

Fishtank Granuloma Treated with Combination of Minocycline and Rifampicine

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Abstract: Fishtank granuloma is atypical mycobacterium infection with *Mycobacterium marinum* as causative agent, primary risk of this condition are exposure with aquatic environment. It has no standard therapy, meanwhile it is imperative to begin therapy as soon as possible before bad prognosis happen due to ascending infection from skin to tenosynovium. Men, 40 years old complains from painful bumps in the back of the hand, ulcerating and indurated. Patient had undergone several therapies, but there were no improvement. Patient got hobby of nurturing koi fishes, similar lesion found on patient's fishes. General examination shows pain score was 6/10. Dermatological examination dorsal manus dextra, with localized distribution, shows erythematous nodules, well defined, quantity 6, size 0,5–2 cm, with ulcers, crusts and scales. Histopathological examination shows poorly formed granulation tissues. Epidermis shows acanthosis and some absent, while dermis shows connective tissue with many blood vessels and sparse inflammatory cells of neutrophil, lymphocyte and histiocyte. No visible datia cells and caseous necrosis. Blood count shows lymphocytosis and slight increase of ESR. Patient being diagnosed as fishtank granuloma, got minocycline 2x100 mg, rifampicine 1x600 mg for three months. Lesion healed with scar, pain score reduced to zero were achieved in second month. Therapy continued one month after complete healing. Fishtank granuloma often misdiagnose and leads to late initial therapy, meanwhile this infection tend to be persistent and unable to heal spontaneously. Combination of minocycline and rifampicine can increase therapeutical efectivity and may support establishing diagnosis of fishtank granuloma.

1 INTRODUCTION

Fishtank granuloma is atypical mycobacterial infection with *Mycobacterium marinum* as causative agent, that obtain its name due to primary risk factor of this condition which are exposure to aquatic environment or water creatures. (Delphine et al, 2012, Wu et al, 2002) This pathogen exist in both tropical or sea water. *Mycobacterium marinum* first time being isolated by Aronson in 1926 from a dead sea fish that being obtained from aquarium in Philadelphia. In 1951, Norden and Linell able to isolating it from swimmer who swim in the contagious swimming pool in Sweden. In the year of 1962, Swift and Cohen begin to report two cases of *Mycobacterium marinum* infection from tropical fishes aquarium, and so it begin the term “fishtank

granuloma.” Since that time, the term “swimming pool granuloma” has rarely being used because chlorination of this reservoir make this condition become rare to occur in swimming pool. (Bonamonte et al, 2013) *Mycobacterium marinum* infection in human that has been proved by culture was reported in 66 patients from 1996 to 1998 in France, with incidence 0.04 cases per 100,000 inhabitants per year. According to published study being held in USA, annual incidence of this illness is 0.27 confirmed cases per 100,000 inhabitants. (Bonamonte et al, 2013) In Asia, fishtank granuloma incidence is not being reported yet in a large publish study. However in 2012, Wu TS et al in Taiwan succeed reporting 27 case finding of *Mycobacterium marinum* from 1999 to 2010 in Changung memorial hospital, while in Indonesia, there are only two case

report found from Fauziah SN et al in 2015 and Barros T et al in 2016 both from RSCM Jakarta, being treated with combination therapy of minocycline and rifampicine with good clinical improvement.(Fauziah et al, 2015,Baros et al, 2015) Being reported within this case report, one case of fishtank granuloma in male 40 years old with good clinical improvement, the lesion healed with scar, reduction of pain score to zero, after 2 months therapy with combination rifampicine and minocycline. Therapy was continued to the third month to prevent recurrence.

2 CASE

Male, 40 years old came to Outpatient Departement of Dermatology and Venereology Saiful Anwar General Hospital with main complain bumps that ulcerate in his hand since five months before admission. Initially the bump was solitary, the size was around 1 cm and look like boils and but a few weeks, it become bigger, indurated and painful. The bump was not itch, on a scale 0 out of 10, but it more painful on a scale 6 out of 10. After a few week occur second bumps next to the first bump and the bump got ulcerate. This past 3 months, occur new two bumps closer to the wrist, with the same characteristic as the previous bumps. No history of punctured or being manipulated with sharp objects, woods or branch of a plant. No history being bite by his pets (patient have turtle and koi fishes as pets). Patient clean the pond once every twice week and patient never use gloves when cleaning the pond. Patient recall that before the occurrence of the bump that he complains, he has small wounds result from boils in his wrist that breaks that he ignore previously. Patient never have any history of chronic cough more than 3 months. No history of losing weight since this past years. Throughout the year, the weight were consistent around 59 kg. After the occurrence of second bumps, taken to General Practitioner got zalf contains antibiotic but there not much improvement. Go to dermatovenereologist, got Injected with intra lesion corticosteroid but there was not much changes. On May 2017 the dermatovenereologist command patient to get FNAB and culture from the ulcers. Because the culture show growth of bacteria, the dermatovenereologist give topical antibiotic therapy. Not much improvement to the lesion. Patient got history try to find therapy for his illness to several dermatovenereologist and follow the instruction carefully of topical therapy but there are no

