Demystifying Morgellons Disease

Jase A Grimm[1]

[1] *University of the People, Pasadena, CA 91101, United States*

Abstract

Morgellons disease is an understudied complex of physical and psychological symptoms that requires further research because medical authorities have diagnosed and treated patients' symptoms as delusional. In contrast, other studies have demonstrated a connection between the hallmark subcutaneous fibers and spirochetal infection. The literature includes case reports of Morgellons treated as delusional infestation with antipsychotic drugs to a certain degree of success, reinforcing the thesis of Morgellons as a purely psychological disease but not addressing the etiology of the somatic symptoms. An under-designed CDC study has similarly concluded that no single joint infectious agent exists in Morgellons disease patients. However, other small sample size case reports identified a common microorganism, Borrelia, and concluded it could cause symptoms as a single species of a more extensive polymicrobial infection. Much literature exists discussing the difficulty in diagnosing polymicrobial infections and the role that they may play in neurodegenerative diseases. This literature review aims to find common ground between these seemingly opposing schools of thought by demonstrating that their findings are not mutually exclusive. The efficacy of antipsychotic drugs does not exclude the possibility of Morgellons having organic pathophysiology. Similarly, studies demonstrating a lack of a single common microorganism in Morgellons patients do not prove that Morgellons disease is not infectious in origin. Establishing that these theories coexist is the aim of this review and demonstrating that further studies, case reports, and clinical trials are necessary to develop a common diagnosis and effective treatments.

Keywords: Morgellons Disease, Delusional İnfestation, Antibiotics, Antipsychotics, Polymicrobial İnfection.

INTRODUCTION

Demystifying Morgellons Disease

The mystery of Morgellons disease (MD) lies in the lack of consensus on a medical definition, a clear cause, and an efficacious treatment. When studying a cohort of MD patients, CDC-sponsored epidemiologists Pearson et al. concluded that "no common underlying medical condition or infectious source was identified, similar to more commonly recognized conditions such as delusional infestation (DI)" [1]. More recently, Balogh et al. reported complete or partial remission in 69% of MD patients prescribed the second-generation antipsychotic medication Risperidone and 72% remission in those prescribed Olanzapine, which is from the same class of drugs [2]. These studies reinforce the idea that MD is a psychosomatic disease because no joint infectious agent has been identified, and symptoms are resolved with medication used to treat psychosis. However, the possibility exists that MD is a multisystem neurodegenerative disease with both physical and psychological symptoms akin to syphilis, Lyme disease, and Alzheimer's and that antipsychotic medications improved psychological symptoms, just like in the aforementioned diseases; logically, successful treatment with antipsychotics does not rule out an underlying infection. The year after the CDC study, an authority on MD, Marianne Middleveen *et al.*, studied a four-person cohort of MD patients and concluded, "the findings suggest that MD has a spirochetal etiology," because of the identification of Borrelia spp. spirochetes in tissue samples from the patients and corroboration by positive seroreactivity to Borrelia antigens [3]. Middleveen et al. acknowledged the limitation of the small sample size but, in the same paper, claimed that these patients were not suffering from DI based on the results of multiple personality, intelligence, and psychiatric tests [4]. Savely and Stricker concluded that 96.8% of the patients in their 122-patient cohort may have had Lyme disease, but that included 54 patients that were non-sero reactive for Borrelia but still "highly-suspect" for Lyme because they demonstrated five of seven clinical criteria for the disease.

There is consensus that MD causes significant patient suffering, but medical professionals cannot agree on a definition; therefore, a cause, or causes, cannot be established from which to establish effective diagnostics and treatments. This paper seeks to demonstrate, through logic deduction, that the existing theories can coexist and that a working definition of the disease can be developed to conduct further research. A polymicrobial infection model satisfies both MD theories and could explain the difficulty in diagnosing the disease and varied results in treatment efficacy. However, further research is needed to

*Corresponding author:
Dr.   Jase A Grimm
University   of   the   People,
Pasadena, CA 91101, United
States
Email: grimm.jase@gmail.com

confirm or deny the possibility of multiple pathogens in the etiology of Morgellons disease to carry out thorough clinical studies to determine an efficacious treatment.

Literature Review

There is no shortage of literature on either side of the fence regarding MD, and much of it seems to contradict the other half. The manuscript summarizes the current findings on the definitions, potential causes, and treatments.

