Seborrheic Dermatitis – An Early and Common Skin Manifestation in HIV Patients

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SUMMARY Seborrheic dermatitis is a common dermatosis occurring on the scalp, face and chest. In the general population, the prevalence of seborrheic dermatitis varies between 3% and 5%, while in HIV positive patients there is an increased prevalence of seborrheic dermatitis ranging between 30% and 83%. Seborrheic dermatitis occurs early in the course of HIV disease and may be an initial clinical marker of HIV infection.

KEY WORDS: seborrheic dermatitis, cutaneous HIV markers, papulosquamous skin diseases, seborrhea, *Malassezia furfur*

INTRODUCTION

Seborrheic dermatitis (SD) is a common chronic papulosquamous dermatosis with remissions and exacerbations, typically located in areas with rich supply of sebaceous glands, i.e. the scalp, face and upper trunk. Clinical manifestations of the disease vary in severity from wild dandruff to exfoliative erythroderma (1-4). Many cross-sectional as well as cohort studies have examined the association between SD and human immunodeficiency virus (HIV) infection. We reviewed current literature regarding SD characteristics, focusing on differences in clinical manifestations, prevalence and treatment between general population and HIV patients. The aim is to demonstrate that SD is more common, has an early onset and presents with severe clinical syndrome in HIV patients, thus posing therapeutic difficulties in this patient population.

EPIDEMIOLOGY OF SEBORRHEIC DERMATITIS

SD affects newborns, infants and adults, occurs in persons of all races, and the clinical syndrome is more severe in males than in females. The prevalence of SD in the general population varies between 3% and 5%, increasing to 30%-83% in human immunodeficiency virus (HIV) positive and acquired immunodeficiency syndrome (AIDS)

patients (1,5). SD is closely related to infantile SD (cradle cap or diaper rash) and to neurological disorders such as Parkinson's disease (2,6,7). It is commonly worsened by changes in environment humidity, changes in seasons, trauma (e.g., scratching) or emotional stress (8).

ETIOLOGY OF SEBORRHEIC DERMATITIS

The etiology of seborrheic dermatitis is poorly understood, although different lines of evidence support the role of *Malassezia (M.) furfur* (previously *Pityrosporum (P.) ovale*) as the causative yeast (9). Furthermore, the success of antifungal medications in treating SD provides new evidence for this view. Many studies describe the effectiveness of antifungal medications, paralleled by a reduction in the number of *P. ovale* and leading to amelioration of SD lesions (10,11).

Gupta *et al.* found *M. globosa* to be the predominant species in SD patients, while Sei confirmed the predominant presence of *M. globosa* along with *M. restricta* in SD patients, in contrast to *M. sympodialis*, which was detected in healthy skin of normal population (2,12).

M. furfur is part of the normal resident skin flora, but under certain circumstances it may cause or aggravate a spectrum of skin diseases including pityriasis vescicolor, atopic dermatitis and SD (13). Currently advanced laboratory methods like RAPD-PCR analyses can offer distinct differentiation between *M. furfur* isolates from pityriasis vescicolor and SD in patients with or without AIDS (14).

However, it is uncertain whether or not SD patients have higher *Malassezia* counts than normal controls (15), although a correlation between yeast density and severity of SD has been reported (16). It has been suggested that the density of *Malassezia* organisms is only important for the individuals who are susceptible to SD. An abnormal immune response to *Malassezia* could be another explanation. Bergbrant *et al.* report that in patients with AIDS who typically show abnormalities of T-cell functions, the activation of the alternative complement pathway by *P. ovale* which does not require T-cell function is depressed and could be an explanation for the inflammatory response (17).

Parry and Sharpe suggest that SD is not caused by an altered immune response to *Malassezia* yeast and propose toxin production or lipase activity as potential mechanisms (9). Other researchers have shown that the lipophilic yeast is able to activate the alternative pathway of complement (18). All the above mentioned processes can induce nonspecific skin inflammation. Briefly, a defect in immune response (specific or not) may facilitate fungal survival in the skin.

Furthermore, endogenous factors have always been implicated in the pathogenesis of SD, along with others factors, e.g., the role of lipid hormones. The lipid amount on the skin in patients with SD was significantly higher than in controls (19).

Similarly, Ostlere *et al.* suggest that the skin surface lipid composition in men with SD differs from that of unaffected controls (20). Since SD is more common in men than in women, hormones may play a role and androgen influence on the pilosebaceous unit has been suggested. In addition, lifestyle and nutrition may be involved in SD development, especially in those suffering from alcoholism (21) or depression (8).

