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Journal of Oral Medicine, Oral Surgery, Oral Pathology and Oral Radiology

Journal homepage: https://www.joooo.org/

Case Report

# Rare oral pigmentation in chronic myeloid leukemia: Melanosis of the hard palate

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## Abstract

Imatinib Mesylate, is a tyrosine kinase inhibitor that has significantly altered the therapeutic landscape of chronic myeloid leukemia (CML), enabling most patients to experience extended survival and a better quality of life. Despite its clinical benefits, the drug is known to produce certain adverse effects, including pigmentation changes in the oral mucosa. Here we are presenting a rare case of a 57-year-old male who had chronic myeloid leukemia and has been under the chemotherapeutic agent Imatinib, since 2008 and in 2024 he discovered a large pigmented palatal mucosa lesion during a routine dental visit.

**Keywords:** Tyrosine kinase inhibitor, BCR-ABL gene, Hyperpigmentation

**Received:** 10-05-2025; **Accepted:** 01-07-2025; **Available Online**: 04-08-2025



## 1. Introduction

Pigmented lesions in the oral cavity are commonly encountered and can arise due to various factors, including medication side effects, isolated occurrences, or indications of systemic conditions. The origins of oral pigmentation can range from simple, non-threatening lesions like blue nevi to more complex and potentially cancerous conditions such as oral melanoma. The differential diagnosis for these lesions includes natural pigmentation seen in African Americans, post-inflammatory melanosis, amalgam tattoos, smoking-induced pigmentation, blue nevi, and oral melanoma. Additionally, oral pigmentation may be associated with rare conditions such as Peutz-Jeghers syndrome, Addison's disease, polyostotic dysplasia, hyperthyroidism, and Nelson syndrome.

Imatinib mesylate is a selective tyrosine kinase inhibitor widely used in the management of chronic myeloid leukemia (CML). It targets the BCR-ABL fusion protein, a constitutively active tyrosine kinase resulting from the Philadelphia chromosome translocation, which plays a central role in the pathogenesis of CML. By competitively binding to the ATP-binding site of the BCR-ABL kinase, imatinib effectively inhibits its activity, thereby blocking downstream signaling pathways involved in uncontrolled cell proliferation and survival. Although the physiological role of the native BCR protein remains incompletely understood, the ABL component is strongly associated with oncogenic processes. Additionally, imatinib exhibits inhibitory activity against other receptor tyrosine kinases, including c-Kit and platelet-derived growth factor receptors (PDGFR). This broader spectrum of action extends its therapeutic application to solid tumors such as gastrointestinal stromal tumors (GISTs), where activating mutations in c-Kit are commonly observed. In vitro studies have demonstrated imatinib's ability to suppress proliferation and induce apoptosis in GIST cells. Despite these common side effects, Glivek has rarely been reported to produce diffuse hyperpigmentation of the palatal mucosa.

To the best of our knowledge, 23 cases of oral imatinib mesylate-associated hyperpigmentation (IAH) have been present in the literature to date in the world. The most common intra-oral site being the hard palate, similarly in our

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https://doi.org/ 10.18231/j.jooo.v.11.i.2.7

case there is pigmentation of palate was noted because of imitinib and was absent on the buccal and labial mucosae, and it's one of its kind as no such lesions was published by any author on imitinib drug in India. Oral IAH presents as diffuse grey or bluish-brown discolorations, often larger than 6mm.[9] Diagnosis relies on clinical presentation, history, and biopsy, as the mechanism behind imatinib-induced pigmentation remains unclear. Once the diagnosis is established, no treatment is required unless patient want cosmetically changed, here we are presenting a rare case of imatinib induced oral pigmentation which was giving an impression of recurrence.

## 2. Case Report

A 57-year-old male patient reported with a chief complaint of pain in the upper right back region of the jaw for 10 days. The pain was of sudden on the onset, moderate intensity dull aching and aggravating on chewing and then relieving on its own.

The patient presented with a medical history of Chronic Myeloid Leukemia for 17 years and has undergone treatment by targeted therapy and is now continuous on medication for the same. He had a habit of smoking 25 years ago with 4-5 cigarettes per day for 2 years and stopped since.

On general examination the patient was normal and on intraoral examination 16 was carious and endodontically treated and missing with 13, 21 and 46 and on the hard palate, there was a dome-shaped swelling noted at the midline of size 2x2 cm with a bluish-black hue and no burning sensation and taste change was noted (**Figure 1** and **Figure 2**). On palpation, the swelling was hard in consistency, non-tender and had no paraesthesia, or numbness and the patient wasn't aware of it, based on the clinical history and examination a provisional diagnosis of malignancy of the hard palate was made and differential diagnosis of salivary gland neoplasm, post-inflammatory melanosis and lichenoid reactions and palatal torus was given and patient was advised for OPG, CBC and biopsy.