Morgellons as psychosomatic disease

The majority of literature that exists approaches MD with the assumption that it is a psychiatric disease with secondary cutaneous symptoms that may be self-inflicted. For example, Harth *et al*. recognize MD as a subcategory of DI, citing a lack of medical evidence supporting the existence of the disease and "unverifiable fibers or filaments in or on the skin" [6]. To support that conclusion, Balogh *et al*. report that antipsychotic drugs have proven the most efficacious treatment for MD to date, but also presented a case in which MD was resolved by adding doxycycline to the patient's existing psyche med protocol of Risperidone and lithium. The study also conclude that MD is simply DI and that treatment with antipsychotic drugs like Risperidone and Olanzapine is the most effective course for these patients, the majority of whom present with other psychiatric comorbidities such as anxiety and depression [2]. It is also important to note that Pearson et al. reported that half of the patients in their cohort tested positive for at least one illegal substance, and 24% presented with clinically significant drug or alcohol use [1]. This data, taken at face value, points to MD as a psychological disorder with secondary, cutaneous lesions of an unknown etiology.

Morgellons as somatopsychic disease

To complicate matters, a mounting volume of peer-reviewed literature exists that appears to correlate spirochetal infections with both the lesions and filaments of MD and the psychological symptoms. The bulk of this literature comes from a few key researchers, one of whom is veterinary biologist Marianne Middelveen. Middelveen & Stricker present convincing serological, historiographical, and polymerase chain reaction (PCR) evidence demonstrating a link between MD lesions and infection with spirochetal bacteria, specifically Borrelia spp [4]. In addition, the study also conclude that MD fibers can be observed under unbroken skin, allegedly debunking the theory that the lesions are self-inflicted, and fibers are foreign contaminants [4]. In a bit of cruel irony, when patients approach their doctors with concerns of MD, they often provide photographs, or samples of the fibers, which are collectively known as the "matchbox sign" for when patients brought specimens to their doctors in a matchbox; according to Middelveen *et al*. physicians are taught to recognize this sign as a diagnostic tool for DI [7]. This teaching is poor practice because DI is a diagnosis of exclusion in that the practitioner must rule out infectious and environmental etiologies first, as well as assess the patient's overall psychiatric health first before diagnosing a patient as delusional; there is no shortcut to diagnosing DI, just the scientific method [7]. In another study, Middelveen et al. concluded that the fibers collected from MD patients comprised of keratin or collagen contain melanin and originate in human keratinocytes and fibroblasts, validating patients' beliefs that these fibers are the result of an organic process and not delusional [8]. Figure 1 presents a collection of patient-presented evidence of these fibers; with the advent of powerful and inexpensive digital microscopes, patients can now collect convincing evidence of their symptoms to present to their medical team.

Figure 1: Patient presented fibers associated with Morgellons Disease. Sub-panels show (A) multi-colored filaments embedded under skin on toe, (B) black and yellow fiber embedded in fungus-infected nail, (C) white, tangled filaments erupt from fingertip, and (D) primarily white filaments embedded in fingertip lesion.

Polymicrobial Infections

The study of polymicrobial infections and associated biofilm formation concerning the virulence, identification, and treatment of disease has progressed since Morgellons was first discovered. According to Brogden and Guthmiller polymicrobial infections can be notoriously tricky to diagnose and treat but are likely responsible for Lyme disease, multiple sclerosis, and periodontal disease [9]. In addition, Miller *et al*. concluded that bacterial biofilms had been linked to neurodegenerative diseases like Alzheimer's and Parkinson's, in which microorganisms and human immune cells extrude amyloid fibers to form an extracellular matrix and as an immune response, respectively [10]. It is important to note that Middelveen *et al*. made a strong case that the amyloid proteins and phosphorylated tau associated with mixed *Borrelia burgdorferi* and *Heliobacter pylori* biofilms collected from MD patients may correspond to the progression of the diseases cutaneous and neurological symptoms [11]. Furthermore, Middelveen & Stricker thoughtfully compared the polymicrobial infection model of bovine digital dermatitis, which is thought to be caused in part by spirochetal bacteria and presents as keratin filaments projecting from lesions on the hooves of cows, to the possible etiology of MD and highlighted the common spirochetal component of the biofilms present in both diseases [4].

