

Oral medicine case book 66: Physiological/racial oral melanin hyperpigmentation

SADJ February 2015, Vol 70 no 1 p28 - p29

A Masilana¹, RAG Khammissa², J Lemmer³, L Feller⁴

ABSTRACT

Physiological/racial oral melanin hyperpigmentation is common, is seen more frequently in darker skinned persons and affects both males and females equally. It may involve any oral mucosal site, but particularly the gingiva, and usually develops during the first two or three decades of life, although many persons with this hyperpigmentation are unaware of its presence.

Physiological/racial oral melanin hyperpigmentation is brought about by increased melanogenic activity of a normal number of melanocytes in the basal cell layer of the oral epithelium. However, the intracellular molecular mechanisms and the intercellular and other micro-environmental signalling pathways that mediate this development are unknown.

Although no definitive relationship between oral mucosal melanoma and physiological/racial oral melanin hyperpigmentation has been demonstrated, and although in the vast majority of cases there should not be any cause for concern, nevertheless it has been observed that melanomas sometimes arise at sites of oral hyperpigmentations.

Key words: melanocytes, melanosomes, melanin.

INTRODUCTION

The normal colour of the oral mucosa is determined by several factors. These include the number, and the degree of melanogenic activity, of the melanocytes in the basal cell layer of the epithelium, the type and amount of melanin produced, the thickness of the epithelium, whether it is ortho- or para-keratinized, the vascularity of the lamina propria and the haemoglobin content of the blood.¹

Physiological/racial oral melanin hyperpigmentation (POH) is common, is equally frequent in females and in males, usually develops during the first two decades of life, is asymptomatic,

1. **A Masilana:** BSc, BDS. Department of Periodontology and Oral Medicine, University of Limpopo, Medunsa Campus, South Africa.
2. **RAG Khammissa:** BChD, PDD, MSc(Dent), MDent (OMP). Department of Maxillofacial and Oral Surgery, University of Limpopo, Medunsa Campus, South Africa.
3. **J Lemmer:** BDS., HDipDent., FCD (SA) OMP., FCMSAae., Hon.FCMSA. Department of Periodontology and Oral Medicine, University of Limpopo, Medunsa Campus, South Africa.
4. **L Feller:** D.M.D, MDent (OMP). Department of Periodontology and Oral Medicine, University of Limpopo, Medunsa Campus, South Africa.

Corresponding author

L Feller:

Head: Dept. Periodontology and Oral Medicine. Box D26 School of Dentistry, MEDUNSA 0204, South Africa. Tel: 012 521 4834
E-mail: liviu.feller@ul.ac.za

ACRONYMS

ACTH: Adrenocorticotrophic hormone
α-MSH: α-melanocyte stimulating hormone
POH: Physiological oral hyperpigmentation

does not need treatment and occurs in all ethnic/racial groups. It is more prevalent in dark- than in light- skinned subjects,² but the degree of oral mucosal pigmentation is not necessarily consistent with the degree of skin pigmentation.³ It can manifest as solitary or as multiple discrete macules, with either well-demarcated or ill-defined borders or as diffused generalised hyperpigmentation (Figure 1a-f).^{2,4-6} On the gingiva, the pigmentation may be quite extensive but is always confined by the muco-gingival junction. The pattern of distribution, the shape and the intensity of the POH are highly variable.²

There are similar numbers of melanocytes in the basal cell layers of the oral epithelia of persons with or without POH, and the development of POH can thus be attributed to genetically determined upregulation of melanogenic activity rather than to any increase in number of the melanocytes.² The intensity and extent of POH may be influenced by endogenous and exogenous factors including hormones, neuropeptides, inflammation, drugs, tobacco smoke, and radiation.^{5,6}

DISCUSSION

Melanosomes within the melanocytes in the basal cell layer of the epithelium are the sites of biosynthesis of melanin.⁷ The melanin-containing melanosomes are transported from the cytoplasm of the melanocytes to the ends of the specialised dendritic processes protruding from the cell membrane of the melanocytes. From thence the transported melanosomes are subsequently transferred through the cell membrane to the neighbouring keratinocytes, and the complex of melanocytes which produce, and keratinocytes which receive, the melanin are referred to as the 'keratinocyte-melanin unit'.² In the skin, within the keratinocytes, the melanin forms protective supranuclear 'caps' shielding the nuclear DNA from ultraviolet radiation.⁸ Whether there is any such phenomenon in the oral keratinocytes which are not exposed to ultraviolet radiation is unknown.

