



The Current Status of Seborrheic Alopecia in Young People and Its Correlation with Fungal Infections

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Abstract: The current status of seborrheic alopecia (SA) in young people and its potential association with fungal infections was discussed. Pathological representations, pathogenesis and therapeutic strategies of seborrheic alopecia were introduced. SA is the most common type of hair loss in adults, but it also occurs in adolescents, though its prevalence among this younger population is not well established. Skin biocenosis, in particular the *Malassezia* spp. flora, plays a key aetiologic role, in combination with the unusual capacity of some corneocytes to be coated by these yeasts.

Keywords: young people, seborrheic alopecia, fungal infections

1. Introduction

Hair loss is divided into seborrheic areata (SA) and alopecia areata, according to the clinical symptoms in modern medicine. SA is referred to as the progressive loss of hair on the top region of the head, which might be accompanied by itching, increased dandruff, and extensive secretion of oil. Alopecia areata is defined as a sudden flaking of hair, which showed no other accompanying clinical symptoms [1]. SA is a type of hair loss characterized by slow development of hair on the forehead, prominent areas, and top during puberty. It is the most common hair loss disorder in clinical practice. Modern medical research has shown that seborrheic alopecia is an androgen dependent polygenic hereditary disease. During adolescence, the level of androgens in the body increases, and testosterone is converted into a more active diaminotestosterone under the action of 5 α -reductase. After binding with androgen receptors, it enters the nucleus and produces a series of biological effects, leading to hair follicle miniaturization, shortened hair follicle growth period, and gradually causing hair thinning, even falling off. Currently, it is believed that its occurrence and development are mainly related to endocrine factors and genetic susceptibility [2]. SA is more common in middle-aged and young people aged 20-40. Its onset process is slow hair loss in the forehead, bump, and top during adolescence, gradually forming a high forehead. The hair on the top of the head is sparse, and even all hair on the forehead and top of the head falls off, while the occipital area is less affected. The scalp skin of patients with this disease may be accompanied by symptoms such as greasiness, itching, and scaling, making it the most common hair loss disease in clinical practice. Both men and women can suffer from this disease, but the incidence rate of men is significantly higher than that of women. At present, research results have found that the prevalence of SA varies among different ethnic groups and regions, with Caucasians having the highest prevalence, while yellow and black people have significantly reduced prevalence [3]. Because the disease affects aesthetics, it brings great mental stress and psychological burden to patients. The pathological characteristics of SA are mainly reflected in the following changes: changes in hair growth cycle, changes in subcutaneous blood flow, changes in sebaceous glands, and changes in hair follicle stem cells [4]. Currently, it is widely recognized that seborrheic alopecia is a type of androgen dependent autosomal inherited hair loss. Its hair follicles are more sensitive to androgens and may be accompanied by an increase in serum free testosterone levels. During adolescence, the level of androgens in the body increases, and free testosterone is easily reduced by 5-alpha reductase to diaminotestosterone. The ability of diaminotestosterone to bind with androgen receptors is significantly higher than that of testosterone, which is ten times more than that of testosterone. After the combination of the two, they enter the nucleus and produce a series of biological reactions, leading to hair follicle miniaturization, shortened hair follicle growth period, and gradually causing hair thinning or even shedding. Although scholars at home and abroad have conducted extensive research on its pathogenesis, it has not yet been thoroughly understood [5]. However, to obtain long-term effects as a topical drug, continuous medication is required. In the current situation of multiple and complicated clinical treatments, Western medicine oral medication can delay and control the development of the disease and promote hair regeneration [6].

2. Current status of SA in the young groups

SA is the most common type of alopecia that occurs after adolescence, regardless of sex [7]. At present, this disease

