

# HIDROXYCHLOROQUINE INDUCED PALATAL HYPERPIGMENTATION

## A CASE REPORT

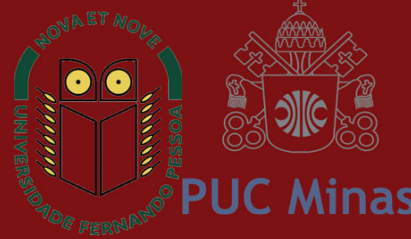
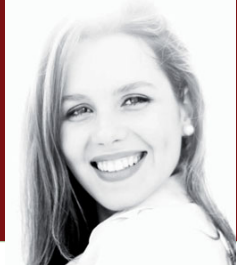
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### Introduction

The presence of melanic pigmentation in the oral mucosa is a diagnostic challenge for the dentist to establish a definitive diagnosis based on an excellent clinical history supported by complementary means of diagnosis. The most common causes of oral mucosal pigmentation are racial / intrinsic; induced by tobacco or drugs, such as antibiotics, chemotherapy, antimalarials, hormones and tranquilizers; post-traumatic or inflammation associated hyperpigmentation; pigmentation associated with systemic diseases such as Addison's disease, hemochromatosis, Peutz-Jegher syndrome, McCune-Albright syndrome, neurofibromatosis and deposition of exogenous pigmented material as amalgam (1,3).

Hydroxychloroquine is an immunomodulatory drug, discovered before the II World War with antimalarial characteristics. Currently, the FDA approves its use in the treatment of discoid lupus, systemic lupus erythematosus and rheumatoid arthritis, as well as in malaria (2). A history of hydroxychloroquine therapy and a biopsy to exclude other possible pathologies are mandatory.

### Case Report

#### Anamnesis

Female Brazilian patient, 78 years old, retired.

She attended the stomatology clinic of PUC Minas in November 2018 after being referred by a general dentist from the community health center after a routine consultation. The patient was totally edentulous and had a alteration in the color of the hard palate mucosa, without pain, reporting never having noticed the lesion on the mucosa.

#### Medical and personal medical history

Hypertension, gastritis, varicose veins, rheumatoid arthritis and hearing loss on the right side. Never smoked and did not drink alcohol.

**Medication** Omeprazole, prednisolone 2.5 mg / day and hydroxychloroquine sulfate 400 mg 3x / week for more than 10 years.

**Extra-Oral Physical Exam** Normal face, without edema and non palpable lymph nodes. PA 150x80 mmHg.

#### Intraoral Examination

Use of upper and lower total removable prosthesis.

Lips, oral mucosa, oropharynx, tongue, floor of the mouth, salivary glands and salivary secretions were normal.

Hard palate altered by a bilateral symmetrical dark grey pigmentation in relation to the palatine raphe.

#### Lesion description

Dark grey pigmentation, unaltered consistency and normal surface, diffuse with irregular borders, located symmetrically on the hard palate, measuring approximately 4 cm in diameter, asymptomatic, and did not disappear when pressure was applied. There is no temporal record of the lesion.

#### Differential Diagnostic

Melanocytic macula, nevus, melanoma, drug-associated pigmentation and pigmentation associated with systemic pathology.

#### Complementary examinations

Incisional biopsy and anatomopathological examination.

#### Microscopic examination of the lesion

Fragment of mucosa covered by parakeratinized stratified squamous epithelium. In the lamina propria, fibrous connective tissue is observed exhibiting diffusely brown pigmentations. Presence of mononuclear inflammatory infiltrate.

#### Diagnosis and prognosis

Hyperpigmentation associated with prolonged hydroxychloroquine therapy. Prognosis is favorable.

**Treatment** No treatment is required.

### Discussion

In pigmented lesions of the oral mucosa, biopsy is always indicated to exclude malignant pathology. In the English literature only 14 cases similar to this are described (1). Since malignancy was not reported on the anatomopathological description and after exclusion of other conditions that induce oral pigmentation the diagnosis of hydroxychloroquine induced palate hyperpigmentation was established supported on the patient's medical history. This is described in hard palate, gums, lips and jugal mucosa (3). The most commonly reported adverse effects of the hydroxychloroquine are retinopathy, hyperpigmentation, myopathy, and cutaneous reactions (2,3). The risk of ocular toxicity increases with dose and time of administration. Prevalence of retinopathy is 2% for use less than 10 years, and 20% at 20 years. It is recommended by the American Academy of Ophthalmology routine ophthalmologic examination, initially in the first year of therapy and after 5 years an annual repeat in low-risk patients (2). From the point of view of oral health these cases do not require treatment.

