Oral medicine case book 63: HIV-associated oral melanin hyperpigmentation

INTRODUCTION

Oral melanin hyperpigmentation (OMH) is not uncommon in HIV+ persons.1 In Venezuela (38%) and in India (30%) HIV-associated OMH (HIV-OMH) is quite common, but by contrast is substantially less common in Italy (6.4%) and in sub-Saharan Africa (Tanzania, 4.7%, Kenya, 6%).5,6 In South Africa, the national prevalence of HIV-OMH is unknown, but Arendorf et al., 1998, reported a prevalence of less than 1% in the population of greater Cape Town, although the authors could not differentiate with confidence between coloured and black South Africans, and they had not been able to exclude other causes for the melanin hyperpigmentation.7

HIV-OMH (Figure 1) may develop secondarily to HIV-induced upregulation of pro-inflammatory cytokines, to drugs used in treating HIV disease or concomitant associated diseases (zidovudine, clofazimine and ketoconazole), or to adrenocortical insufficiency, which frequently occurs in HIV+ persons with low CD4+ T cell counts. HIV-OMH may also be idiopathic. The increased melanin in HIV-OMH is located either in the epithelial basal cell layer, in melanophages in the lamina propria or at both sites.1,8-10

Both brown-black eumelanin and yellow-red pheomelanin are synthesized in melanosomes which are membrane-bound organelles within melanocytes. These melanosomes contain all the proteins and enzymes necessary for melanogenesis. Melanogenesis is a complex process controlled locally by multiple factors including alpha melanocyte stimulating hormone (αMSH) produced by keratinocytes and melanocytes, melanocytic melanocortin-1 receptors (MC1R), adrenergic and cholinergic agents, and cytokines in the microenvironment. The type and the amount of melanin produced is genetically determined.11

Oral mucosal and epidermal melanocytes are histologically and ultrastructurally identical, but it is recognised that oral melanocytes under physiological conditions are inherently less active metabolically.13 Nevertheless, when stimulated by hormones, pro-inflammatory cytokines, tobacco smoke or infectious agents such as HIV, oral mucosal melanocytes may become active, producing melanin hyperpigmentation.12,13

ACRONYMS

ACRoNYMS

αMSH: alpha melanocyte stimulating hormone
HAART: highly active antiretroviral therapy
MC1R: melanocortin 1 receptor
OMH: Oral melanin hyperpigmentation
HIV-OMH: HIV associated oral melanin hyperpigmentation

DISCUSSION

Melanocytes originate from precursor cells which during development migrate from the neural crest, and ultimately differentiate into mature melanocytes that reside in the basal and suprabasal layers of the epidermis, and of the epithelium of mucous membranes.14 Apart from their primary role in melanogenesis, melanocytes function as immune cells producing cytokines which modulate local immunoinflammatory and antibacterial responses, and as neuroendocrine cells producing acetylcholine, catecholamines, opioids and...
Melanocytes, and their neighboring keratinocytes, form epithelial melanin units, each unit consisting of one melanocyte and a group of up to 36 keratinocytes. The melanin-containing melanosomes produced by the melanocytes are transferred via the dendritic processes of the melanocytes to the keratinocytes within the unit. Skin and oral mucosa owe their color to the number and size of melanosomes, which contain eumelanin or pheomelanin, to the state of maturation of the network of melanocytic dendritic processes, and to the efficacy with which these dendritic processes distribute the melanosomes to neighboring keratinocytes.

Melanin biosynthesis is genetically determined and there are substantial differences in the degree of melanin pigmentation among racial/ethnic groups and between subjects of the same group. Both oral mucosal physiological/racial melanin hyperpigmentation and HIV-OMH are more frequently seen in darker than in lighter skinned subjects.

If it occurs, HIV-OMH usually appears within two years of the diagnosis of HIV infection, or after a month or more of antiretroviral medication with zidovudine, and it is observed more frequently in HIV+ persons with a CD4+ T cell count of less than 200 cells/cubic mm. It has been proposed that IL-1, IL-6 and TNF-α, which are upregulated during HIV infection, stimulate keratinocytes and melanocytes to produce αMSH, and stimulate melanocytes to express MC1R, thus resulting in increased melanogenesis of less than 200 cells/cubic mm. Prevalence of oral lesions in HIV+ patients related to CD4 cell count and viral load in a Venezuelan population. Med Oral Patol Oral Cir Bucal 2006;11:E33-9.

HIV-related medication, then a diagnosis of HIV-OMH should be considered.25

Further research is needed in order to discover what mechanisms and environmental factors possibly play a role in the pathogenesis of HIV-OMH and whether HIV-OMH has any clinical significance in HIV disease.

References