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Original Article

Progressive macular hypomelanosis pathogenesis and treatment: a randomized clinical trial

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ABSTRACT

Background: Progressive macular hypomelanosis (PMH) is a cosmetically disturbing skin disorder that is poorly understood with indefinite treatment. The aim of the present study was to clinically outline PMH and study its pathogenesis. Based upon the literature suggesting improvement of PMH with antibiotic therapy to decrease *Propionibacterium acnes* (*P. acnes*) colonization, different treatment modalities were tried to reach the best treatment option.

Patients and methods: This study included 12 newly diagnosed PMH selected patients who attended Tanta University Hospital outpatient clinic of Dermatology and Venereology from June 2009 to March 2010. Patient's lesions were subjected to wood's lamp and potassium hydroxide (KOH) examination as well as biopsies used in histological, immunohistochemical, bacteriological and electron microscopic examination. A randomized clinical trial with different treatment modalities was applied.

Results: The patient's mean age was 25 ± 10.8 with significant female predominance ($P = 0.0001$). Reduction of epidermal melanosomes and tyrosine activity together with difference in distribution of S100 proteins in hypopigmented skin was demonstrated. Abnormal distribution of tonofilaments was noticed inside keratinocytes with increased apoptosis. *P. acnes* were detected in hair follicles of 83.3% hypopigmented lesions. Administration of local and systemic antimicrobial treatment with narrow band ultraviolet B (NBUVB) phototherapy for 3 months was the best treatment modalities.

Conclusion: The etiology of PMH is multifactorial where genetic predisposition, the presence of *P. acnes* and hormonal imbalance play the main role. Administration of local and systemic antimicrobial treatment with NBUVB phototherapy for 3 months is an effective treatment regimen for PMH.

1. Introduction

Progressive macular hypomelanosis (PMH), also known as idiopathic multiple large-macules or nummular and confluent hypomelanosis of the trunk [1], is poorly understood and often misdiagnosed cosmetically disturbing skin disorder [2,3]. It occurs all over the world in young adults of

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all races and is characterized by symmetrically distributed ill-defined nummular, non-scaly, hypopigmented macules mainly on the trunk. Inflammatory predisposition is absent and the lesions tend to progressively increase in number, sometimes extending to the neck, face, buttocks and upper half of extremities [4,5]. These lesions appear to be less densely pigmented with less mature melanosomes than normal skin as indicated by histological and electron microscopic (EM) examination [6]. Up till now the course and prognosis as well as specific treatment to PMH is not well known [4].

Many theories have been proposed to clarify its pathogenesis, however, hard facts in support of these ideas are lacking [4]. Melting of genes between white and black parents in patients of mixed racial background was speculated by Guillet et al. [2]. Switching between type IV singly aggregated melanosomes to type I–III aggregated melanosomes in the hypopigmented skin lesions of PMH provided an evidence for such theory [7]. Because he noticed the disorder only in family members, Borelli [8] suggested that PMH is a genodermatosis. According to Lesuer et al. [9], PMH might be related to tinea versicolor although its causative organism, the yeast Malassezia furfur, was never detected. In a case study report, Lo Schiavo et al. [10] pointed to the possible role of antiretroviral drugs in the pathogenesis of PMH as they noticed that receiving post HIV prophylaxis was the only risk factor reported.

Westerhof et al. [4] was the first to offer *Propionibacterium acnes* (*P. acnes*) impact based on its presence in high density in their lesional skin pilosebaceous units and the observed red fluorescence inside the hypopigmented spots by ultraviolet (UV) radiation. However, the mechanism by which *P. acnes* may induce PMH is uncertain, although several hypotheses were proposed. First, the production of bacterial enzymes with degradative properties that target the integrity of epidermal skin cells and the barrier function of sebaceous follicles [11]. Second, *P. acnes* might be involved in triggering inflammation by constitutively produced factors such as porphyrins, surface determinants like a glycocalyx polymer or stress proteins, an acid shift, or heat shock [11,12]. Last, *P. acnes* contain genes encode CAMP factor homologs that act as pore-forming toxins [13,14], which may affect the function of melanocyte [4]. In contrary, Relyveld et al. [15] hypothesize that the species causing PMH differ from that causing acne, and cannot be differentiated by conventional culture and biochemical methods.

The aim of the present study was to clinically outline PMH, study its histological and immunohistochemical pictures and determine its bacteriological aspect to throw a light on its pathogenesis. Based upon the literature suggesting improvement of PMH with antibiotic therapy to decrease *P. acnes* colonization [16], different treatment modalities are tried to reach the best treatment option.

2. Patients and methods

2.1. Patients

This study included 12 newly diagnosed PMH selected patients who attended Tanta University Hospital outpatient clinic of Dermatology and Venereology in the period from June 2009 to March 2010. The disease was discussed with the patients who signed an informed written consent.

2.1.1. Inclusion criteria

The chosen enrolled patients were selected according to the following criteria: (a) clinically diagnosed cases of acquired, non scaly, confluent, hypopigmented macules and patches with normal sensation, (b) wood's light examination for accentuation of the clinically diagnosed lesions and diagnosis of subclinically undiagnosed one, (c) exclusion of fungal infection by KOH examination, and (d) histopathologically proven from biopsies taken from lesion and adjacent normal skin [2,7,16].

2.1.2. Exclusion criteria

Patients were excluded if they had hypopigmentation due to other diseases, they were under medical treatment or phototherapy for the disease or they refused skin biopsy.

2.1.3. Controls

Control samples were taken from the apparently normal nearby skin of the selected cases.

2.2. Methods

After complete history taking and thorough general and cutaneous examination, patient's lesions were subjected to wood's lamp and KOH examination to confirm the diagnosis and exclude fungal infections. Skin of the selected patients was disinfected and two punch biopsies (4 mm each) were taken from each patient, one from the hypopigmented and the other from the normal nearby skin. Specimens were divided into many parts for histological, immunohistochemical, bacteriological and EM examination.

2.2.1. Wood's lamp examination

Wood's lamp (Waldmann W^{TM}) examination was done according to Gilchrest et al. [17], with the following precautions: (a) patient's skin was examined from a distance of 5–20 in. after cleaning with alcohol in perfectly dark room, and (b) common sources of error as bluish or purplish fluorescence produced by ointments on the skin-containing petrolatum, green fluorescence by salicylic acid containing medicaments on the skin and light reflected from the examiner's white coat producing a light blue fluorescence were avoided.

2.2.2. KOH examination

After cleaning the skin with alcohol, scraping of the hypopigmented skin on a clean sterile glass slide was done, followed by adding a drop of 15% KOH, then mixing. A cover glass was put over the preparation and was allowed to remain at room temperature until the material has been cleared which may be warmed to speed the clearing process. Slides were examined by light microscope at X^{10}, and X^{40} power [18].