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Association between Piscine Mycobacteriosis and Morgellons Disease: Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Piscine Mycobacteriosis (PM) or sometimes called fish tuberculosis, is a deadly zoonotic disease found in both fresh and marine fish throughout the world. More than 20 strains of *Mycobacterium spp.* are known to cause PM, but their pathogenesis is currently unclear. This is a chronic progressive disease with a variety of clinical symptoms including skin ulcerations, loss of color, scoliosis, and weight loss. Advanced technical molecular methods have now allowed us to different *Mycobacterium* to the individual species level. Out of the 20 known strains, *M. marinum* is the commonest and the most pathogenic organism and it is found in marine and freshwater fish. Morgellons Disease (MD) is a multi-system disorder where patients commonly present with multiple, non-healing, cutaneous wounds. Patients report seeing multi-colored filaments/fibers under the skin and often provide samples to the clinician. However, most clinicians thought this is a delusional disorder and treated the patients with antidepressant drugs. However, recent studies have linked MD with systemic manifestations of Lyme Disease (LD). Other studies have found correlation between MD and tick-borne co-infections. Despite these studies, the definite causative agent of MD has not yet been confirmed. Since the clinical symptoms of PM and MD are somewhat similar, it could be hypothesized that PM and MD could be related to each other. Therefore, the objective of this literature review is to find any link between PM and MD based on the current literature available. However, it should be noted that there is no study done specifically looking into

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this hypothesis. The primary search engine used to find information for this review is PubMed and ScienceDirect. More than 30 research articles and case reports were reviewed and only 19 were shortlisted and used as references. None of the studies were limited to study design, number of participants or the study year. However, only articles written in English language were considered for this review.

Keywords: Morgellons Disease; piscine Mycobacteriosis; Borrelia spirochetes; Mycobacterium marinum.

1. INTRODUCTION

Morgellons disease (MD) is a multisystem dermatological disorder characterized by the presence of multi-coloured filaments embedded under the skin [1]. The beliefs regarding MD have evolved significantly with the light from recent discoveries. Previously, MD was thought to be purely a delusional disorder as patients described crawling and tingling sensations under the skin. However, recent research has completely falsified this belief as it shows histological evidence that multi-coloured filaments are present under the skin and they arise from different layers of the skin, which also eliminates the possibility of self-inflicted implantation of cotton or other fabric.

It has been observed that patients with MD experience symptoms involving cardiovascular, neurological, and musculoskeletal systems similar to those who have been diagnosed with Lyme disease. This finding is supported by the recent research that shows various species of *Borrelia* (causative agent of Lyme disease) in serology and tissue samples of patients with MD. Although a causative link has yet not been established, a strong correlation seems to be present between *Borrelia* species and MD.

Piscine mycobacteriosis (fish mycobacteriosis) is a zoonotic infection present in marine and fresh-water fish [2]. Among the 150 known species of mycobacteria, of which tuberculosis is the major obligate organism for humans, 20 species have been recorded to cause fish mycobacteriosis. Of these 20 species, *Mycobacterium marinum* is the most common bacteria known to cause this disease. It can develop acute illness in both fish and some other vertebrates including humans. The typical presentation includes single or multiple nodules or granulomatous ulcers usually on the extremities [2].

This review will highlight the relation between MD and PM based on their etiology, transmission, clinical features and treatment.

2. ASSOCIATIONS BASED ON ETIOLOGY

Piscine mycobacteriosis is associated with multiple *Mycobacterium spp.* [3]. So far, more than 20 strains *Mycobacterium spp.* have been isolated from fish throughout the world. However, the commonest agent identified in PM is *M. marinum*. It should be noted that the clinical symptoms seen in PM caused by *M. marinum* are different from that of other *Mycobacterium spp*. For example, lesions seen in histology caused by *M. Marinum* is more severe and the symptoms are more acute [3].

M. marinum was also the first agent to be isolated in PM [4]. It was found in fish in an aquarium in Philadelphia in 1926. At that time, researchers thought *M. marinum* only infected marine fish. However, now we know that it is an ubiquitous species and can infect humans as well [4].

Unlike Piscine mycobacteriosis, the etiological agent of MD was not known for many years [1]. Even today, some doctors consider it as a delusional disorder despite the ample amount of evidence suggesting otherwise. For example, multiple studies have shown the association between MD and *Borrelia burgdorferi* infection [5-6]. *B. burgdorferi* is the same spirochetal agent causing Lyme Disease (LD). Therefore, there might be a connection between MD and LD with one infection predisposing the individual to a second infectious agent. However, whether all patients of MD have Lyme *borreliosis* is yet to be determined.