Melanin biosynthesis is regulated by a complex interaction between multiple biological mediators. Adrenocorticotrophic hormone (ACTH), α-melanocyte stimulating hormone (α-MSH), β-endorphins, prostaglandins, endothelin-1, histamine and oestrogen are some of the agents in the microenvironment which have the capacity to stimulate production of melanin; while melatonin, glucocorticoids, and some cytokines can inhibit melanin biosynthesis.⁹

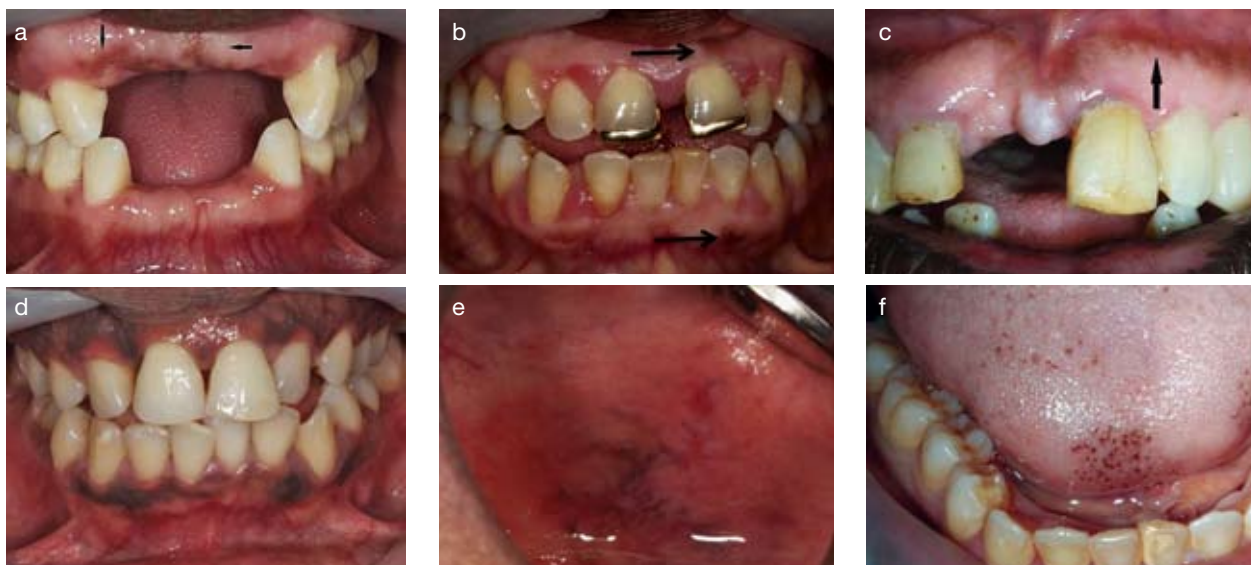


Figure 1: (a) Melanin hyperpigmentation confined to the maxillary masticatory mucosa, not transgressing the mucogingival junction. (b) Discrete pigmented macules on the maxillary and mandibular gingiva. (c) Diffuse melanin hyperpigmentation of the maxillary attached gingiva bordering but not transgressing the mucogingival junction. (d) Diffuse generalized black-brown melanin hyperpigmentation on the maxillary and mandibular attached gingiva, sparing the interdental papillae and not transgressing the mucogingival junction. (e) Irregular striate hyperpigmentation of the buccal mucosa. (f) Scattered melanin hyperpigmentation of the fungiform papillae.

