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The role of infection in morphea disease

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ABSTRACT

Morphea is a skin disorder that leads to the sclerosis of the dermis and subcutaneous tissue. In epidemiologic studies, the incidence rate of approximately 0.4 to 2.7 per 100,000 people has been reported that is equal in adults and children. Based on clinical findings of disease and presentations, morphea disease has been divided into four major types including plaque-type, linear, generalized and a miscellaneous group with morphologically distinct phenotypes. Overall, plaque-type is the most common type of morphea. This disease is characterized by three main histopathologic features that include deposition of collagen in the dermis sometimes with extension to subcutis, vascular changes and an inflammatory cell infiltration, particularly in early lesions. Morphea is a multifactorial process that its main underlying cause is not completely known but the most common causes related to the genesis of morphea including trauma, radiation, medications, infection, autoimmunity and microchimerism. In this paper, we review the literature about the role of infection in the genesis of morphea.

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Introduction

Morphea (subgroup of the localized scleroderma) is a skin disorder that leads to the sclerosis of the dermis and subcutaneous tissue but it can sometimes spread to the fascia, muscle and underlying bone. Clinically, morphea indicates an asymmetric distribution and is usually limited to one body zone (1).

In epidemiologic studies, its incidence is reported to be approximately 0.4 to 2.7 per 100,000 individuals that is equal in adults and children.

Children and adults with morphea are more likely without morphea to have a positive family history of morphea and other autoimmune diseases compared to their peers (2).

In recent years, several groups of researchers have attempted to understand various forms of morphea presentation. Based on clinical findings, the disease has been divided into four major types including plaque-type, linear, generalized and a miscellaneous group of morphologically distinct phenotypes. Overall, plaque-type is the most common type of morphea (1).

In this paper, we review the literature about the role of infection in the genesis of the morphea.

Literature review

Morphea is characterized by three main histopathologic features that include deposition of collagen in the dermis sometimes with extension to subcutis, vascular changes and an inflammatory cell infiltration, particularly in early lesions (3).

The epidermis is usually normal; however, incidence of atrophy or even slightly thickness than usual is also reported (4).

The dermis thickness increases and composes of thick sclerotic collagen bundles, which stains

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strongly with the trichrome. Subcutis and the fat around the sweat glands replaced with collagen are observed in late stage (5).

Morphea is a multifactorial process that its underlying cause is not completely known. The most common causes are summarized in Table 1.

Table 1. Presumptive causes of morphea and related evidences

Cause	Evidences
Trauma	Morphea after vaccination for measles, mumps, rubella, [1]DTP, [2]BCG, hepatitis B and tetanus
Radiation	Radiation recieved for the treatment of breast cancer
Medication	Development of morphea-like lesion after medications such as bisoprolol, bleomycin, peplomycin, D-penicillamine, bromocriptine, L-5-hydroxytryptophan in combination with carbidopa, pentazocine, balicatib
Infection	Association with borrelia spp, [3]CMV
Autoimmunity and family history	Association with autoimmune disease (vitiligo, insulin-dependent diabetes mellitus, hashimoto thyroiditis, graves' disease and ulcerative colitis)
Microchimerism	Similarities between morphea and [4]GVHD

[1]DTP: Diphtheria, tetanus, pertussis ;[2]BCG: Bacillus Calmette–Guérin;[3]CMV: Cytomegalovirus;[4]GVHD: Graft versus host disease.

In a study in 2007, Pope et al. assessed increasing infection (bacterial and viral) in scleroderma compared with non-inflammatory musculoskeletal disorders (MSD). They studied 351 patients with systemic sclerosis and 83 patients with MSD as controls (tendonitis, arthritis or fibromyalgia). They determined the history of exposure to infectious agents during one recent year, vaccination and trauma. Finally, the study did not support the role of infection and vaccination as a cause or trigger for systemic sclerosis (6).

In a review article, Eisendle et al. assessed 16 studies with positive results of borrelia infection in patients with morphea (approximately 51% of patients with morphea revealed positive results for borrelia). Wide range of diagnostic tests were used (immune peroxidase, culture, silver stain, polymerase chain reaction [PCR] and focus-floating microscopy) and lack of a standard criterion for active borrelia infection was the main cause for performing difficult interpretation. Furthermore, no evidence of association could be a confusing problem between two entities in some studies (7).

The reports is obtained from Europe, which often reflect uniform results of positive Borrelia.

European strains of borrelia are different from the United States cases (Borrelia afzelii or garinii vs. Borrelia (B.) burgdorferi). Although Borrelia may be considered as a likely cause of morphea, there is scant evidence to support this issue (8).

Fujiwara et al. illustrated the geographic and genospecific association of Borrelia with morphea and lichen sclerosus et atrophicus (LSA), by evaluating biopsy specimens of patients` skin (19 morphea and 34 LSA) in the United States, Japan and Germany through DNA PCR. Five cases of morphea and two cases of LSA in Germany and Japan manifested positive signals for B. garinii or B. afzelii (the European species). None of the American samples was positive for Borrelia PCR. Borrelia burgdorferi sensu stricto was not detected in any of the specimens. They concluded that morphea and LSA in Germany and Japan could be related with European genotypes of Borrelia (9).

In 2009, Arnson et al. evaluated serological reaction against various infectious agents in 80 patients with systemic sclerosis (SSc) and compared them with 296 healthy controls. All samples were collected from the presence of antibodies against hepatitis B virus, hepatitis C virus, toxoplasmosis, rubella, CMV, Epstein barr virus (EBV) and treponema pallidum. Patients with SSc had increased IgM and IgG titres against toxoplasma gondii and CMV. Higher titers were also found against the hepatitis B virus core protein (recombinant HBc antigen). A significantly higher rate of IgM antibodies against the capsid antigen of the EBV was detected in SSc patients compared with healthy controls. These data showed that antibodies against CMV, HBV and toxoplasmosis were detected more often in patients with SSc. This association indicates that infectious agents might have a role in disease pathogenesis and expression (10).

In 2004, Ohtsuka et al. assessed the prevalence of CMV in skin samples of patients with systemic sclerosis using PCR for detecting DNA. There was no significant statistical difference between the case group compared with healthy controls and the hypothesis of CMV as a cause of systemic sclerosis was not supported (11).

Conclusion

Morphea is a multifactorial process that its underlying cause is not completely known but the most common causes related to the genesis of morphea includes trauma ,radiation , medications, infection, autoimmunity, and microchimerism. The most likely disease cause is the Infection and according to the previous articles. Borrelia spp. and CMV are the most common infectious agents; however, newer molecular and genetic research are needed to confirm these results.

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Conflict of Interest

The authors declare no conflict of interest.

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