Researchers around the world have made different hypotheses regarding the etiology of MD. One far-fetched but entirely possible hypotheses is that MD could be related to Piscine mycobacteriosis. MD presents with a primary symptom of multi-colored filaments which extrude from the skin. Similarly piscine mycobacteriosis (mainly caused by *M. marinum*)

also presents with superficial crusting ulcers and purple nodules [7]. Since this is an opportunistic disease, it is possible to be a co-infection associated with LD which could somewhat overlap with skin symptoms of MD.

In addition to that, piscine mycobacteriosis also presents with multi-systemic manifestations just like MD. These include loss of weight, white nodule formation, abdominal swelling, etc. [7]. Therefore, it could possibly be argued that MD is the 'human version' of PM. While no study stands to support this notion, there is no literature that falsifies and rules out this possibility either.

3. TRANSMISSION OF MD AND PM

Back when Morgellons disease was thought to be a delusional infestation it was said to be transmitted through internet [1]. However, with recent discoveries suggesting MD to have a strong association with Lyme Disease the transmission of MD could be similar to that of LD.

The *Borrelia burgdorferi*, bacteria that causes LD is transmitted through tick-bites. Blacklegged tick (or deer tick, *Ixodes scapularis*) attach to certain regions of the body such as the groin, armpits and scalp and suck blood for several days [8]. To date, there is no proof that LD can spread from human to human. It also does not seem to transmit through food, water, air and mosquito bites. Since the bacteria can survive in the blood stream, blood donation and maternal transmission is possible, but rare [8]. Although association of MD and LD has been evidently established, the causation has not yet been concluded. Therefore, the exact transmission of Morgellons disease still needs to be further evaluated.

The most common route of transmission of fish mycobacteriosis is through the skin when people rest their hand on the border of ponds. Exposure to *mycobacterium* among swimmers has significantly reduced after ponds were being chlorinated regularly. In addition, handling shellfish or fish after a trauma has also been associated with transmission of the disease. Human to human transmission has not been recorded for this disease in history [8].

There are no direct connections or associations between the transmission of both Morgellons disease and Fish Mycobacteriosis. A cross sectional study that was done on patients in Kaiser Permanente Northern California Hospital who reported fibres, threads or fuzz balls coming out of their skin reported that none of the lesions had mycobacteriosis. However, the validity of this study is questionable since the case definitions were by self-reporting which could lead to bias and misclassification [9].

4. PATHOPHYSIOLOGY AND CLINICAL SYMPTOMS OF MD AND PM

As mentioned previously, Morgellons Disease was previously thought to be self-inflicted and due to psychiatric conditions, such as Delusional Parasitosis. Since the fibres found in the lesions are bright and multi-coloured, which is contrasting to other similar lesions found in humans (as shown in Fig. 1.), it was also thought these fibres are coloured fabric materials. Regardless of their colour, these filaments were found to be arising from follicular sheaths and hyaline from the stratum Basale of the skin. In addition, some of these fibres also had scaling and follicular bulbs similar to that of human hair [10].

Histology samples of Morgellons patients were tested for keratin, collagen, melanin and spirochetes in a study published in Dove Press. The results of this study showed that some of the filaments were positive for all these substances whereas others were not. Also, it was noted that red and white coloured filaments were positive for melanin while blue filaments were positive [11]. Dermatological tissue from these patients also showed hyperkeratosis and hyperplasia. Calluses that were observed in some patients arises from the stratum Basale towards stratum corneum whereas in other patients it originated from the stratum corneum. Fibroblast proliferation was observed in some filaments which caused the rupture of them [11].

To date, not much work has been done on an accurate diagnostic tool for Morgellons Disease. However, recent studies which related staging of MD with syphilis has devised a clinical diagnostic criterion as shown in Table 2. [12]. Middelveen has also come up with a staging criterion for MD based on the histology. Summarised version of the criteria is outlined in Table 1. Apart from the dermatologic symptoms, MD patients also experience an array of systemic symptoms such fatigue, arthralgia, cardiac complications, difficulties with cognition, neuropathy, all symptoms that are commonly reported in patients with Lyme Disease [1].

Table 1. Primary, Secondary and other complications seen in Morgellons Disease and Piscine Mycobacteriosis

Symptoms	Morgellons Disease	Piscine Mycobacteriosis
Primary	a. Multicolored filaments embedded within or protruding from the skin (Fig. 1)	a. single violet or red coloured plaque or nodule (Fig. 2)
	a. Development of calluses	- NIL
	b. Ulcerative lesions	
Secondary	c. Papules	
	d. Burning, itching, stinging, biting	
	e. Hair loss	
	f. Atypical hair/nail production	
	g. Dry appearance with or without flaking skin	
	h. Edema	
	i. Hyper- or hypopigmentation from scarring	
	j. Hypertrophic scarring	
	k. Excoriations	
	l. Slowly healing lesions	
	m. Aging skin	
Additional complications	fatigue, arthralgia, cardiac complications, difficulties with cognition, neuropathy, all symptoms that are commonly reported in patients with Lyme Disease.	Unresolving ulcers, deep infections such as osteomyelitis, tenosynovitis, and disseminated disease.