is mainly diagnosed clinically. The main clinical manifestation is that it is more common in males aged 20-40 years old. In the early stage, it is characterized by hair loss at both sides of the hairline, and varying degrees of hair loss may also occur at the hairline of the forehead, even gradually forming a "high forehead" with an M-shaped front hairline; As the condition progresses, the hair on the top of the head shows sparse shedding, and the two areas of hair loss can merge into patches; In the late stage, it may develop to only retain a small amount of hair in the occipital and bilateral visible areas. The skin in the hair loss area is smooth, without atrophy, and may be accompanied by symptoms such as greasiness, cancer itching, and scaling. Most patients have a family history [7]. Moreover, a genetic predisposition and serum androgen hormone levels are known to play an important role in the pathogenesis of SA in adolescents [8]. Adolescence is a transition period from childhood to adulthood, when mental maturity and physical changes due to growth spurt, secondary sex characteristics, and reproductive function are completed [9]. In recent years, many studies have shown that this disease is mainly related to genetic factors and androgen levels, among which excessive production of dihydrotestosterone (DHT) is an important pathogenesis of seborrheic alopecia. Serum (T) and free (FT) DHT are involved in multiple aspects of male sexual characteristics, development, and reproductive function. As age changes, the concentrations of T, FT, and DHT in serum also change. Studies have shown that with age, T, FT, and DHT gradually decrease, indicating a negative correlation between age and T, FT, and DHT, respectively [4-5]. As a result, the expression level of T, FT, DHT in young people is relatively high, and the relationship between DHT and seborrheic hair loss is very close. This provides a theoretical basis for us to study the correlation between hormone levels in young people and seborrheic hair loss. DHT is a product of testosterone catalyzed by 5-reductase in target tissues, widely distributed in the bloodstream throughout the body. DHT can bind to specific receptors to form complexes that enter cells, then connect to nuclear receptors and bind to chromatin, thereby affecting RNA and DNA synthesis and exerting a series of physiological effects. In adult males, excessive DHT can lead to pathological phenomena such as sores and hair loss. Modern research has shown that 5 α reductase has two types of isomerases in the human body, namely type I and type II reductase. Type I reductase is mainly present in the sebaceous glands, chest and back skin, liver, adrenal gland, and kidneys. Type II reductase is mainly present in the scalp, hair follicles (i.e. the innermost layer of the outer hair root sheath), and tissues around hair follicles. Type II reductase is mainly present in the prostate and beard areas. The DHT formed by the conversion of testosterone by 5-reductase causes hair follicle atrophy, leading to hair loss [10]. Similarly, it has also been reported that those visiting Korean hospitals with hair loss are becoming younger [11].

In SA, the anagen becomes shorter and number of hair follicles in telogen increases during repeated hair cycles. Clinically, the hair on the frontal and parietal areas of the head becomes vellus hair, which is thinner and shorter, and finally there is no hair on the scalp [12]. In Japanese males, SA becomes evident in the late 20s to 30s, then gradually progresses to completion after 40 years of age. The average incidence of SA is approximately 30% in Japanese males of all ages [13]. Genetic predisposition and hormonal changes are involved in SA pathogenesis [14]. Studies on monozygotic and dizygotic twins have shown that genetic factors are strong [15], while studies on monozygotic twins have shown that internal and external factors affect alopecia [16], suggesting the involvement of factors other than heredity. Environmental factors affecting the scalp include sebum and microorganisms.

The prevalence and type of SA are known to be dependent on race and age [17]. In the USA, one study found that 77 of 496 15- to 17-year-old males (15.5%) had symptoms more severe than grade II according to the Hamilton–Norwood classification [18]. Another study found that symptoms, such as reduced frontal and parietal hair diameters occurred at age 14.8 years in males and at 13.8 years in females among 448 androgenetic alopecia patients aged 7–17 years old [19]. Moreover, the prevalence of SA among Koreans is lower than that among Caucasians by 10 to 20%, and its prevalence among Korean adolescents seems to be lower than among same-aged Caucasians [20].

Due to the irreversible transformation of DHT by 5 α reductase, the disease cannot be completely cured at present. However, if detected early, early intervention can be taken to block the progress of this reduction reaction, thereby achieving the goal of preventing further deterioration of hair loss. Therefore, the early diagnosis and treatment of seborrheic alopecia is of great significance. Finasteride is a selective type II 5 α reductase inhibitor that can reduce serum and hair follicle DHT levels and is currently widely used in clinical practice. Although finasteride has a good therapeutic effect, due to the long treatment cycle and lack of monitoring methods during the treatment process, there is a certain degree of blindness in the treatment, which leads to poor patient compliance. The research significance of this project is to statistically analyze the DHT levels in young student patients and the relationship between various clinical stages of hair loss and DHT. For patients with high DHT levels of seborrheic hair loss, finasteride treatment is used. By monitoring the patient's serum DHT levels, the diagnostic value of DHT for seborrheic hair loss is evaluated, and more evidence is provided for the study of seborrheic hair loss.

3. Correlations between SA and fungal infection

The human body is covered with various microorganisms, which constitute a microbial society termed a “microbiome.” Cutibacterium acnes and Staphylococcus species (bacteria) and Malassezia fungi predominate on the scalp [21]. Chronic inflammation of the scalp is involved in the occurrence and development of SA. Some studies suggest that changes in hair follicle cycle and apoptosis of related cells caused by chronic scalp inflammation may have a promoting effect on hair loss [21]. Among them, the resident microorganisms of human skin, such as Propionibacterium acnes (P.acnes), Staphylococcus aureus (S.aureus), Malassezia, or Demodex mites, can cause local chronic inflammation of hair follicles and participate in hair loss in SA patients [22]. Malassezia, as the most common symbiotic fungus in the human body, is considered a part of the skin microbiota and often resides in lipid overflow areas such as the scalp. Some scholars believe that it may play a certain role in the pathogenesis and disease process of SA [23].

