CASE REPORT

J Mycol Infect 2018; 23(4): 111-114
pISSN:1226-4709, eISSN:2465-8278
http://dx.doi.org/10.17966/JMI.2018.23.4.111

JMI

A Suspected Case of Hyperkeratotic Head and Neck *Malassezia* Dermatosis Presenting with Acanthosis Nigricans

Min Kyun An, Ji Ha Yoon, Eun Byul Cho, Eun Joo Park and Kwang Ho Kim†

Department of Dermatology, College of Medicine, Hallym University, Anyang, Korea

A 19-year-old woman presented with an asymptomatic cutaneous discoloration on her nape. Dermatological examination revealed localized dark brown to dark pigmented velvety macules and patches. She denied a past medical history, except for a 7-kg weight gain over a 6-months period. Histopathologically, the specimen showed hyperkeratosis, epidermal hyperplasia, mild acanthosis, and papillomatosis. In addition, keratin material and fungal spore were noted between the papilloma ridges. Periodic acid-Schiff special stain showed a positive result for the fungal spore in the horny layer. She was treated with a daily oral dose of terbinafine and topical flutrimazole. After 12 weeks of treatment, she is currently under observation without pigmentation and adverse effect. We considered the initial diagnosis as acanthosis nigricans because of weight gain, similar clinical features, and histological findings. However, the final diagnosis was hyperkeratotic head and neck *Malassezia* dermatosis considering the presence of yeast and the dramatic improvement after antifungal treatment. To the best of our knowledge, hyperkeratotic head and neck *Malassezia* dermatosis is not well characterized in the literature. It is an unusual variant of pityriasis versicolor. The skin lesion appears brown to dark, scaly, and hyperkeratotic macules and patches located on the face and neck. Here, we reported an unusual case of hyperkeratotic head and neck *Malassezia* dermatosis.

Key Words: Acanthosis nigricans, Fungal spore, Hyperkeratotic head and neck *Malassezia* dermatosis, *Malassezia* species

INTRODUCTION

Hyperkeratotic head and neck *Malassezia* dermatosis (HHNMD) was the first disease condition reported by Boralevi et al.[1] Clinical features of HHNMD include scaly hyperkeratotic dermatosis involving the face and neck. Examination of the skin lesion revealed *Malassezia* colonization. Clinical manifestations of acanthosis nigricans (AN) are systemic hyperpigmented, hyperkeratotic, and verrucous velvet-like patches and plaques. It mainly occurs in the intertriginous areas, such as the axilla, posterior neck, and genital area. AN develops because of several different causes, and it can be classified into eight subtypes, namely malignant-associated, benign, acral, obesity-associated, syndromic, drug-induced, unilateral, and mixed[2]. AN is more commonly associated with insulin resistance or obesity. To the best of our knowledge, no cases of AN-associated fungal infection have yet been reported. Here we reported a case of HHNMD caused by yeast infection presenting with AN.

Received: June 19, 2018 Revised: November 21, 2018 Accepted: December 11, 2018

†Corresponding: Kwang Ho Kim, Department of Dermatology, Hallym University Sacred Heart Hospital, 22, Gwanpyeong-ro 170beon-gil, Dongan-gu, Anyang, Gyeonggi-do, 14068, Korea.
Phone: +82-31-380-3765, Fax: +82-31-386-3761, e-mail: dermakkh@naver.com

