



Malassezia infection associated with stucco keratosis

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ABSTRACT

We report a case of a 20-year-old young woman with a large stucco keratosis in the mons veneris, one of the clinical variants of Seborrheic keratoses (SKs). Periodic acid-Schiff staining revealed a large number of *Malassezia* spores in the stratum corneum. After oral antifungal treatment with itraconazole for 4 weeks, the benign tumor was completely cleared without residue or recurrence, which may open a new perspective for exploring the pathogenesis of SKs.

1. Introduction

Seborrheic keratoses (SKs) are the most common benign epithelial tumor in humans with high clinical variability. Traditionally, SKs have been regarded as a sign of skin aging, which may be related to ultraviolet (UV) exposure [1,2]. However, the exact etiopathology of SKs is still not fully understood, and the relationship between potential infectious factors and the occurrence of this benign tumor is even less well studied [3]. Here, we demonstrated a large stucco keratosis in the mons veneris of a young woman, one of the clinical variants of SKs, with a large presence of *Malassezia* spores in the corneum. Surprisingly, the benign tumor was completely cleared after oral itraconazole antifungal treatment, with no trace or recurrence.

2. Case presentation

A 20-year-old female from the southwest China was admitted to the outpatient Department of Dermatology (day 0) in March 2022 due to proliferative brown plaques on her mons veneris for 2 years. The lesions started as brown macules (day -720), ranging from the size of mung beans to peanuts, with gradual verrucous proliferation on the surface (day -680). Some proliferative granules can be peeled off (day -650), not easy to bleed, no pain or itching. Normal sweating. Before the eruption, no trauma or other clear source of infection was identified, and there was no history of sexual contact. The female college student was otherwise healthy, with no constitutional symptoms or history of immunosuppression. All other serum chemistries were within normal limits. Physical examination showed dense peanut-sized brown macules

on the mons veneris, fused into patches, with a center of dark brown warty hyperplasia with a size of 6cm × 7cm, and a granular surface that was not easy to peel off (Fig. 1A). Network-like (NL) structures and sharp demarcation were observed by the dermoscopy (Fig. 2A and B) [4]. Histopathological examination of the skin revealed basket shaped hyperkeratosis, parakeratosis, papilloma-like hyperplasia of the epidermis, resembling a church spire, and pseudo-horn cysts formation. The blood vessels in the papillary dermis were dilated, and a small number of lymphocytes and histiocytes were infiltrated (Fig. 3A). Periodic acid-Schiff staining (PAS) showed a large number of ovo-shaped yeast spores in the stratum corneum, some of which were budding (Fig. 3B). *Malassezia* was considered morphologically. Itraconazole was given orally at a dose of 100 mg twice daily, Hydroxychloroquine sulfate 200 mg twice a day; Topical 10 % salicylic acid ointment once a day; The total course of treatment was 4 weeks. One week later (day 7), the verrucous hyperplastic particles began to fall off. Four weeks later (day 30), all the rashes subsided, leaving only surgical scars resembling peanuts in size (Fig. 1B). During one year follow-up (day 360), the skin was still intact without any sign of recurrence.

3. Discussion

Stucco keratosis is a special type of SKs, usually occurs in the distal limbs, the skin lesions are generally less than 3cm in diameter, gray brown, easy to scratch without bleeding [4]. Histologically, it is similar to common seborrheic keratosis (CSK), but characterized by upward papillary growth and hyperkeratosis forming a church steeple-like appearance (Fig. 3A) [4]. Dermoscopy generally lacked the common

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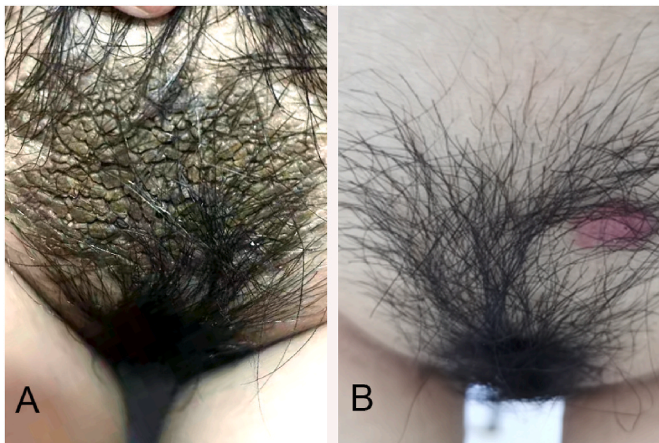


Fig. 1. A well-demarcated brown patch on the mons veneris with granular verrucous hyperplasia measuring 6cm × 7cm on the surface (A); Resolution of lesions after one month treatment (B). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

