Swimming pool granuloma - difficult diagnostic problem

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Abstract

Swimming pool granuloma is a rare infection of the skin caused by *Mycobacterium marinum*. The primary skin lesion is defined as a blue/red papule or nodule with verrucous surface and secondary ulceration in some cases. The skin lesions are usually localized on upper limbs, especially fingers. Usually, at the very early beginning they are misdiagnosed as a deep mycotic infection, tuberculosis, skin abscess, leishmaniasis or warts. Here we analysed retrospectively 5 patients diagnosed and treated between June 2009 and September 2010 because of swimming pool granuloma in the Outpatient Ward of the Department of Dermatology, Medical University of Gdansk. We also followed the newest publications relating to this problem.

Key words: swimming pool granuloma, Mycobacterium marinum, diagnostic procedures, treatment.

Introduction

Mycobacterium marinum was first isolated by Aronson in 1926 from marine fish in an aquarium in Philadelphia [1-7]. The first case of human disease after the use of swimming pools in Sweden was described in 1951 by Linell and Norden [8]. Several years later, Swift and Cohen published a case of M. marinum infection associated with natural water reservoirs [9].

Mycobacterium marinum belongs to group I bacilli according to the classification by Runyon [10]. In fish it causes a deadly disseminated tuberculosis-like infection [6]. In humans, the infection occurs when the pathogen penetrates the skin at places of minor injury (needle pricks, scratches or abrasion) of the skin while in water, in which the bacillus is a naturally occurring saprophyte [1]. Mycobacterium marinum is naturally found in closed reservoirs, rivers, lakes, shallow parts of the ocean, as well as heated swimming pools and aquariums [11]. Its vectors include marine or freshwater fish, dolphins, snails and crustaceans [12].

After an incubation period of 2-6 weeks [13], at the site of injury a single erythematous papule or nodule develops. The lesion then progresses to papillary purple plaques, which can undergo ulceration with haemoserous secretions [3]

The lesions are located mainly in the upper limbs, especially fingers. Less common sites are elbows, knees,

feet and in some cases the face, which closely correlates with traumatic exposure [2].

Case reports

Case 1

A 64-year-old tropical aquarium fish breeder, with no previous history of systemic disease, presented in April 2010 to the Outpatient Clinic Medical University of Gdansk (MUG) due to red/purple nodular changes located on the fifth digit of the right hand. There were also several smaller nodules on the forearm of the same side. The primary lesion on the finger appeared two months prior to the visit to the clinic. The diagnosis of furunculosis was made. Treatment in an outpatient clinic with clavulanic acid, amoxicillin, azithromycin and clindamycin lasted 3 weeks, with no effect.

The history revealed that two weeks before the skin change first appeared, the patient had cleaned an aquarium. Physical examination found no abnormalities, peripheral lymph nodes were not enlarged. Basic laboratory tests were within normal values. Histological examination of a skin fragment revealed abscess-like granulomatous inflammation with skin ulceration and reactive hyperplasia. Tissue cultures for *M. marinum* came back negative after a waiting period of 8 weeks. Diagnosis of fish tank granuloma (FTG) was established based on clinical and

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histological findings. Treatment with doxycycline at a dose 2×100 mg was initiated. After 8 weeks of therapy, complete remission of skin lesions was achieved with a remnant of a bluish coloured scar.

Case 2

A 33-year-old professional diver reported to the clinic in December 2009 due to a erythematous skin change with a diameter of 4 cm. The lesion was described as hyperkeratotic, seeping from time to time, located on the back of the right hand and also with several small nodules on the right forearm (Fig. 1 A). The skin change on the hands was first noticed in January 2009 and originally had the appearance of a red/blue painless nodule. For nearly 12 months the patient was unsuccessfully treated by several specialists. Initially the lesion was diagnosed as a skin abscess and was treated with topical antibiotics, and later with oral antibiotics (amoxicillin, azithromycin). This treatment had no positive clinical effect. Another diagnostic suggestion was deep skin mycosis, which was then treated for months with oral antifungal agents, in spite of a negative mycological culture. After several months, the patient noticed the appearance of more widespread nodules in the proximal right forearm. At the time of reporting to our centre the patient was applying topical corticosteroids on the lesions.