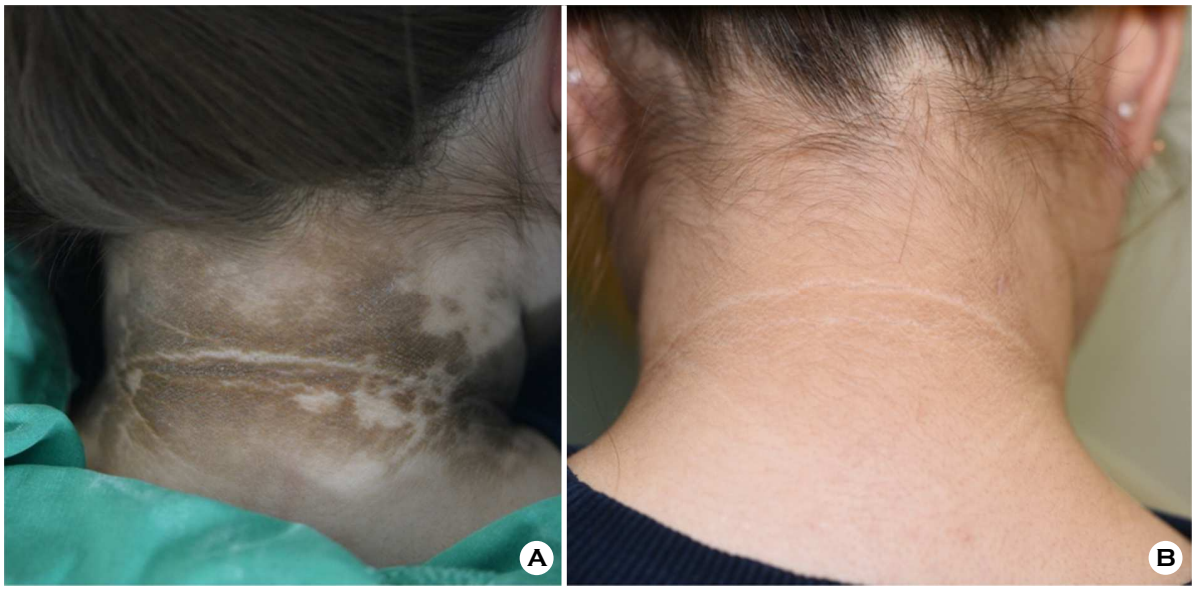

Fig. 1. (A) Localized dark brown to dark pigmented velvety macule and patch on the nape of the neck before treatment (B) Background hyperpigmentation disappeared after treatment for 12 weeks

CASE

A 19-year-old woman presented with asymptomatic cutaneous discoloration. A dermatological examination revealed localized dark brown to dark pigmented velvety macules and patches on the nape (Fig. 1A). No pruritus or pain was detected in the skin lesions. She denied any medical history except for a 7-kg weight gain over the past 6 months. Her grandfather has diabetes, but there is no familial history of AN. Laboratory results were positive with fluorescent antinuclear antibody-speckled pattern, and all findings, including blood sugar test and HbA1c levels, were normal.

A skin punch biopsy was performed to differentiate among HHNMD, confluent and reticulated papillomatosis, and AN. Histopathologically, the specimen revealed hyperkeratosis, a thinned epidermis above papillomatous projection, mild acanthosis, and an upward finger-like projection of dermal papillae (Fig. 2A). Keratin material and fungal spores were detected between the papilloma ridges. The upper dermis revealed mild perivascular lymphocytic infiltration. No other specific findings were observed in the dermis. Periodic acid-Schiff (PAS) staining revealed a positive result for fungal spores in the horny layer (Fig. 2B).

AN and HHNMD were not excluded based on clinical and histological findings. The initial treatment was performed with 250 mg terbinafine and 1% topical flutrimazole cream daily. After 3 weeks, the velvety pigmented patches improved. After 12 weeks of continuous treatment, the symptoms disappeared, leaving no residual pigmentation and without any adverse effect (Fig. 1B). Considering the dramatically improved skin lesions after antifungal treatment, HHNMD was considered as the final diagnosis. She is currently undergoing observation without any special treatment.

DISCUSSION

HHNMD is a rare cutaneous infection caused by *Malassezia*. Until date, there have been only two reports on HHNMD[1,3]. Boralevi et al.[1] confirmed *Malassezia* species in the fungal culture and considered it an unusual variant of pityriasis versicolor (PV) based on clinical features in adolescents and young adults. Pham-Ledard et al.[3] inferred it to be a facial presentation of confluent and reticulated papillomatosis (CRP) based on clinical features of brown, scaly, hyperkeratotic macules, and patches.