Table 2. Staging of MD and PM

Morgellons Disease		Piscine Mycobacteriosis	
Stage	Defining Features	Stage	Features
Mild – A	1. Filaments small and not prominent. 2 No hemorrhage, little or no infiltration. 3. Infected keratinocytes.	Type I	self-limiting verrucal lesion
Moderate – B	1. Filaments present. 2. Epidermal parakeratosis and hyperkeratosis. 3. Minimal hemorrhage with infiltration. 4. Infected keratinocytes and macrophages.	Type II	single or multiple subcutaneous granulomas, with or without ulceration
Severe - C	1. Filaments are a prominent feature. 2. Hemorrhage, lymphocytic infiltration and cell disarrangement. 3. Infected macrophages. 4. Borrelia aggregates.	Type III Type IV	deep infections involving tenosynovium, bursa, bones or joints causing tenosynovitis, septic arthritis or osteomyelitis. disseminated infection with lung disease and other systemic manifestations

Similar to MD, the pathophysiology of Piscine Mycobacteriosis is also not well understood nor researched. The low incidence of non-tuberculous mycobacterial infections reduces the ability to correctly identify and diagnose such diseases [13]. *M. marinum* infections usually present as a single violet or red coloured plaque or nodule. The surface maybe crusty and rough or verrucous as well. It is sometimes purulent and shows spread through lymph nodes in a sporotrichoid fashion as seen in Fig. 2. [14]. Further complications seen in fish mycobacteriosis is listed in the staging in Table 2. from the current evidence, it is known that both Morgellons disease and Fish Mycobacteriosis manifests initially with dermatological symptoms. Regardless, the presentation of the of the lesions in both diseases are distinct. PM shows more of a nodular sometimes purulent lesions whereas Morgellons lesions look scratchy with filaments projecting out [13], [15]. In addition most Morgellons patient come to the clinic with the chief complaint of multi-coloured fibres coming out of skin while patients with mycobacteriosis complain of pain and itching mainly [1], [16].

5. ASSOCIATIONS BASED ON MANAGEMENT

To control *M. marinum* infection in fish, all affected stocks must be destroyed and holding tanks must be disinfected. Studies have shown that ethanol and lysol is effective in destroying *M. marinum* in aquaria. However, due the resistance of *mycobacteria* to common disinfectants, researchers found that disinfecting is not very successful to control fish mycobacteriosis [7].

It is also possible to vaccinate fish against *Mycobacterium* [17]. For example, injecting heat-killed *M. marinum* results in the production of IgM and TNF-α in European Seabass. As a result of this, less fish was found dead due to Mycobacteriosis. Heat-killed *M. bovis* can also be used and it provided cross-protection in zebra fish. Finally, DNA vaccines is used too which

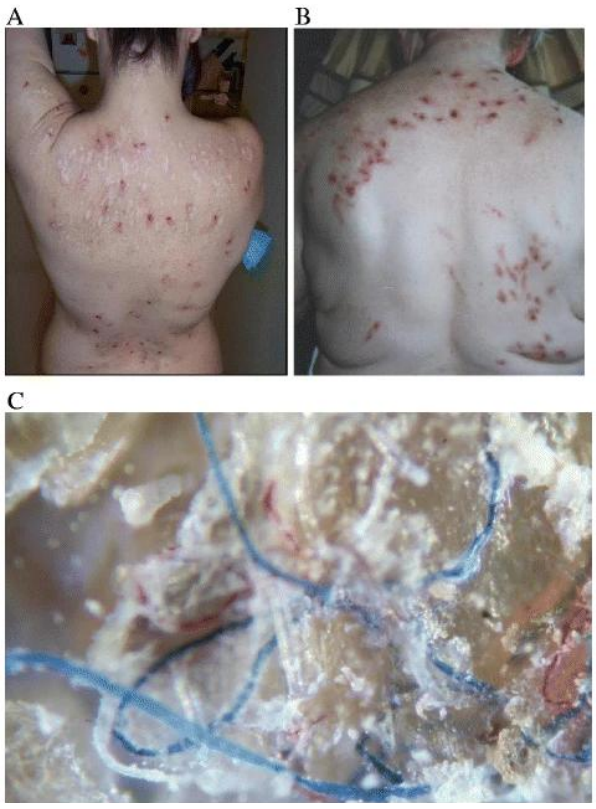

Fig. 1. A, MD patient back showing lesions covering entire surface, including areas out of patient's reach. B, Back of patient with scratching-induced lesions showing distribution limited to patient's reach. C, Multicolored fibers embedded in skin callus from MD Patient 2 (100x)