### Conclusion

Intraoral melanin pigmentation can have several etiologies and malignancy must always be excluded with the help of a biopsy. The patient was on hydroxychloroquine for rheumatoid arthritis for more than 10 years. Given the rarity of this oral manifestation, it is important to alert dentists to the potential adverse effects of this drug. When used in long-term treatments may lead to other more severe complications, such as retinopathy. The dentist has an important role in the early detection of these cases.

#### References

(1) de Andrade, B. A. B. et al. (2017). Hyperpigmentation of hard palate induced by chloroquine therapy. *Journal of Clinical and Experimental Dentistry*, 9(12), pp. e1487-e1491.

(2) Shippey, E. A., Wagler, V. D. and Collamer, A. N. (2018). Hydroxychloroquine: An old drug with new relevance. *Cleveland Clinic Journal of Medicine*, 85(6), pp. 459-467.

(3) Tosios, K. I., Kalogirou, E. M. and Sklavounou, A. (2018). Drug-associated hyperpigmentation of the oral mucosa: report of four cases. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. Elsevier Inc., 125(3), pp. e54-e66.



Fig. 1 – Hard palate with alteration of color

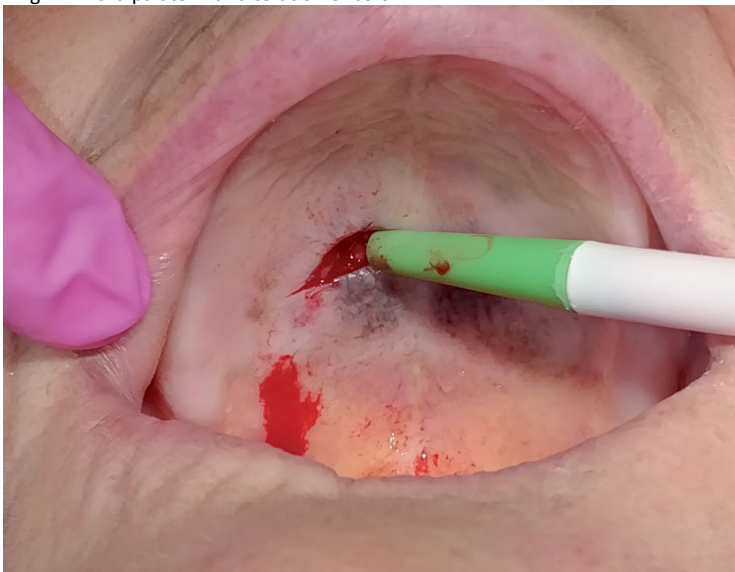


Fig. 2 – Incisional biopsy



Fig. 3 – Suture, single stitches

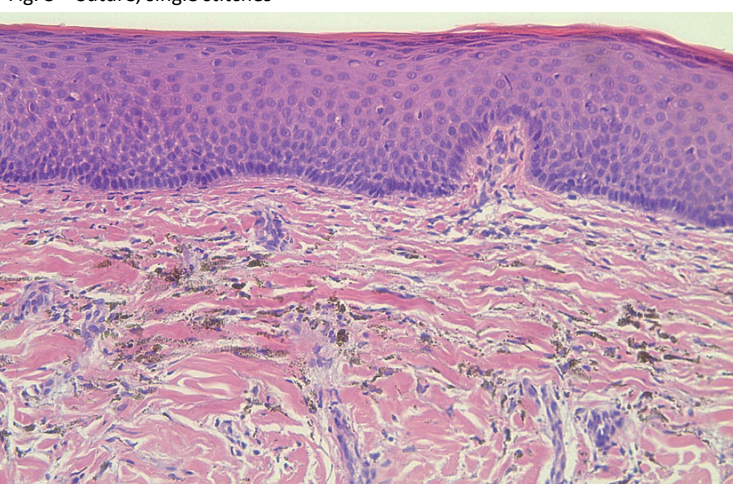


Fig. 4 – Microscopic histological examination



Fig. 5 – Follow-up at two weeks post biopsy