Histological features of PV are characterized by slight hyperkeratosis, slight spongiosis, and minimal perivascular lymphocytic infiltration[4]. CRP is characterized by mild hyperkeratosis, papillomatosis, and focal acanthosis[5]. Histological findings of this case showed significant hyperkeratosis, thinned epidermis at the tips and sides of protruding dermal papillae,

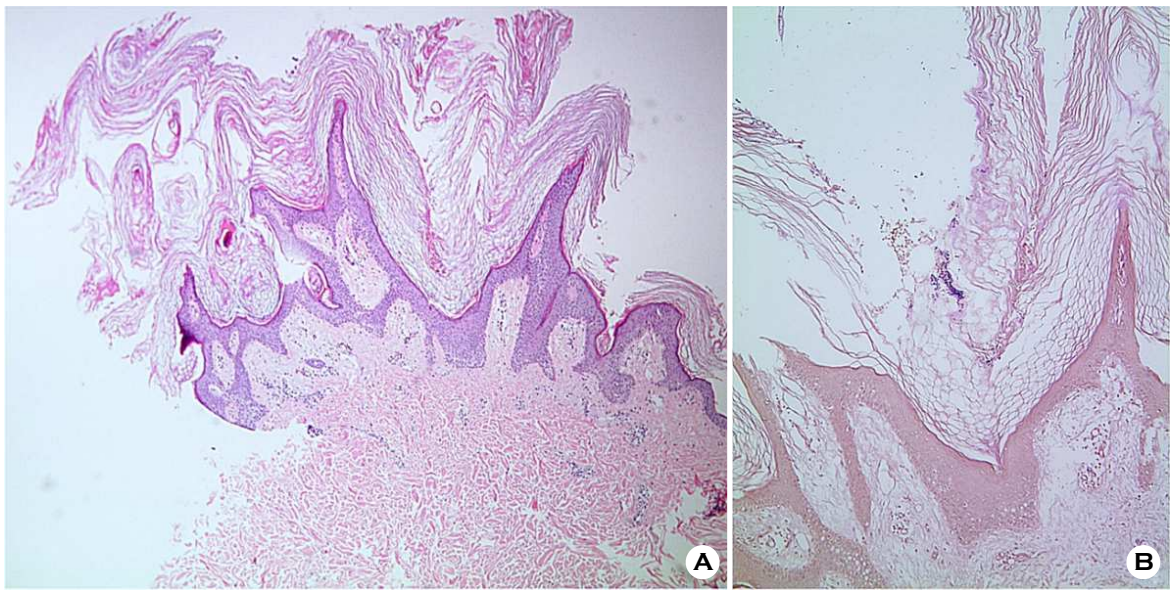

Fig. 2. (A) Histopathological examination revealed hyperkeratosis, epidermal hyperplasia, mild acanthosis, and papillomatosis (H&E, ×40). (B) A high-powered view of immunohistochemistry for PAS showing keratin material and fungal spores (PAS, ×100)

and upward projection of the dermal papillae. Therefore, PV and CRP were excluded.

This case showed weight gain, typical skin appearance of AN, and histological findings. However, fungal spores were observed with the keratin material between the hyperkeratotic ridges. No cases of cutaneous fungal infection have yet been reported. The response to treatment of AN is extremely poor. However, this case was treated, and dramatically hyperkeratotic scaly hyperpigmentation of the skin was observed after antifungal treatment. Although we did not conduct any evaluation, such as fungal culture or genomic sequencing, the cutaneous infection of *Malassezia* yeast was the most suspected based on the observed fungal spores. The epidermal stripping or scrapping, performed before the skin punch biopsy, could exclude terra firma forme dermatosis but not the skin lesion. The stable psychological status and willingness for therapy excluded the possibility of dermatitis neglecta. These clinical features and histological findings suggest that the final diagnosis was more appropriate for HHNMD than for AN.

Cutaneous changes in AN are caused by growth factor stimulation of keratinocytes and dermal fibrosis of the skin, and hyperpigmentation is caused by epidermal hyperkeratosis[2]. Tamraz et al.[6] reviewed 10 cases of CRP and observed *Malassezia* yeast in six, which demonstrated clinicopathological hyperpigmentation and hyperkeratosis similar to that in HHNMD. In CRP, an abnormal keratinizing response to *Malassezia* has been hypothesized to underlying pathological keratinization[6]. We believe that hyperkeratosis in HHNMD is similar to that in CRP, considering the improper response of keratinocytes to fungal spores. Histological findings of this case also demonstrated a significant increase in hyperkeratosis but not in melanin pigmentation. Histological findings of the two cases reported by Boralevi et al.[1] showed no increase in melanin pigmentation. Thus, hyperpigmentation of HHNMD is believed to occur due to hyperkeratosis rather than due to an increase in melanin pigmentation.