improvement were achieved. Topical therapy that patient ever got were nadifloxacin, erythromycine, metronidazole, sulfur, salicylic acid and dexpanthenol. Patient never apply traditional herbals or any other substances to his wounds. Patient is single. Working as computer technician. Patient got hobbies of nurturing koi fishes in aquarium, ponds and have turtles. He clean the fishtank and pond once a week. No history got bite by his turtle or any wound appear from his hobbies. But according to the patient he has history of having boils that breaks and leave a wound in his wrist and that time, he keep cleaning the fishtanks anyway with the existing wound. According to the patient some of his fishes have ulcer in their body part. Patient clean his yard twice a month by unplug the wild grasses with bare hands. He do it to make his garden clean. Patient do not like gardening or nurturing a specific plant. Physical examination shows patient compos mentis, with good general condition.



Figure 1. Clinical improvement after 3 month of rifampicine 1x600mg and minocycline 2x100mg

Dermatological examination from dorsal manus dextra, with localized distribution, shows erythematous nodules, well defined, round to oval, some confluence, quantity 6, size 0,5 cm – 2 cm, with ulcer, crust and scales. Zeehl Neelsen stain examination from the lesion did not show acid fast bacillus. Blood count examination show limphocytosis and increase of erythrocyte sedimentation rate. Chest X-ray within normal limits, no sign of tuberculosis.

Histopathological examination with HE & PAS stain shows poorly formed granulation tissues with no malignancy. Epidermis absent in some part and acanthosis in the other, while dermis area shows connective tissue with many blood vessels and sparse inflammatory cells of neutrophil, lymphocyte and histiocyte. No visible datia cells and caseous necrosis. Patient being diagnosed as fishtank granuloma and being planned for therapy with rifampicine 1x600 mg and minocycline 2x100 mg for three months.

3 DISCUSSION

Fishtank granuloma is pathologic condition causing granulomatous skin and soft tissue lesions in humans that occur because of *Mycobacterium marinum*, aerobic, waterborne atypical mycobacterium that belongs to Runyon’s classification Group I photochromogenic non-tuberculous mycobacteria. This pathogen causing chronic systemic infections in fish and amphibians, commonly found in non-chlorinated water occupying many aquatic environments. In one large published study by Jernigan *et al* in 2000, they observed 193 infections reported from 1962 through 1996 and found that this pathogen were majority aquarium-related. (Rallis, 2007, Jernigan, 2000, Petrini, 2006) *M. marinum* infection occurs two weeks after direct inoculation of the organism either from fish fins, bites or from the handling of aquariums. In 90% of cases, this takes place via trauma to the upper extremity and do not transmittable from person to person. (Delphine *et al*, 2012, Rallis, 2007, Bhatta *et al*, 2000) In this case patient got hobby of nurturing koi fishes, and direct contact with koi fishes and turtle. He also has habit of cleaning the pond and aquarium without latex gloves. Patient recall that he has minor lesion few weeks before the occurrence of the lesion.

Fishtank granuloma begins as a violaceous papule at the site of a trauma 2-3 weeks after inoculation. Dermatological examination shows nodule or psoriasiform or verrucous plaque, usually

occur in hands, feet, elbows or knees. Infections with *M. marinum* can be classified into 4 clinical categories; Type I (1–3 lesions), Type II: numerous (> 3) lesions) Type III: deep infections (tenosynovitis until osteomyelitis), Type IV: disseminated infection, lung involvement and other systemic manifestations. (Delphine *et al*, 2012, Rallis, 2007, Bhatta *et al*, 2000) Diagnosis is usually delayed, because most physicians are unfamiliar with the disease and a failure to establish a history of exposure to aquatic environments. Therefore, key diagnostic elements for *M. marinum* infections are a high index of suspicion raised by negative bacterial tissue cultures, poor response to conventional antibiotic treatments and a history of aquatic exposure.⁴ Bonamonte *et al* in 2013, report acid-fast bacilli identification only can be found in 6.7% case using Ziehl-Neelsen stain, in accordance with the low detection rates reported in the international literature. (Bonamonte *et al*, 2013) In this patient, regarding the clinical manifestation, Patient suffer from fishtank granuloma type II with history of poor response to various antibiotics and and history of exposure with aquatic environments. Disseminated distribution from the lungs can be excluded since there were no history of chronic cough, or lung tuberculosis an chest X-Ray of this patient was normal. The diagnosis of fishtank granuloma was established based on clinical manifestation and was then confirmed with histopathological examination of skin tissues.