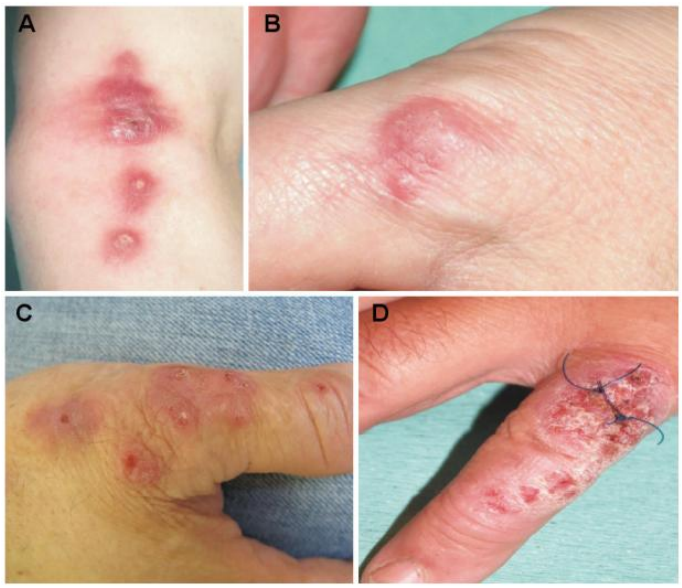

Fig. 2. Mycobacterium marinum cutaneous infection. Sporotrichoid lesions on the arms of patient 1 (A) and patient 3 (C), nodular inflammation presented in patient 2 (B), and abscess formed and presented in patient 4 (D). Photographs are by M. Bodnarova

Aims at fibronectin-binding protein of *Mycobacterium spp.* These vaccines help in developing an immune response against *M. marinum.* This increases survival of the vaccinated fishes. Although promising developments are made with regards to vaccines, no vaccines are commercially available to be used against *Mycobacteriosis* in fish [17].

The treatment of *M. marinum* in man is different. Since *M. marinum* is a multi-drug resistant organism, it is difficult to treat it with just one drug. Monotherapy is effective only if skin and soft tissue is infected. It is not effective if the infection spreads to deeper tissues [7].

In superficial infections, *clarithromycin*, *trimethoprim,* and *ciprofloxacin* can be used. It takes a longer time to treat deeper infections. In these cases, a combination therapy of two drugs (*ethambutol* and *rifampicin*) is recommended. *Streptomycin*, *isoniazid* and *pyrazinamide* cannot be used as *M. marinum* is resistant against these drugs [7].

As for Morgellons Disease, an effective treatment method has not yet been established. This is because of the controversy and lack of understanding of the disease [18]. Because some still consider MD as a delusional disorder, treatment of MD often consists of low-dose antipsychotics [19]. These antipsychotics are usually combined with corticosteroids, phototherapy, and antibiotics for higher efficacy [19]. Antibiotics help to reduce itching and are prescribed if the doctor thinks MD is caused by an infection [18].

Unlike Piscine mycobacteriosis, there is no available vaccine for MD. This is mainly because the etiological agent causing MD is still not identified. And since there is no definite treatment for MD, it is not possible to correlate MD with PM based on their treatment. However, it is worth noting that antibiotics can be used to treat both MD and PM. Nevertheless, this alone is not a strong point to make any correlations between MD and PM. Therefore, further research needs to be done if we are to make connections between MD and PM based on their treatment options.

6. CONCLUSION

Both Morgellons disease and Piscine Mycobacteriosis in humans are poorly studied and researched. It is possible for both MD and PM to be caused by the same organism, but further research needs to be done to confirm or rule out this possibility. The transmission of Morgellons disease is not completely understood yet. However, since it is closely associated with Lyme disease, the transmission could be through the black legged ticks. Fish Mycobacteriosis on the other hand is transmitted

through water and other marine organisms. Both diseases are not known to spread from human to human. MD and mycobacteriosis both present with dermatologic symptoms initially. Regardless of this, the morphological, histological and site of lesions are distinct in both diseases. Furthermore, the chronic manifestations of mycobacteriosis are infections whereas it is more of a systemic inflammation in Morgellons disease. Although similarities are found in the clinical symptoms of both diseases, without further cross-sectional studies on recent cases of both diseases, it is not possible to establish a strong association nor dissociation.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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