However, there is a lack of direct evidence from Malassezia on the pathogenicity of SA, and the above viewpoint is still controversial. Malassezia is also a lipid dependent yeast. Due to the lack of fatty acid synthase in the body, its growth and reproduction are highly dependent on lipids on the surface of the skin [24]. Therefore, Malassezia prefers to inhabit skin areas rich in sebum, such as the scalp, face, chest, and back. As a biphasic fungus, it normally inhabits the epidermis of the human body, but may transition to a pathogenic state under certain factors. The pathogenic mechanism of Malassezia may be the transformation of spores into hyphae, which then invade the stratum corneum and cause disease.

At present, it has been confirmed that the diseases caused by Malassezia are Pityriasis versicolor (PV) and Malassezia folliculitis (MF), while the relationship between Malassezia and atopic dermatitis (AD), seborrheic dermatitis (SD), psoriasis (PSO) and other diseases is still unclear and controversial [13]. The relationship between Malassezia and SA has also been controversial. For SA patients, the development of the disease is often accompanied by an increase in sebum secretion from the sebaceous glands, and a high lipid environment may promote the colonization and growth of Malassezia. And the increase in androgen levels, as a pathogenic factor, can not only cause hair follicle miniaturization, but also stimulate the proliferation and secretion of sebaceous glands, creating a favorable environment for the colonization and growth of Malassezia. In recent years, some scholars have found that a certain proportion of patients with SA exhibit an increase in the abundance and density of Malassezia when exploring the colonization of scalp microbiota. In addition, Huang et al. observed under electron microscopy that Malassezia spores invaded the hair of SA patients, causing damage to the hair shaft [25]. Two to three weeks after stopping treatment, the initial clinical situation recurs as Malassezia spp. increase to their initial levels.

Mostafa et al. found in PV that Malassezia's invasive damage to hair follicles and stratum corneum is based on Malassezia's lipid dependent characteristics. These studies all suggest that Malassezia may be involved in the occurrence or development of SA. At present, there is no direct evidence to prove that Malassezia can lead to the occurrence of SA disease or promote disease progression. The transformation of Malassezia from spore state to hyphal state is considered a key step in Malassezia's invasion and pathogenesis. With the application of direct immunofluorescence detection technology in clinical practice, we unexpectedly discovered the presence of varying degrees of Malassezia hyphae in the scalp hair loss area of SA patients. We speculate that the Malassezia hyphal state in SA may not be an accidental phenomenon, and Malassezia hyphae may be involved in the occurrence or development of SA. [26]. Malassezia is a resident fungus in the human body. Under various susceptibility factors, Malassezia is widely recognized as a pathogenic fungus for SA [27]. A detailed definition of Malassezia's pathogenic ability in the human body remains a challenge, and currently, host susceptibility is considered a prerequisite for pathogenicity, Because not all individuals will develop symptomatic diseases.

In recent years, due to the development of improved fungal identification, genetic engineering and other technologies, people's research on Malassezia has surged, which has led to the discovery of its pathogenicity in many skin diseases, and also proved that it plays an important role in inflammatory bowel disease and pancreatic cancer [28]. At present, it is speculated that its pathogenicity may be caused by the transformation from spore state to hyphal state, which in turn leads to pathological changes in the stratum corneum and hair follicles [20], leading to scalp inflammation and hair loss. With the application of immunofluorescence in clinical practice, we have found that "short rod-shaped" hyphae appear on the scalp of SA patients. The mycelial pattern of Malassezia may be the result of its high replication and proliferation under the stimulation of abundant sebum and sex hormones in the scalp, leading to the growth of hyphae. And we found that Malassezia hyphae are present in SA patients of different ages (male and female), and it is not an accidental phenomenon. Therefore, we reasonably speculate that Malassezia hyphae may play a potential role in the occurrence or development of SA diseases [29].

4. Conclusions

The growth of hair is regulated by the interaction signals between epithelial cells and dermal papilla cells, among which

various cytokines, growth factors, hormones, neuropeptides, and enzymes are involved in hair cycle control. The regulatory factors in SA are currently not fully understood. However, there are still many gaps in the research and understanding of the mechanisms by which *Malassezia* affects the structural functions of keratinocytes, hair follicle sebaceous gland units, and hair in healthy individuals and patients with skin lesions. In summary, we showed the possible involvement of *Malassezia* hyphae in the pathogenesis of SA, or at least in the exacerbation of clinical symptoms of SA, as evidenced by antifungal therapy for symptom relief. Reducing or eliminating the *Malassezia* bacterial load in the lesion area may be a promising treatment option for improving SA.

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