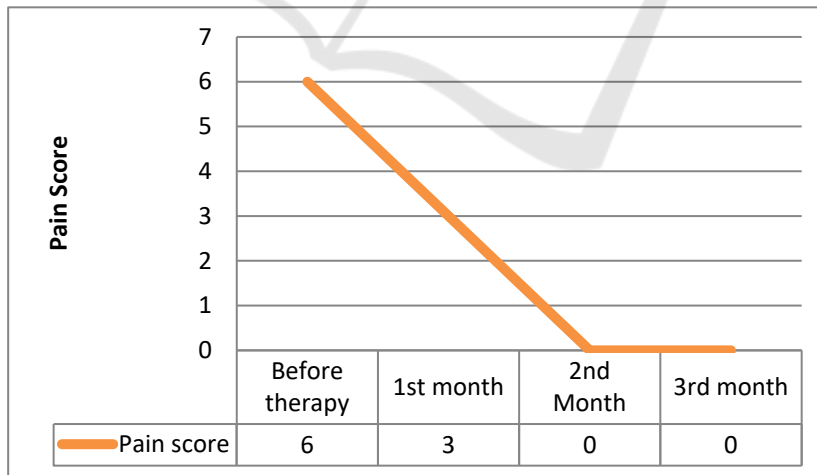


Figure 2. Pain score reduce from 6 to 3 on 1st month, completely zero in second month and the third month

There is no standard regimen for therapy of choice for fishtank granuloma because low incidence of this infection, and *M. marinum* is naturally multi-drug resistant species and treatment is based primarily on the personal experience and

preference of individual investigators, without any large studies or randomized controlled trial. In superficial cutaneous infections, minocycline, clarithromycin, doxycycline and trimethoprim-sulfamethoxazole being reported as effective

monotherapy, but drug resistance varies and thereby combination therapy using two drugs may be required. (Rallis, 2007, Doug et al, 2012) Like other atypical mycobacteria, patients suspected of having atypical mycobacterial skin infections are generally treated empirically. (Rallis, 2007, Jernigan, 2000) Minocycline, The second-generation tetracyclines are the most frequently reported effective treatments. It inhibits bacterial protein synthesis by preventing the association of aminoacyl-tRNA with the bacterial ribosome. (Delphine et al, 2012, Jernigan, 2000) Cummins *et al* 2005 describe a case of *M. marinum* that improved rapidly with minocycline despite a lack of response to doxycycline after 6 weeks. Recent in vitro studies with wild-type *M. marinum* Strains have shown minocycline to be more potent than doxycycline. In addition, at least one minocycline-sensitive strain has shown resistance to doxycycline. (Cummins et al, 2005, edelstein et al, 1994) Bonamonte *et al* 2013 collecting 15 case report from 1987 to 2011 and found 13 cases effectively treat by minocycline 200 mg per day with clinical improvement after 2-3 months. (Bonamonte et al, 2013) Rifampicine in a dose of 600 mg daily, has been used effectively in fishtank granuloma either alone or in combination with other agent. Inhibit RNA synthesis and result in termination of bacterial replications. (Bonamonte et al, 2013, Cummins et al, 2005) Speight *et al* in 1997 has succeed giving rifampicine as single therapy for fishtank granuloma in 14 month old girl, the patient got rifampicine as single therapy because ethambutol and minocycline were contraindicated due to the patient's age. In 1994 Elstein *et al* collected 31 case report of fishtank granuloma and conclude that among other treatment, rifampin in combination with other antimycobacterial appeared to be more successful and in the next best for fish tank granuloma therapy is minocycline treatment. (edelstein et al, 1994, Speight et al, 1997) Duration of therapy that consider effective for management of atypical mycobacteria is ranging from four to thirty eight weeks, depends on how the lesion reponse clinically. It is suggest that the treatment is continued for next four week after lesion has resolved to prevent recurrence of illness. Monotherapy with antimycobacterial agent reported to be effective but since there are variety in drug resistency in *M. marinum*, combination therapy of usually two drugs were strongly suggested. (Rallis, 2007, Fauziah et al, 2015, Baros et al, 2015) Fauziah *et al* in 2016 was reported *Mycobacterium marinum* infection that successful being treated with combination of rifampicine and minocycline, after 2 months. (Fauziah et al, 2015)

4 CONCLUSIONS

Clinical, histopathological feature and clinical response to minocycline and rifampicine support establishing diagnosis of fishtank granuloma. There are clinical improvement, the lesion healed with scar and reduction of pain score to zero after two months giving rifampicine 600 mg daily and minocycline 200 mg twice daily, and application of wet gauze (Na Cl 0,9%) twice daily in this patient. Therapy were being continued 1 month after resolved of lesion and pain, to prevent recurrence (Baros et al, 2015) Laboratory examination after release from treatment shows no elevated liver and renal enzyme, normal erythrocyte sedimentation rate (ESR) and other normal laboratory counts. Blue black discoloration, as side effect of minocycline in the lesion appear after 3 months therapy but subside after 1 months release from treatment.

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If any, should be placed before the references section without numbering.

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