METHOD

In order to establish common ground from which to build our knowledge base of MD, the literature from all schools of thought on the disease was reviewed and their findings were broken down into similar terms, possible explanations were established for the varied data, and connections among existing models of microbial infection mediated psychologic, cutaneous illnesses, and MD were defined. To find this literature, peer reviewed articles were searched using "Morgellons disease," "delusional infestation," and "polymicrobial infections" as keywords. Further, a workable definition was synthesized, feasible models of etiology were explored, and a research plan of action was presented with which to further our understanding of MD and diagnosis, treatment, and prevention.

Merging Definitions

The best existing definition of MD gleaned from the literature is "a dermatologic condition in which lesions that contain unusual filamentous inclusions," with "Lyme-like symptoms such as musculoskeletal, neurological and cardiovascular manifestations

suggestive of spirochetal etiology" [12]. This definition acknowledges the existence of the controversial fibers while also addressing the psychological component of the generally accepted model of DI presented by Pearson *et al* [1]. However, it downplays the neurological scope of the disease, alienating mental health practitioners who maintain a psychiatric-only stance on the disease, and limits research to establishing a single-pathogen pathophysiology. A new, more unified working definition must be synthesized to pursue the type of research that will provide answers.

Considering all Possible Etiologies

Even the authority on MD, acknowledges that the etiology of MD is yet unknown; similarly, researchers who consider MD a type of DI have yet to provide a common etiology to explain patients' symptoms [4]. Moving forward, researchers and practitioners must consider all possible etiologies. The polymicrobial infection model fits neatly into what we already know about MD and could explain the difficulty in diagnosing and treating MD. This type of spirochete anchored mixed microorganism infection has been demonstrated to produce unusual keratin filaments in the epithelial tissue of ruling out or confirming the involvement of biofilm-producing microbial communities as the etiology of MD is paramount [4]. Throughout this review, a lack of data relating to other common comorbidities like herpes simplex virus 1 (HSV-1) was observed, or human papillomavirus (HPV), that also have been linked to cutaneous lesions, polymicrobial and biofilm infections, and neurodegenerative processes [13].

Potential Treatments

When reviewing the literature on effective treatments for MD, emphatic reports from researchers were found, claiming antipsychotics were most effective at reducing the severity of symptoms [2]. while others made the same claim about antibiotics [14]. To demonstrate the consensus between these two differing prescriptions, one can consider the case study Zhang presented in which the antibiotic doxycycline was administered, in addition to an established lithium and risperidone regimen and resulted in complete resolution of symptoms in two weeks [15]. While this is a tiny sample, the point is that the treatment worked. It consisted of a two-pronged approach treating the neurodegenerative symptoms of MD and targeting a potentially culpable underlying infection. In addition, the mechanism of action of drugs like Risperidone and Olanzapine is not entirely understood but is thought to block the interaction of the neurotransmitters dopamine and serotonin and receptors; these two chemicals are also immune system modulators correlated with T cell regulation and the resulting abnormal immune system response that can lead to Parkinson's and Alzheimer's [16]. This insight requires more research on how these widely available antipsychotic medications and immunoregulators could be used to develop new therapies for many diseases affecting the body and the brain, MD included.

Coexisting theories

Many neurological diseases have organic etiology, and infectious factors have been linked to Alzheimer's [17]. multiple sclerosis [18]. Defining MD as a complex, multisystemic disease of currently unknown etiology that is characterized by fibers of human origin embedded in skin, hair, or nails as well as adverse neurological effects would allow both schools of thought to collaborate on the research necessary to demonstrate a cause for the symptoms (whether it be infectious or otherwise) and develop effective treatments.

Findings

The aim of this literature review and analysis was to unify opposing schools of thought on the etiology of the contested illness MD and establish an actionable research plan to demystify the definition, cause, and potential treatments. Although seemingly contradictory definitions of MD exist, common ground is found in that patients suffer from both cutaneous and psychological symptoms. Moreover, both antibiotics and antipsychotics have shown some efficacy in resolving symptoms, reinforcing a multisystem pathologic model. Finally, polymicrobial infections could plausibly account for the difficulty in isolating a single common infectious organism in the CDC's study and the limited efficacy of antibiotic treatments. This new model for the pathophysiology responsible for MD can serve as a framework for future extensive and carefully designed studies to either confirm or deny this thesis and, regardless of the result, further the research necessary to demystify Morgellons disease.