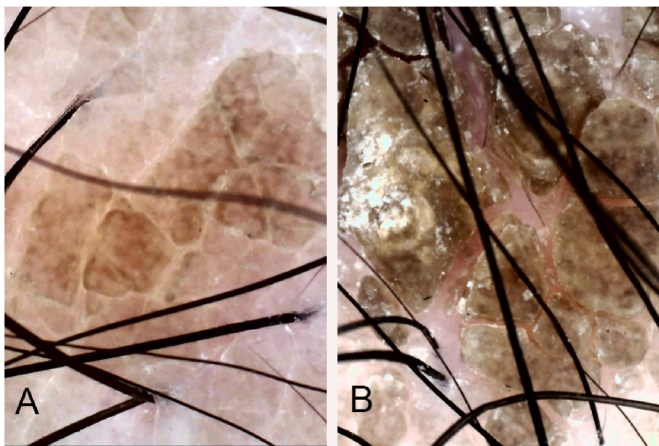


Fig. 2. Dermoscopy showing network-like (NL) structures and sharp demarcation. Dull, flat and brown patches at the edge (A), central waxy verrucous or "stuck-on" appearance, darker in color (B). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

findings of SK, such as comedo-like (CL) openings, fissures and ridges (FR) and fingerprint (FP)-like structures. The main manifestations were network-like (NL) structures and sharp demarcation (SD) [2,4]. Combined with clinical, pathological and dermoscopic examination, our case was completely consistent with the diagnosis of stucco keratosis, and the particularity lies in the site and size of occurrence. The mons pubis is warm and moist with abundant sebaceous glands and is the niche of *Malassezia*, the most common fungus in the skin microbiome [5,6]. So, the very intriguing question arises, does this fungus contribute to tumor initiation and progression?

It is well established that chronic infection can induce tumorigenesis, such as human herpesvirus 8 (HHV-8) and Kaposi's sarcoma [7]. A small number of previous studies have indeed suggested that infectious factors may be associated with SKs, with the presence of human papillomavirus in about half of the genital lesions [2,3], and *Malassezia* species often found in this benign hyperplasia in the seborrhea area of the head, face and back, but the exact mechanism and causal relationship are not clear [8]. Although papillomavirus DNA detection was not completed in this case, no typical vacuolar cells were found in the upper layer of the proliferating epidermis, and there was no history of sexual contact, so

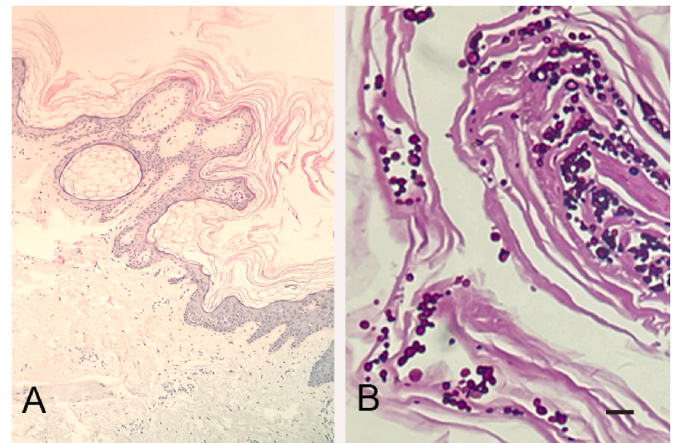


Fig. 3. H&E section revealed basket shaped hyperkeratosis, parakeratosis, papilloma-like hyperplasia of the epidermis, resembling a church spire, and pseudo-horn cysts formation (200 ×) (A). Periodic acid-Schiff staining (PAS) showed a large number of ovoid budding yeast spores in the stratum corneum, some of which were budding. Scale bar 10µm (B).

the coexistence of papillomavirus can be basically ruled out. In contrast, the abundance of ovoid budding spores in the stratum corneum provided evidence for the presence or infection by the fungus, *Malassezia* sp. Most importantly, this large tumor regressed completely after standardized systemic and topical antifungal treatment, avoiding the traditional disadvantages of local treatment of SKs, which are usually uncomfortable and have cosmetic sequelae [2,3]. To the best of our knowledge, this is the first case of SKs with complete resolution of antifungal therapy.

Of course, it is worth debating whether systemic administration of itraconazole and hydroxychloroquine resulted in the elimination of this benign tumor by inhibiting *Malassezia*. As a classic systemic triazole antifungal drug, itraconazole has been confirmed to inhibit angiogenesis and proliferation while leading to increased apoptosis, thus expanding its new role in the treatment of hemangioma and non-small cell lung cancer [9–12]. However, no inhibitory effect of itraconazole on the proliferation of keratinocytes has been found so far. In this case, the target of itraconazole was *Malassezia*, and the combined use of hydroxychloroquine sulfate, which our previous study has confirmed has a synergistic antifungal effect with itraconazole [13].

Based on the above, this case provides a new perspective for us to understand SKs. The special onset age and location of this benign tumor are contrary to the traditional mechanism of light exposure and aging. The existence of *Malassezia* and successful antifungal treatment provide new ideas for the potential pathogenesis of this benign tumor. *Malassezia* may not be an "effect" but a potential "cause" in the occurrence of this clinical subtype. Moreover, as the most common benign skin tumor, which remains benign and rarely mutates to malignancy and metastasis, does *Malassezia* also act as a protective factor?

CRedit author statement of "It's you: *Malassezia* is indeed the "cause" of stucco keratosis"

Yanping Jiang: Conceptualization, Methodology, Supervision, Software.

Zhan Zhou: Data curation, Writing- Original draft preparation.

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Ethical statement

The authors confirm that this material is original and has not been published in whole or in part elsewhere; that the manuscript is not

currently being considered for publication in another journal; and that all authors have been personally and actively involved in substantive work leading to the manuscript, and will hold themselves jointly and individually responsible for its content.

Declaration of competing interest

There are none.

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