In the patient interview, it was found that a few weeks before the appearance of the first changes, the patient suffered an injury to the same region while diving in a river. Physical examination and basic laboratory tests showed no abnormalities. Histological diagnosis revealed chronic granulomatous perifolliculitis. Tuberculin test was positive (Fig. 1 B), but the tissue culture was negative. With the typical history, characteristic swimming pool granuloma clinical picture and positive tuberculin test, the patient was started on doxycycline 2×100 mg for 6 weeks. During the treatment, a reduction in size, significant flattening of the primary lesion and complete disappearance of the nodules on the forearm was observed. The therapy was supplemented with cryosurgery on the back of the hand, with a good clinical effect (Figs. 1 C, D).

Case 3

A 35-year-old pet store employee reported to the local clinic in May 2010 due to blue/red nodules located on the hands and forearms on the right side (Fig. 2), which had



Fig. 1. A – erythematous-infiltrative change with a hyperkeratotic surface in the course of FTG (patient 2), B – a positive tuberculin skin test (patient 2), C-D – significant flattening of the lesions after combination therapy (doxycycline + cryosurgery)



Fig. 2. Changes in the course of FTG blue/red nodules (patient 3)

appeared 2 months ago. The patient was under no treatment for this disease. The patient's work, among other things, included frequent cleaning of aquariums containing tropical fish. There was no associated injury prior to the appearance of eruptions on the affected limb. The diagnostic tests performed, except for a positive tuberculin test, did not reveal any abnormalities. On physical examination enlarged axillary lymph nodes were found on the right side. The histological lesion biopsy was described as an overgrowth of akeratocytic epidermis with dermal inflammatory infiltration that was mainly located around small blood vessels. Also, small, isolated epithelioid granuloma giant cells were described. Despite the negative result from tissue culture on Löwenstein-Jensen medium, the diagnosis of swimming pool granuloma was made. The patient was initiated on doxycycline 2 × 100 mg. After 3 weeks of therapy the disease progressed and the emergence of new nodular eruptions on the forearm spreading along the course of lymphatic vessels was observed. Doxycycline was discontinued, and the patient was treated with ciprofloxacin at a dose of 2×500 mg. The treatment was continued for another 8 weeks with complete remission of skin lesions, only leaving discoloured scars.

Case 4

The 73-year-old patient reported to the Outpatient Clinic MUG in July 2010, due to colour changes of red/purple nodules located on the middle finger of the right hand and forearm. In outpatient care, the patient was treated for 4 weeks with clavulanic acid plus amoxicillin and clindamycin for an extra 2 weeks, without improvement. After a thorough history taking, it was found that a few weeks before the appearance of the first changes on the finger, the patient was exposed to an injury while working at a marine fish cookery. Pathological examination showed extensive leukocytes concentrated around the hair follicles and other appendages of the skin within the granulomatous site in the dermis. Tissue culture was negative, despite the characteristic clinical picture of the disease. The patient was treated with ciprofloxacin 2 × 500 mg for 8 weeks with good therapeutic effect.

Case 5

A 49-year-old professional fisherman appeared in the clinic in June 2009 for diagnosis of an erythematous skin lesion located on the dorsal surface of the left hand and spreading to the arm on the same side (Fig. 3 A). The first change occurred about 4 weeks after a fish scale stick injury. Initially the patient was treated with amoxicillin with clavulanic acid for 3 weeks, but without effect. In laboratory studies there were no irregularities. Pathological examination showed intense inflammatory infiltration in the dermis composed mainly of small lymphocytes, and a single small granuloma (Fig. 3 B). After treatment with ciprofloxacin 2 × 500 mg for 6 weeks, there was a complete remission.