A New Working Definition

I have attempted to synthesize a working definition for MD that fits the current data set available, unifies the conflicting theories, and lays the groundwork for future constructive research: "MD is a multisystem disease of the nervous and integumentary systems hallmarked by neurodegeneration and cutaneous lesions embedded with unusual filaments of human cellular origin, of which the etiology is yet unknown." I present this as a working definition, meant to facilitate communication and collaboration between historically opposing authorities on the subject and inspire the research that is needed.

Polymicrobial Infections fit Model of MD

Once the scope and signs of the disease have been defined, corroborating or ruling out plausible etiologies is the next step. In the twenty years since Morgellons was first reported in the US, the involvement of polymicrobial infections and associated biofilms in multisystem diseases like Lyme, Alzheimer's, and Parkinson's have been established [9,10]. Considering the similarities in symptoms, causes and treatments between MD and these well researched and defined disease, it would be logical to try to establish or disprove a polymicrobial infection can cause MD.

What Treatments Work and Why

Psychiatrists were more likely to report diagnosis of MD as DI and treat as such with antipsychotics, with which they had some success [2]. Microbiologists and Lyme specialists generally searched for, and found, bacterial pathogens which they sometimes had success treating with antibiotics [8]. The most conclusive case report of treatment was one patient of Zhang *et al*. whose symptoms completely resolved after adding antibiotics to their current antipsychotic regimen [15]. It is apparent that to some degree, both medications are effective in controlling MD symptoms, therefore more research as to the specific mechanism of action is of the efficacious treatments is required.

DISCUSSION

This paper aimed to unify the two predominant views on MD; one, it is a psychological condition best treated with antipsychotics, and two, a microbial infection mediated multisystem disease with cutaneous and psychologic symptoms. We attempted to demonstrate that both thoughts can be true and that the only recourse is to continue studying MD and form a consensus on a definition, so we can identify the cause to ultimately develop an effective treatment.

Limitations in design

The paper is merely a retrospective literature review, analysis, and synthesis, and it is limited to the existing data and conflicting definitions of the disease in question. Although I objectively reviewed a diverse sample of the peer reviewed literature available, my conclusions are ultimately speculative; that being said, forming this hypothesis is simply the next necessary step in the scientific process that the medical community relies upon to expand upon existing

knowledge. Ideally, this review could lead to a larger-scale research study, further case reports, and clinical trials.

Limitations in generalizability

Because the definitions and diagnosis of MD vary, it is possible that not all of the patient data available in the literature is indicative of actual MD as defined in this analysis. Because MD is not an officially recognized condition, the fact that many MD patients are "self-diagnosed" also calls into question the validity of the information gathered. Furthermore, MD may be a purely psychological condition, and supposed physical manifestations are psychosomatic. MD patients may not share common infections, and symptoms are simply an immune response, or current medical science does not possess the tools or knowledge to solve the mystery of Morgellons.

CONCLUSION

After analyzing the available literature, creating a consensus in the medical community that MD is a severe, very real condition affecting both the mind and body. We cannot yet rule out that a polymicrobial infection is a key to resolving the enigma surrounding the condition. Existing literature paints a picture of MD as a multisystemic disease affecting, but not limited to, the skin and nervous system and responding positively to antibiotic, antipsychotic, or a combination of both therapies, and maybe a result of a spirochete anchored polymicrobial infection which would complicate both diagnosis and treatment of this distressing condition.

Future Prospects

With a unified, cohesive definition of MD, an open mind about possible etiologies (including polymicrobial infections), and some promising treatment options, we can collaborate and move forward on the research still needed to fully understand the condition and what to do about it. The quickest, most accessible, and most illuminating data set would be a standardized, exhaustive medical history focusing on establishing common infectious organisms, environmental agents, and lifestyles that have been overlooked in previous studies, including but not limited to: HPV, HSV-1, *Candida albicans*, Malassezia spp., Dermatophytes, Epstein-Barr Virus, *Mycoplasma pneumonia*, Streptococcus spp., *Treponema denticola*, *Staphylococcus aureus*, *Staphylococcus lugdunensis*, and *Pseudomonas aeruginosa*. The history should include instances of the following diagnosis or symptoms: gynecomastia, benign fibroadenoma, psoriasis, cherry angioma, Raynaud phenomenon, Lhermitte's sign, bi-polar disorder, anxiety, depression, genetic diseases, and hernias. In addition, an environmental and historical breakdown of exposure to possible health hazards: international travel, contact with farm animals/wild animals, exposure to chemicals or radiation, diet, substance use, career, and lifestyle. To validate the information provided by patients, corroborating evidence of the hallmark fibers of MD would be required, in the form of pictures or videos, alongside the survey for researchers to consider with the rest of the information gathered to determine the reliability of the data set. Hopefully, a large enough sample size could demonstrate a pattern as to who develops MD and what causes it. With that knowledge, large-scale diagnostic and clinical trials could begin with particular attention paid to discovering the potential polymicrobial community or communities responsible for MD by utilizing shotgun metagenomics and other techniques suited for studying these complex infections. Additionally, collecting, categorizing, and archiving a collection of validated Morgellons specimens for medical practitioners and patient advocates to utilize to identify and treat MD in the future more quickly.