In this case, additional evaluations, such as fungus culture, were not performed to identify the pathogen, which is a limitation. Boralevi et al.[1], who first reported HHNMD, reported HHNMD as a variant form of PV. Pham-Ledard et al.[3] considered HHNMD as a facial presentation of CRP with contingent yeast colonization. Considering the lack of reports on HHNMD, it remains controversial to consider HHNMD as an independent disease entity.

Antifungal agents should be considered as the first-line treatment for HHNMD. Boralevi et al.[1] confirmed *Malassezia globosa* and *M. sympodialis* as causative agents in two cases. A 26-year-old man, treated with oral ketoconazole and imidazole cream, improved after 6 months of treatment. A 42-year-old woman was treated with oral and topical ketoconazole as well as 1% salicylic acid topical ointment, and the skin lesion improved after 1 month of treatment. In this case, the

patient was also treated with oral terbinafine and topical flutrimazole for approximately 12 weeks.

These antifungal agents may be helpful not only for the direct treatment of *Malassezia* yeast but also for hyperkeratosis —the cause of hyperpigmentation. Ketoconazole exerts an anti-inflammatory effect through the inhibition of the arachidonic acid cascade[7] and directly acts on a somatomedin C/insulin-like growth factor I receptor to reduce keratinocyte replication[8]. Until date, no studies have reported that terbinafine and flutrimazole reduce human keratinocyte proliferation; however, terbinafine is commonly used for the treatment of seborrheic dermatitis in *Malassezia* infection[9]. The effect of terbinafine can be attributed to the combination of its antifungal activity against *Malassezia* yeasts and its anti-inflammatory activity[9]. Topical flutrimazole has demonstrated an anti-inflammatory effect in animal studies, which reduces edema by targeting arachidonic acid[10].

In the present case, we demonstrated that HHNMD presenting with AN can be effectively and safely treated with antifungals. The improvement in pigmentation can be explained by the elimination of *Malassezia* yeast. The authors believe that antifungal agents are effective for the treatment of hyperkeratosis. Therefore, we hypothesized that cutaneous fungal infection is associated with hyperkeratosis and hyperpigmentation. Therefore, the antifungal agents could be considered as keratolytics in patient.

CONFLICT OF INTEREST

In relation to this article, We declare that there is no conflict of interest.

REFERENCES

1. Boralevi F, Marco-Bonnet J, Lepreux S, Buzenet C, Couprie B, Taïeb A. Hyperkeratotic head and neck *Malassezia* dermatosis. Dermatology 2006;212:36-40
2. Sinha S, Schwartz RA. Juvenile acanthosis nigricans. J Am Acad Dermatol 2007;57:502-508
3. Pham-Ledard A, Ezzedine K, Couprie B, Begueret H, Boralevi F, Taieb A. Facial confluent and reticulate papillomatosis (Gougerot-Carteaud syndrome) or hyperkeratotic head and neck *Malassezia* dermatitis? Ann Dermatol Venereol 2010;137:451-454
4. Elder DE. Lever's histopathology of the skin. Lippincott Williams & Wilkins, 2014:732
5. Park YJ, Kang HY, Lee ES, Kim YC. Differentiating confluent and reticulated papillomatosis from acanthosis nigricans. J Cutan Pathol 2015;42:944-952
6. Tamraz H, Raffoul M, Kurban M, Kibbi AG, Abbas O. Confluent and reticulated papillomatosis: clinical and histopathological study of 10 cases from Lebanon. J Eur Dermatol Venereol 2013;27:e119-123
7. Cutsem JV, van Gerven F, Cauwenbergh G, Odds F, Janssen PAJ. The antiiflammatory effects of ketoconazole. J Am Acad Dermatol 1991;25:257-261
8. Nickoloff BJ, Misra P, Morhenn VB, Hintz RL, Rosenfeld RG. Further characterization of the keratinocyte somatomedin-C/insulin-like growth factor I (SM-C/IGF-I) receptor and the biological responsiveness of cultured keratinocytes to SM-C/IGF-I. Dermatologica 1988;177:265-273
9. Faergemann J. Treatment of seborrhoeic dermatitis with oral terbinafine? Lancet 2001;358:170
10. Merlos M, Vericat ML, Garcia-Rafanell J, Forn J. Topical anti-inflammatory properties of flutrimazole, a new imidazole antifungal agent. Infalmm Res 1996;45:20-25