

The Dark Side of the Tongue: The Stomatology Point of View on Oral Hyperpigmentation

O Lado Negro da Língua: O Ponto de Vista da Estomatologia sobre Hiperpigmentações Orais

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Dear Editor,

We read with great interest a case report about tongue hyperpigmentation associated with temozolomide as a single agent.¹ In the article, the authors point out the uniqueness of the case since temozolomide was the only drug causing oral hyperpigmentation, which was never reported, as well as its relevance for healthcare professionals regarding pharmacological side effects of specific drugs.

Oral hyperpigmentation can cover a broad spectrum of diagnoses that may include physiological variations associated with ethnic differences, with a predominance in dark-skinned populations, benign lesions such as amalgam tattoos, oral repercussions due to systemic disease, such as Addison's disease, malignant lesions such as oral melanoma and, as stressed by the authors, an adverse effect of pharmacological therapy.²

In the literature, oral and skin hyperpigmentation due to chemotherapy has been well-documented.^{2,3} One of the most common drugs associated with oral pigmentation is the tyrosine kinase inhibitor, imatinib, commonly used in chronic myeloid leukemia. Additionally, studies report that treatment duration or the synergic effect in patients who had treatment with hydroxyurea before commencing imatinib therapy are risk factors for more extensive and darker lesions.²

In this case, the onset of hyperpigmentation was related to the initiation of temozolomide. However, an evaluation by a stomatologist might aid the diagnosis by discarding other possible diagnoses or factors, although less likely, that might contribute to the oral pigmentations, for example,

amalgam tattoos or chewing tobacco, which can mimic the observed lesions. Additionally, levetiracetam has already been reported as being associated with cutaneous hyperpigmentation.⁴ While that report does not mention the oral mucosa, oral hyperpigmentation due to this drug could not be discarded, including a synergetic effect with temozolomide. Antiepileptic drugs like oxcarbazepine or retigabine have already been reported to induce oral pigmentation.⁵

Diagnosis of oral pigmented lesions is challenging, with definitive diagnosis typically requiring histopathological examination. Although most hyperpigmented lesions are benign, diagnosis based on a detailed history and clinical examination alone only provides a provisional diagnosis. Clinicians may consider the use of biopsy, especially in less suggestive cases. As an adverse effect, oral hyperpigmentation is innocuous, but surveillance is advised in order to monitor changes in lesions over time.²

Physicians must be aware of pigmented oral lesions while treating cancer patients. We advise referral to the Department of Stomatology, in which the clinician wants to ensure their clinical suspicion, exclude contributing factors, or rule out other lesions of a malignant nature.

AUTHOR CONTRIBUTIONS

RS: Draft of the paper, approval of the final version.

NR, CM: Critical review, approval of the final version.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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Rui SEIXAS^{✉1,2}, Natacha RIBEIRO¹, Carlos MATOS¹

1. Serviço de Estomatologia. Hospital São Bernardo. Centro Hospitalar de Setúbal. Setúbal. Portugal.

2. Instituto Superior de Educação e Ciências. Lisboa. Portugal.

✉ **Autor correspondente:** Rui Seixas. rui.seixas@chs.min-saude.pt

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