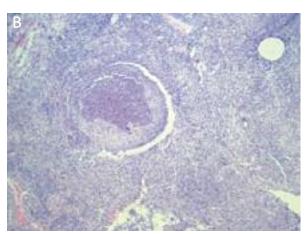


Fig. 3. A – erythematous-infiltrative changes in the course of FTG (patient 5), B – histopathology of swimming pool granuloma – intensive inflammatory infiltration in the dermis composed mainly of small lymphocytes and a single granuloma

Discussion

The incidence of swimming pool granuloma is not really known. According to various reports, occurrence is about 0.05-0.27 cases per 100,000 inhabitants [14, 15]. The number of patients observed by us in a relatively short time (16 months) suggests that the infection occurs much more frequently than previously thought. In the past, a small outbreak among persons using swimming pools was observed [16], but this number of cases has decreased significantly (up to 2.6-4.4% of all *M. marinum* infections), undoubtedly due to the chlorination of swimming pools occurring nowadays [17]. Currently, the majority of cases are linked to aquarium activities and are estimated to be as high as 49% of infected patients [18], which is also confirmed by our observations.

Mycobacterium marinum usually causes superficial skin infections. Hurst et al. [19] isolated the 3 types of skin lesions in swimming pool granuloma (fish tank granuloma – FTG) (Table 2). Deeper structures such as tendons, joints and bones becoming affected is rarely seen, but according to some authors, may complicate up to 29% of infections [20].

In 20-40% of cases observed, the sporotrichoid form of FTG exists, where nodular or ulcerative changes spread along the course of lymphatic vessels. The lymph nodes are usually enlarged [13, 21, 22]. Our patients presented with this form of the disease.

Diffuse type of FTG is often correlated with an underlying cause. Most of these cases are observed in immuno-compromised patients, mostly due to the use of systemic corticosteroid therapy [23, 24], and very rarely in people with AIDS [25–27].

Accurate diagnosis is often difficult to establish, which explains the delay in the initiation of appropriate treatment [28]. In our patients the time from the appearance of the rash to diagnosis ranged from 2 months to 1 year. Similar observations have also been reported by other authors. Hess $et\ al.$ [28] analysed 29 cases of swimming pool granuloma and found that the average time to final diagnosis was 5.2 months (1-14 months).

The disease is uncommonly recognized by doctors who are not dermatologists. In the initial period, especially if together with a poorly collected history, the changes can be misdiagnosed as a skin abscess [3], inflammation of the subcutaneous tissue [3], deep fun-

Table 1. Clinical characteristics of the patients in our study

Patient	Age	Sex	Preceding trauma	Type of exposure	Time from onset to diagnosis	Type of infection	Localisation of lesion	Treatment	Outcome
1	64	M	Yes	Aquarium	2 months	Sporotrichoid form	Finger/forearm	Doxycycline 200 mg/day 8 weeks	Cured
2	33	M	Yes	Diving	1 year	Sporotrichoid form	Hand, forearm	Doxycycline 200 mg/day 6 weeks Cryosurgery	Partial remission, cured
3	35	M	No	Aquarium	2 months	Sporotrichoid form	Hand, forearm	Doxycycline 200 mg/day 3 weeks; ciprofloxacin 1000 mg/day 8 weeks	Progression, cured
4	73	М	Yes	Sea fish	3 months	Sporotrichoid form	Finger/forearm	Ciprofloxacin 1000 mg/day 8 weeks	Cured
5	49	М	Yes	Sea fish	2 months	Sporotrichoid form	Hand, forearm	Ciprofloxacin 1000 mg/day 8 weeks	Cured

Table 2. Morphological changes in swimming pool granuloma according to Hurst

Type	Morphology
I	Blue and red sore nodules with a diameter of 1-2 cm, self-limiting, lasting from a few to several months
II	Single or multiple subcutaneous granuloma, which may undergo ulceration
III	Changes in deep structures: tendons (tendosynovitis), joints (septic arthritis), lymphatic vessels (lymphangitis), bones (osteomyelitis)

Table 3. Includince of injury and exposure to containinated water reservoirs in infected M. Maritain attended	Table 3. Incidence of inju	ry and exposure to contamina	ated water reservoirs in	infected M. marinum –	· literature data
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Author	Preceding trauma [%]	Contact with water environment [%]	Number of cases
Aubry	7.9	84	63
Kullavanijaya	61.1	66.7	44
Ang	31.5	44.7	38
Hess	Not documented	69	29

Table 4. Methods of treating swimming pool granuloma

Invasive methods	Non-invasive methods
Cryosurgery Laser therapy X-ray therapy Surgery	Antibiotic mono-therapy (minocycline, doxycycline, clarithromycin, ciprofloxacin, trimethoprim-sulfametho-xazole) Combined therapy (ciprofloxacin + clarithromycin, ciprofloxacin + doxycycline, ciprofloxacin + rifampicin) Rifambucin + ethambutol

gal infection of the skin, leishmaniasis [4], and even ordinary warts [5]. In the differential diagnosis of these types of lesions, furunculosis, skin tuberculosis, atypical mycobacterial infection, sporotrichosis, sarcoidosis, tularemia, *Nocardia* infection, anthrax, cat scratch disease, tumours and foreign body reaction should also be included and considered [2].