SEBORRHEIC DERMATITIS IN HIV INFECTED PATIENTS

Cutaneous manifestations including SD may occur at any stage of HIV infection (22,23). In fact, the first clinical manifestations related to HIV infection are often located on the skin. SD is a common dermatosis occurring most frequently on the scalp, face and chest in HIV positive patients. In these patients, SD tends to occur early in the course of the disease (CD4^{+} T-cell count range 450-550 cells/µL) (24-26), and is usually more severe and difficult to diagnose and treat than in the general population (27). The butterfly distribution of the rash when followed by a non-diagnostic biopsy, as sometimes happens, may mislead to the diagnosis of discoid lupus erythematosus unless the clinician is aware of the underlying immunodeficiency (26,28). Additionally, because tinea infections such as tinea faciei may occur in this patient population and mimic SD, a potassium hydroxide examination for hyphae should be performed if the diagnosis is in doubt (29).

It has been shown that during the course of HIV disease almost 85% of patients will manifest SD at least once, although these data seem to be closely linked to the type of the patient population and the duration of follow-up (31). In Mali, where SD is quite rare, development of this dermatosis has been used as a predictor for HIV infection (31,32).

The introduction of highly active antiretroviral therapy (HAART) has led to a dramatic reduction in the incidence of opportunistic disorders and HIV-related mortality (30,33,34). Hengee *et al.* re-

port that 25.3% of HIV patients develop SD lesions prior to HAART (35). In this series, the cumulative incidence of SD did not change significantly (17.6%) among patients under HAART. In a study reported by Rosatelli *et al*., 223 HIV patients were examined during the 1989-1993 period, and 152 of these 223 patients had full-blown AIDS, whereas the remaining 71 patients were asymptomatic. It was concluded that SD was the most frequent disorder affecting 24% of patients in the initial stages of HIV and 30.3% of those with AIDS (36).

In addition, many studies, mainly cross-sectional or cohort studies, have examined the association between skin disease prevalence and CD4 counts, concluding that a low CD4 cell count or higher viral load were linked with extended skin abnormalities (37-39). Also, patients suffering from SD and decreased CD4 cell counts were more likely to experience rapid progression to advanced disease (40).

TREATMENT

Antimycotics remain a popular treatment for SD, in the form of shampoos or creams. Many double-blind studies have documented the efficacy of ketoconazole 2% in reducing flaking and *Malassezia* counts (41,42); furthermore, ketoconazole 2% shampoo has been shown to have a significant prophylactic effect when used once weekly (11). Nevertheless, low potency topical corticosteroids (e.g., hydrocortisone) and emollients have been used in the initial stages of treatment (43).

Additional measures including shampoos with coal tar, pyrithione zinc, then selenium sulfide and lithium succinate ointment may be effective treatment for SD both in immunocompetent individuals and in those with AIDS (44).

Newer topical successful therapeutic options for facial SD in HIV patients are pimecrolimus 1% and tacrolimus cream (45-47). These modulators are nonsteroid calcineurin inhibitors that exert their anti-inflammatory effects by inhibiting the release of pro-inflammatory cytokines and mediators from T-cells and other cells, involved in skin inflammation (48,49).

A recent open-label pilot study conducted by de Moraes *et al*. documented that all patients responded to therapy despite their immune status and that pimecrolimus did not alter CD4$^+$ and CD8$^+$ T-cells counts or viral load during the treatment period (5). Furthermore, metronidazole has been used in the treatment of SD, with some promising results (50,51).
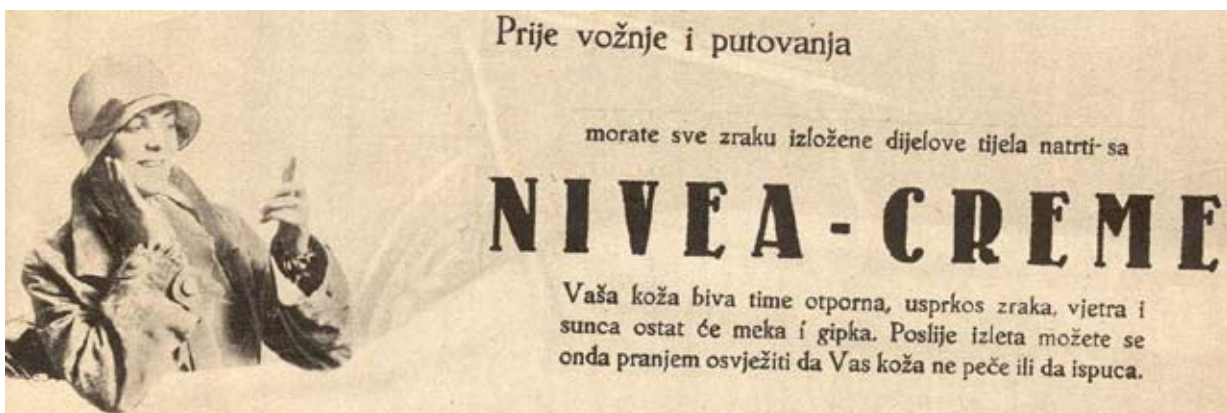
CONCLUSION

SD is one of the earliest and common skin diseases in the course of HIV disease. Careful examination of the skin may be highly useful for the diagnosis of HIV infection and the severe forms of common skin diseases in HIV patients (such as SD) may provide a clue for the clinician to suspect the underlying HIV infection (27,36).

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