Cryptic deep dermatophytosis in a renal transplant recipient with hidradenitis suppurativa

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INTRODUCTION

Anthropophilic dermatophyte infection is one of the most commonly encountered skin and nail pathologies. Invasive disease occurs in immunocompromised individuals through follicular invasion, traumatic infiltration, or localized infiltration in pathologies inducing epithelial barrier disruption. It typically presents as purplish ulcerated nodules of the lower extremities, but corporal manifestations vary in extent and appearance, ranging from scaly nodules and plaques to tumor-like pseudocysts, vegetative nodules, coalesced pink-purple plaques, or papulopustular lesions with or without pain.1

Mimicking disease states or infections can blur differential diagnosis, but their concomitant presence is seldom described. We report a unique case of Trichophyton rubrum deep dermatophytosis in an immunocompromised host with a previous diagnosis of hidradenitis suppurativa (HS).

CASE DESCRIPTION

A 61-year-old man with a history of kidney transplantation, onychomycosis, gout, tinea cruris and pedis, and diabetes presented for a violaceous and purulent nodule on the inguinal aspect of the right thigh. The lesion was asymptomatic, and there were no signs of systemic infection. Of note, similarly appearing, relapsing lesions of the groin and thigh progressively worsened over the past 4 months despite the use of ketoconazole cream, topical chlorhexidine, and clindamycin swabs as well as numerous courses of antibiotics for Escherichia coli urinary tract infections and bacteremia. Culture of drainage from an inguinal nodule produced scant colonies of Corynebacterium and sterile white mold, presumed to be contaminants. A biopsy of this inguinal nodule revealed perifollicular suppurative and granulomatous inflammation suggestive of HS on hematoxylin-eosin—stain (H&E). Additional staining was not performed. This diagnosis, failure of medical treatment, and the development of additional purulent papules and nodules with scarring tracts in the groin, prompted referral to plastic surgery for excision. Histopathology of the inguinal excision displayed abscesses, scars, candida pseudohyphae, and inflammation on H&E, and numerous yeast and hyphae on Grocott methenamine silver (GMS), again being consistent with HS.

By the time of his post-operative visit 3 weeks later, no groin nodules had returned, but the patient's...
ankle lesion had developed into a large and purulent mass. Also since the time of surgery, he developed a new eruption of nodules on the left side of his face. The patient denied fever or chills and remained compliant with his post-transplant regimen of tacrolimus, mycophenolate, and prednisone.

Physical examination revealed well-healed scars in the groin, several draining nodules on the face (Fig 1), and the previously biopsied large, painless, and purulent tumor on the right ankle (Fig 2). Repeat biopsy and culture of the face and ankle were performed (Fig 3). Laboratory evaluation revealed a normal white blood cell count and beta-D-glucan levels greater than 500 pg/mL, raising concern for deep fungal infection. Other fungal antigen tests were negative. Microscopic inspection revealed pseudoepitheliomatous hyperplasia with suppurative inflammation, and GMS highlighted deep dermal branching hyphae, with some organisms demonstrating asymmetrical walls, which could be suggestive of Blastomyces.

Fungal culture ultimately grew T. rubrum sensitive to itraconazole, and the patient was diagnosed with T. rubrum deep dermatophytosis in the setting of immunosuppression. The patient experienced significant clinical improvement after 2 months of itraconazole, with complete resolution of facial nodules and decrease in size and purulence of the ankle lesion.

DISCUSSION

Less than 100 cases of invasive T. rubrum have been reported in the literature since its description by Majocchi et al. in 1883.2 The disease has 4 distinct clinical manifestations: Majocchi granuloma, deep dermatophytosis, disseminated dermatophytosis, and (pseudo)mycetoma (Table I). In the context of immunosuppression and active tinea without systemic antifungal treatment, it is likely that our patient insidiously progressed from superficial to superimposed deep dermatophytosis while being treated for HS. Moreover, it is possible that the epithelial compromise induced by his uncontrolled HS hastened deep fungal infections in areas of active superficial tinea.

The association between HS and infectious disease has not been fully elucidated; significant dysbiosis, increased inflammatory cytokines, inhibited notch signaling, and anti-microbial peptide synthesis3 may play a role in self-perpetuation of the condition. However, it is well known that terminal follicle hyperkeratosis and subsequent follicular rupture results in expulsion of epithelial components and bacteria into the dermis, where acute and chronic infection exacerbate the disease. Immunodysregulation and epithelial barrier disruption foster higher rates of all-cause infection; HS is associated with a more than three-fold increased risk of fungal infection.4 This overlap between auto-inflammatory and chronic infectious pathologies, in which suppuration, abscesses, and scarring are abundant, can significantly complicate the clinical and microscopic examination. Although biopsy and culture of the patient’s ankle mass would prompt the final diagnosis of deep dermatophytosis, a history of prolonged granulomatous inflammation, suppurative nodules, and associated sinus tracts in his groin, previously diagnosed as HS, initially obscured any infectious etiology.

On histopathologic examination, deep dermatophytosis is characterized by extrafollicular granulomas and hyphal invasion of the dermis and subcutis without follicular involvement.1 This presents a diagnostic challenge, as T. rubrum often displays atypical morphology in deeper tissue.
sections, as observed in our case.\textsuperscript{5} It is hypothesized that the diminished innate immune system and alkaline environment of the dermis facilitate uninhibited differentiation required for adaptation. Histologically, pleomorphic features including chlamydoconidium, arthroconidium, pseudobudding, branching hyphae, and broad-based budding have been reported in this population, suggesting a broad variety of possible fungal infections.\textsuperscript{2,5,6} Tissue section plane, hyphal orientation, and tissue viability also influence the histological appearance of these structures.\textsuperscript{7} Therefore, polymerase chain reaction or culture are often required to determine the causative organism.

In the solid organ transplant population, renal transplant recipients have the highest incidence of invasive dermatophytosis. It is a late complication, and the majority of immunosuppressed patients who develop dermatophytosis have concurrent superficial infection, which predisposes them to self-infection.\textsuperscript{8} Clinical suspicion in combination with histological findings of hyphae in the dermis warrants prompt treatment with appropriate antifungal therapy.

This case highlights the atypical nature of dermal \textit{T. rubrum} in patients with a diminished immune system, and its potential for invasive infection underscores the importance of treating superficial dermatophytoses in solid organ transplant patients. It also brings to attention the importance of ruling out infectious processes in patients with HS, and the difficulty in differentiating superinfections from infections mimicking HS.

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### Table I. Variants and presentations of invasive dermatophyte infections\textsuperscript{1,9,10}

| Variant                  | Presentation                                                                 |
|--------------------------|-----------------------------------------------------------------------------|
| Majocchi granuloma       | - Localized suppurative folliculitis near trauma-exposed area with pre-existing superficial dermatophytosis in immunocompetent patient  |
|                          | - Generalized nodular granulomatous perifolliculitis due to chronic follicular invasion in immunocompromised patient |
| Deep dermatophytosis     | - Large (>1 cm) purple nodules or plaques, often on the extremities, with suppurative, non-follicular abscesses caused by fungal organisms in the deep dermis or subcutis in immunocompromised patient |
| Disseminated dermatophytosis | - Systemic disease involving vascular or lymphatic spread to internal organs |
| (Pseudo)mycetoma         | - Clusters of fungal organisms or associated pyogranulomatous reactions develop chronic sinus tracts |

![Fig 3. Histopathology of ankle biopsy.](image)
Conflicts of interest
None disclosed.

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