Conflict of Interest

None declared.

REFERENCES

1. Pearson ML, Selby JV, Katz KA, Cantrell V, Braden CR, Parise ME, *et al*. Clinical, epidemiologic, histopathologic and molecular features of an unexplained dermopathy. PLoS One. 2012;7(1):e29908.
2. Balogh EA, Beuerlein KG, Feldman SR. Choosing the appropriate pharmacotherapy for Morgellons disease: an expert perspective. Expert Opin Pharmacother. 2022;23: 527–30.
3. Middelveen MJ, Mayne PJ, Kahn DG, Stricker RB. Characterization and evolution of dermal filaments from patients with Morgellons disease. Clinical, Cosmetic and Investigational Dermatology. 2013;6:1.
4. Middelveen MJ, Stricker RB. Filament formation associated with spirochetal infection: a comparative approach to Morgellons disease. Clin Cosmet Investig Dermatol. 2011;4: 167–77.
5. Savely VR, Stricker RB. Morgellons disease: Analysis of a population with clinically confirmed microscopic subcutaneous fibers of unknown etiology. Clin Cosmet Investig Dermatol. 2010;3:67–78.
6. Harth W, Hermes B, Freudenmann RW. Morgellons in dermatology. J Dtsch Dermatol Ges. 2010;8:234–42.
7. Middelveen MJ, Fesler MC, Stricker RB. History of Morgellons disease: from delusion to definition. Clin Cosmet Investig Dermatol. 2018;11:71–90.
8. Middelveen MJ, Burugu D, Poruri A, Burke J, Mayne PJ, Sapi E, *et al*. Association of spirochetal infection with Morgellons disease. F1000Research. 2013;2:25.
9. Brogden KA, Guthmiller JM (eds). Polymicrobial Diseases. Washington (DC): ASM Press, 2011.
10. Miller AL, Bessho S, Grando K, Tükel Ç. Microbiome or infections: Amyloid-Containing biofilms as a trigger for complex human diseases. Frontiers in Immunology. 2021;12:514.
11. Middelveen MJ, Filush KR, Bandoski C, Kasliwala RS, Melillo A, Stricker RB, *et al*. Mixed Borrelia burgdorferi and Helicobacter pylori biofilms in Morgellons disease dermatological specimens. InHealthcare. 2019;7:70.
12. Middelveen MJ, Martinez RM, Fesler MC, Sapi E, Burke J, Shah JS, *et al*. Classification and staging of Morgellons disease: lessons from syphilis. Clinical, Cosmetic and Investigational Dermatology. 2020;13:145.
13. Itzhaki RF. Overwhelming evidence for a major role for herpes simplex virus type 1 (HSV1) in Alzheimer's disease (AD); Underwhelming evidence against. Vaccines (Basel). 2021;9:679.
14. Harvey WT. Morgellons disease. Journal of the American Academy of Dermatology. 2007;56:705–06.
15. Zhang JF, Gopalakrishnan K, Molloy DJ. Treatment of Morgellons disease with doxycycline. Clin Case Rep. 2021;9: e05148.
16. Sarkar C, Basu B, Chakroborty D, Dasgupta PS, Basu S. The immunoregulatory role of dopamine: an update. Brain, behavior, and immunity. 2010;24(4):525-8.
17. Sait A, Angeli C, Doig AJ, Day PJ. Viral involvement in Alzheimer's disease. ACS Chemical Neuroscience. 2021;12(7):1049-60.
18. Bjornevik K, Cortese M, Healy BC, Kuhle J, Mina MJ, Leng Y, *et al*. Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis. Science. 2022;375:296–01.