became ill at the same time.

Somatic status is unremarkable. There are no data on accompanying diseases. All routine hematological and biochemical laboratory tests were normal. Bacterial and fungal cultures were negative, as well as Quantiferon and HIV-antibody tests. Chest x-rays did not show pulmonary tuberculosis. Histological examination revealed a granulomatous inflammatory infiltrate with tuberculoid granulomas and scattered giant cells in the dermis. (fig. 2)

Fig. 2. Skin and subcutaneous tissue - Pseudoepitheliomatous hyperplasia; in the deep deep dermis, extensive necrosis mixed with leukocytes (abscessing necrosis) is observed; proliferation of epithelioid cells and young blood vessels, among which numerous multinucleated giant cells are found. **a)** – H&E x 10; **b)** – H&E x 100;



In terms of differential diagnosis, infections with a similar clinical picture (Pyoderma, Tinea profunda, Sporotrichosis, Chromoblastomycosis, Tuberculosis cutis, Leishmaniosis cutis) have been discussed, including infections with atypical mycobacteria (*M. marinum*, *M. kansasii*, *M. chelonae*, *M. avium-intracellulare*, *M. ulcerans*). For the purposes of the diagnosis, a molecular-genetic study was carried out for species identification of clinically significant mycobacteria (GenoType Mycobacterium CM, Lab.No 38/22.02.2022), in the reference laboratory of the National Center of Infectious and Parasitic Diseases, Sofia, and *Mycobacterium marinum* was verified (01. 04. 2022).

The patient was consulted by a pulmonologist who prescribed therapy with Clarithromycin 500 mg bid, Rifampicin 300 mg bid and Ethambutol 750 mg/day for a period of 6 months, which was extended by three months after a control examination at the 5th month from the start of therapy. After a nine-month treatment with the indicated triple drug combination, all pathological changes disappeared. (fig. 3)

Fig. 3. Effect of the therapy **a)** – 5 months; **b)** – 9 months





DISCUSSION

Mycobacterium marinum is a nontuberculous mycobacterium first isolated by Joseph Aronson from dead saltwater fish in a Philadelphia aquarium in 1926. In 1954, Linell and Norden reported *M. marinum* infection in 80 patients from a swimming pool in Sweden. [5] In 1962, Swift and Cohen first reported 2 cases of *M. marinum* infection from an aquarium with tropical fish. [6] The first two etiologically confirmed cases of infection with *M. marinum* in Bulgaria were described by Bachiiska E, et al. in 2020. [7]

Clinically, the upper limbs are affected in 90% of patients. [8, 9] In about 60% of cases, *M. marinum* is a skin infection, manifesting as a single papular or nodular lesion at the site of inoculation on the finger or hand, 2-6 weeks after inoculation. In a quarter of the patients, the disease takes a sporotrichoid form, which is the case described by us. Sometimes skin lesions appear as pustular, nodulo-ulcerative, granulomatous or verrucous plaques. Lymphadenopathy is rarely observed. [1, 2, 10, 11]

Usually, the evolution of the infection is benign, and it may be able to heal spontaneously up to 2-3 years after infection, leaving atrophic cicatrixes. Generalized infection is rarely seen, mostly in immunocompromised patients. In humans, *M. marinum* infection does not cause permanent immunity. [5]

Due to the non-specific clinical picture and the wide differential diagnosis, the diagnosis of the disease can be difficult and delayed, especially if there is no his-

tory of contact with fish, fish products and/or potentially contaminated water. Histological examination is non-specific and presents with granulomatous inflammation with necrosis in the deep dermis and the presence of giant cells. Ziel-Neelsen staining is positive for the bacterium in only about 30% of cases, and microscopy cannot distinguish *M. marinum* from other mycobacteria. The most reliable is the cultural method, and the sowing is carried out on the specific medium of Löwenstein-Jensen at a temperature of up to 30°C. After the isolation of a pure bacterial culture with a molecular genetic test, species identification of the clinically relevant mycobacteria is performed by amplification and hybridization. [1, 7, 12]

There is currently no single approach to treating *M. marinum* infection. In addition to the wide range of antibiotics, local antibacterial agents, cryotherapy, photodynamic therapy, electrodissection, debridement are also applied, and most often, the treatment is combined. Systemic corticosteroids are not administered because of the risk of recurrence of the condition. [1, 13] *M. marinum* is sensitive to clarithromycin, which drug is more effective in combination with rifampicin. [14, 15] For a 67-year-old patient treated with clarithromycin, ethambutol and rifampicin reported by Johnson RP, et al. (2007), and in the course of a three-month treatment, the lesions disappeared completely for two months. [16]

During the last decade, *M. marinum* infection has also gained a significant role as an infection in individuals treated with biologics; however, recent publications recommend continuation of biologic therapy after elimination of the bacteria by adequate antibiotic therapy. [17, 18]

CONCLUSIONS

M. marinum is a nontuberculous mycobacterium widely distributed in fresh and salt water environments. More often, nodular granulomas are found on the skin of the upper extremities. The diagnosis is made from material for histological examination, culture culture in a specific medium for mycobacteria and species identification with a molecular genetic test. Treatment mainly involves double or triple antibiotic combinations with anti-tuberculosis agents.

We present a case of a healthy 47-year-old white male with a history of contact with contaminated aquarium water after trauma to a finger on the right hand, demonstrating a sporotrichoid form of Fish tank granuloma. The causative agent, *M. marinum*, was culture- and species-verified, and treatment with clarithromycin, rifampicin, and ethambutol resulted in complete recovery after nine months of therapy.

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