Etiopathogenesis of seborrheic dermatitis

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Seborrheic dermatitis (SD) is a common inflammatory disorder of the skin, characterized by erythema covered with greasy-looking scales and seen over areas rich in sebaceous glands-namely, the scalp, face, chest, back and flexural areas. Though much remains to be learned, there is increasing understanding of the etiopathogenesis of seborrheic dermatitis. This should eventually lead to more effective management of the disease.

SEBORRHEA

Seborrheic dermatitis is not a disorder of sebaceous glands. Many normal young adults have an oily-looking skin but no SD. Moreover, the sebum secretion rate from the forehead of SD patients is normal.[1] Though Parkinson's disease is associated with seborrhea and seborrheic dermatitis,[2] its treatment with L-dopa reduces sebum secretion if it is in excess but has no effect if the sebum secretion is normal.[3] It has been suggested that the increased sebum levels in patients of Parkinson's disease have permissive effect on the growth of *Malassezia*. It may be concluded that seborrhea may be a predisposing factor but is not the primary etiological factor for seborrheic dermatitis. This is supported by the fact that low-dose oral isotretinoin, a known sebostatic agent, given for several months, is useful in stubborn seborrheic dermatitis.[4] However, the effects of isotretinoin on the regularization of disturbed keratinization may also be responsible for this improvement.

Newborns have high sebum production from active sebaceous glands due to their stimulation by circulating maternal androgens.[5] Infantile seborrheic dermatitis (ISD) clears spontaneously within 3 to 4 weeks after birth and is attributed, albeit without much scientific support, to decreased levels of sebum production.[6] Besides that, it is not established that ISD is the same condition as SD seen in adolescents and adults. Most infants with ISD become normal in adult life; only 7 of 88 ISD patients had persistent seborrheic dermatitis when reviewed 10 years later.[7] Sometimes, typical ISD transforms into atopic dermatitis later.[7] In two different studies, 19 and 27.5% of ISD patients, when reviewed 12 and 13 years later respectively, were diagnosed as having atopic dermatitis.[8,9] This confusion is due to a clinical overlap between the two conditions, particularly in the early stages. Cohen concluded that ketoconazole is at least as effective at treating seborrheic dermatitis as steroid creams and may be better at preventing recurrences, providing a good alternative to steroid creams in infants.[10]

PITYROSPORUM OVALE

Schuster proposed that the organism *Malassezia furfur* or its yeast form, *Pityrosporum ovale,* plays an etiological role in SD.[11] The organism is increased in number in SD and can be cultured from the lesions. Experimental infection with the organism causes the disease. Patients with dandruff have high antibody

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titers to Malassezia compared with controls.[11] A good therapeutic response to antipityrosporal drugs proves the point. Improvement in the disease corresponds with a reduction in the number of Malassezia, while recolonization results in disease recurrence.[12] In patients with pityriasis versicolor[13] and pitysporum folliculitis,[14] seborrheic dermatitis has been found in a higher percentage than expected.

Although correlation between yeast density and severity of SD has been reported,[15] it is not certain that SD patients have higher Malassezia counts than controls.[16] Also, some investigators have found no difference in the amount of Malassezia yeasts in lesional versus non-lesional skin of SD patients. Moreover, the response of SD to antifungal drugs like azoles and imidazoles may be due to their anti-inflammatory action.

SKIN LIPIDS AND INFLAMMATION

How *Malassezia* yeasts initiate the inflammation of seborrheic dermatitis is not clear. They or their byproducts may cause inflammation by inducing cytokine production by keratinocytes[17] or through involvement of Langerhans cells and T-lymphocyte activation.[4] However, the occurrence of SD in early HIV infection, where the cell-mediated immunity is impaired, goes against the hypothesis that SD is mediated by T-lymphocyte activation by *Pityrosporum ovale*.

Another factor that may cause inflammation is the lipase activity of *P. ovale,* which generates inflammatory fatty acids from skin lipids.[18] Though qualitative abnormalities in the composition of sebum have not been demonstrated in SD, mild abnormalities in the surface lipids could result from the ineffective keratinization that is often demonstrated histologically.[19] In infants with active SD, levels of essential fatty acids 18:1W9 were increased and levels of 18:2W6 were decreased compared to healthy children.[20] All deviant values became normal at the time of spontaneous remission, which can be explained by a transient impaired function of the enzyme δ-6 saturase. In another study, SD patients had lower free fatty acids (FFAs) and raised triglycerides, whether they were HIV-positive or not.[21]

IMMUNE DYSFUNCTION

Though antimycotics 'clear' the condition with a reduction in the number of the organisms, recolonization and relapse occur on stopping treatment. This could be explained by an underlying immunological deficit. The increased prevalence of seborrheic dermatitis in HIV-positive patients also supports the hypothesis that seborrheic dermatitis has a strong immunological basis.

There may be a defective cell-mediated immune response to *Pityrosporum ovale* in patients with seborrheic dermatitis, although the evidence for this is incomplete and confusing.[22-26] Though the relationship between seborrheic dermatitis and *Malassezia* yeasts is not yet completely understood, these studies support the postulation that strong skin colonization with *P. ovale* in seborrheic dermatitis is due to altered cell-mediated immunity and that the development of seborrheic dermatitis depends upon the way the patient's immune system reacts to antigens derived from *P. ovale*.

SEBORRHEIC DERMATITIS AND AIDS

The prevalence of SD in HIV-positive and AIDS patients is between 34%[27] and 83%[28] as opposed to 3% in the general population. Its incidence and severity are closely related to the stage of HIV infection and inversely correlate with the absolute CD4 and helper T cell counts.[29] More severe, widespread disease in the HIV infected, with more erythematous, hyperkeratotic and psoriasiform lesions, has led to the suggestion that the clinical picture seen in HIV infection-AIDS should be termed as SD-like dermatitis of AIDS and should be regarded as a distinctive entity caused by immunological defects. As the disease becomes more advanced, the lesions spread and exacerbate, presumably due to the enhanced growth of yeasts secondary to immunosuppression.

SD-LIKE DERMATITIS

Many drugs like auranofin, aurothioglucose, buspirone, chlorpromazine, cimetidine, ethionamide, gold, griseofulvin, haloperidol, interferon-α, lithium,

methoxsalen, methyldopa, phenothiazines, psoralens, stanozolol, thiothixene and trioxsalen are known to induce a SD-like dermatitis by an unknown mechanism.[30] Nutritional deficiencies, especially of riboflavin, pyridoxine, niacin, zinc and EFA, also cause a SD-like dermatitis by an unknown mechanism.[31] The distinction between SD and SD-like conditions is not easy to make.

The cause of SD is yet to be resolved. Until then, the choice of therapy in SD will be between antimycotics, topical steroids, sebostatics or their combinations. The future may see more studies with topical immunomodulators[32] or other nonsteroidal agents like metronidazole,[33] whose mechanism of action is yet to be elucidated.

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