Keratinocytes appear to have some control over the regulation of skin and oral mucosal melanin pigmentation as they have the capacity to produce and to secrete ACTH, α -MSH, β -endorphins and endothelins; and also to have some influence over the transfer of melanosomes from the melanocytic dendritic processes to the keratinocytes of the keratinocyte-melanin unit of which they themselves are a part.¹⁰

Besides their role in influencing the colour of skin, hair and eyes, melanin has the capacity to neutralize reactive oxygen species and free radicals in the local microenvironment and to neutralize bacteria-derived enzymes and toxins, to sequester metal ions, and to bind to organic molecules, thus acting as a physical barrier against microorganisms. As keratinocytes ascend through the cell layers of the oral epithelium to desquamate at the surface, melanosomes within the keratinocytes disintegrate releasing melanin 'dust' that protects the oral mucosa against microbial toxins and other microenvironmental stressors.⁸

The population of melanocytes of the oral epithelium appears to be more or less constant throughout life, despite the fact that some melanocytes are lost owing to the natural process of programmed cell death, and to mechanical, thermal or chemical injury. The mechanism by which the population of oral melanocytes is maintained in a steady state is unknown and the location of the reservoirs of undifferentiated melanocytes stem/progenitor cells containing the genetic information and the regenerative capacity of the oral melanocyte population is obscure. However, since there is clearly a source of melanocyte stem/progenitor cells capable of maintaining a stable number of oral epithelial melanocytes, such a niche reservoir of melanocyte stem/progenitor cells must exist.

COMMENTS

- Further research is needed into why most POH develops in the first two or three decades of life and thereafter diminishes; and into whether POH plays any role in maintaining the homeostasis of the oral epithelium and lamina propria.
- It is not possible to differentiate between a melanotic macule and POH manifesting as a solitary macule or as multiple discrete melanotic macules, because of the clinical and microscopical similarities of these two entities.

This naturally leads one to question whether these two 'entities' exist separately.

- Although up to thirty percent of oral mucosal melanomas develop at sites previously affected by melanin hyperpigmentation,¹¹⁻¹³ and although in most cases the nature of the hyperpigmented pre-melanoma cases has not been determined, there must be concern about any POH being a potential site for future melanoma.
- Although both POH and oral mucosal melanoma most frequently affect the gingiva, the biopathological significance of this is unknown.

References

1. Dummett CO. Physiologic pigmentation of the oral and cutaneous tissues in the Negro. *J Dent Res* 1946;25:421-32.
2. Chandra S, Keluskar V, Bagewadi A, Sah K. Extensive physiologic melanin pigmentation on the tongue: An unusual clinical presentation. *Contemp Clin Dent* 2010;1:204-6.
3. Gaeta GM, Satriano RA, Baroni A. Oral pigmented lesions. *Clin Dermatol* 2002;20:286-8.
4. Caldeira PC, de Sousa SF, Gomez RS, Silva TA. Diffuse pigmentation of the oral mucosa. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;110:550-3.
5. Eisen D. Disorders of pigmentation in the oral cavity. *Clin Dermatol* 2000;18:579-87.
6. Meleti M, Vescovi P, Mooi WJ, van der Waal I. Pigmented lesions of the oral mucosa and perioral tissues: a flow-chart for the diagnosis and some recommendations for the management. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;105:606-16.
7. Kauzman A, Pavone M, Blanas N, Bradley G. Pigmented lesions of the oral cavity: review, differential diagnosis, and case presentations. *J Can Dent Assoc* 2004;70:682-3.
8. Feller L, Masilana A, Khammissa RA, Altini M, Jadwat Y, Lemmer J. Melanin: the biophysiology of oral melanocytes and physiological oral pigmentation. *Head Face Med* 2014;10:8.
9. Slominski A, Wortsman J, Plonka PM, Schallreuter KU, Paus R, Tobin DJ. Hair follicle pigmentation. *J Invest Dermatol* 2005;124:13-21.
10. Hirobe T. Role of keratinocyte-derived factors involved in regulating the proliferation and differentiation of mammalian epidermal melanocytes. *Pigment Cell Res* 2005;18:2-12.
11. Lourenco SV, Bologna SB, Hsieh R, Sanguenza M, Fernandes JD, Nico MM. Establishment and characterization of an oral mucosal melanoma cell line (MEMO) derived from a longstanding primary oral melanoma. *Am J Dermatopathol* 2013;35:248-51.
12. Mohan M, Sukhadia VY, Pai D, Bhat S. Oral malignant melanoma: systematic review of literature and report of two cases. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013;116:e247-54.
13. Thiloe MM, Khammissa RA, Bouckaert M, Altini M, Lemmer J, Feller L. Oral mucosal melanoma: some pathobiological considerations and an illustrative report of a case. *Head Neck Pathol* 2014.