Detailed medical history, demonstrating an injury prior to and exposure to contaminated water, can make the diagnosis much easier, but is not always present [12] (Table 3). In a retrospective analysis of 63 cases made by Aubry *et al.* [20] trauma prior to the occurrence of FTG was found only in 7.9% of patients. However, Ang *et al.* [2] reported that only 44.7% of patients infected with *M. marinum* have had contact with an aquatic environment.

In the diagnosis of *M. marinum* infection, helpful tests are histological examination of skin lesions and the tuberculin test, whose outcome is usually positive due to the cross-reaction with *M. tuberculosis* [13].

Histologically, swimming pool granuloma is characterised by significant expansion of the epidermis, purulent inflammation and granulomatous reaction [29]. Because the histological findings are often non-specific, it is necessary to take a tissue culture and identify *Mycobacterium* to undoubtedly confirm the diagnosis [30]. The most used medium for this purpose is Löwenstein-Jensen medium, and the result is read after 6-8 weeks. *Mycobacterium marinum* is photochromogenic; its colonies are cream coloured, and when exposed to light produce a yellow dye [12]. This bacillus grows best at 30-32°C, much worse at warmer temperatures around 37°C, hence the tendency to occupy the distal part of the body in infected people [28].

However, sometimes the tissue culture is negative and the diagnosis of FTG is based on history, typical clinical picture and histopathology, and confirmed with a good response to treatment [31, 32]. In these cases, modern molecular biology techniques, such as PCR, can be crucial in the diagnosis of FTG [11, 33-35]. In our material, *M. marinum* infection was diagnosed on the basis of the characteristic medical history and morphology of lesions and by histological examination. Therapy is implemented just after the cultured material is sent to the lab. In the group of five patients with FTG, the result obtained in tissue culture after 8 weeks was negative. All patients obtained complete remission of skin lesions after treatment.

The optimal treatment regime is not yet determined and the multitude of treatment options shows the limited effectiveness. The choice of treatment depends on individual experience and centre preferences [36]. The therapeutic spectrum includes non-invasive and invasive treatment options (Table 4).

In superficial infections, antibiotics are recommended as monotherapy. The most commonly used are doxycycline, clarithromycin, trimethoprim-sulfamethoxazole and ciprofloxacin. In severe infections, including the sporotrichoid form, rifampin + ethambutol or antibiotic combination therapy consisting of two drugs is recommended. The average duration of treatment should be no less than 6 weeks [1]. Pearson recommends continuing treatment for 4-8 weeks after complete resolution of skin lesions [3]. Cryotherapy and surgery are used as adjuvant therapy in selected cases. However, surgical treatment should not be routinely used and is reserved only for cases resistant to antibiotics and changes with deeper involvement of tendons, joints and bones [12, 17, 36].

In this study, in 3 cases doxycycline was used as first-line treatment and gave complete resolution in one patient, and in 1 patient partial remission, with the need to supplement with cryosurgery treatment. In the other one, the lack of therapeutic effects and progression of the lesion led to a change to ciprofloxacin with good results. In 2 consecutive patients who received as initial treatment ciprofloxacin, relatively rapid remission of skin lesions was observed.

In conclusion, the occurrence of swimming pool granuloma is more common than indicated by data from the literature. The disease is diagnosed late, and the key to proper diagnosis is careful history taking, and demon-

strating an injury prior to exposure to contaminated water. The FTG treatment is difficult, not determined only by the treatment regimen or duration of therapy. Our experience shows that ciprofloxacin is more effective in the treatment of infections caused by *M. marinum* than doxycycline and should be considered as the first line treatment in superficial infections.

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