OPG shows reduced joint space in the left side and thickening (radiopacity) of the hard palate with increased pneumatization of both the maxillary sinus (**Figure 3**).

Patient was not willing for biopsy as he was already undergoing treatment in other institute.

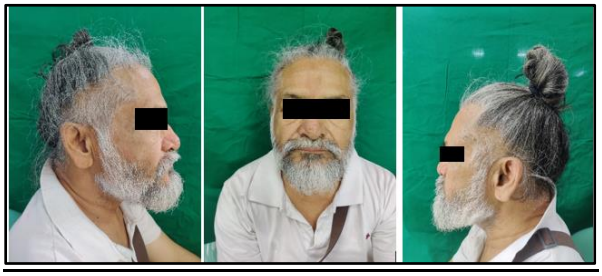

**Figure 1:** Extraoral images

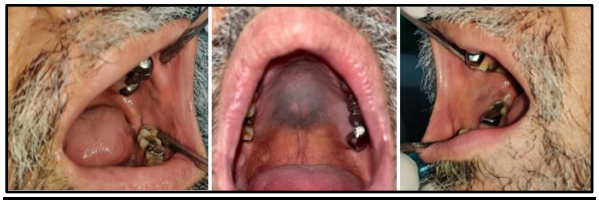

**Figure 2:** Introral images investigations

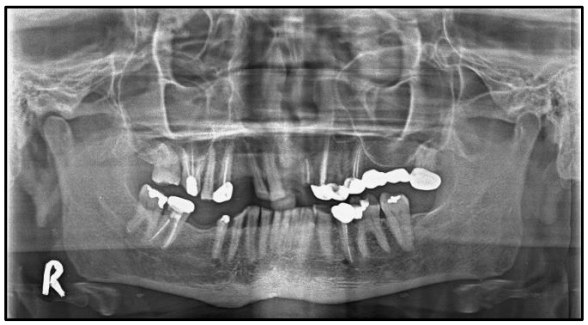


**Figure 3:** OPG shows reduced joint space and pneumatization of the maxillary sinus.

**Table 1:** Medications that have been reported to be associated with oral hyperpigmentation.[10]

| Category | Medication |
|---|---|
| Antibiotic | Tetracycline, Minocycline |
| Antiviral | Zidovudine |
| Antifungal | Ketoconazole |
| Antiarrhythmic | Amiodarone |
| Antipsychotic | Phenothiazine |
| Anti-epileptics | Retigabine |
| Antimalarial | Chloroquine diphosphate, Quinacrine hydroxychloroquine, and Amodiaquine and other quinine derivatives |
| Chemotherapeutic | Imatinib mesylate, Bleomycin, cyclophosphamide, 5-fluoruoracil, doxorubicin, busulfan |
| Laxatives | Phenolphthalein |
| Leprosy | Clofazimine |
| Tranquilizers | Chlorpromazine |
| Hormones related drugs | Oestrogen, Premarin |

**Table 2:** Summary of previous case reports on palatal pigmentation associated with imatinib therapy

| Author(s) | Dosage (mg/day) | Patient Details | Histological Observations | Condition Treated |
|---|---|---|---|---|
| Lewis[1] | 800 | 70-year-old Male | Histological diagnosis given | Chronic Myeloid Leukemia (CML) |
| Wong et al.,[2] | Unknown | 43-year-old Female | Histological diagnosis given | CML |
| Mattson et al.[3] | 400 | 66-year-old Female (x2), 64-year-old Female | Melanin deposits; Clinical diagnosis for two cases | Metastatic GIST (1), CML (2) |
| Li et al.[4] | 400 | 64-year-old Male 53-year-old Male, 29-year-old Female | Histological diagnosis given | CML (2), Pelvic Fibromatosis (1) |
| Steele et al.[5] | 400 | 48-year-old Male | - | CML |
| Yu et al., | Unknown | 42-year-old Male | - | CML |
| Resende et al.[5] | 600 | 38-year-old Male | Clinical diagnosis only | Post-Hematopoietic Stem Cell Transplant |
| Khoo et al.[12] | 400 | 58-year-old Female | Clinical diagnosis only | CML |
| Hindocha and Clark, | - | - | - | - |
| Song and Kang, | Unknown | 58-year-old Male | Clinical diagnosis only | CML |
| Roeker and Wolanskyj, | Unknown | 65-year-old Female | Clinical diagnosis only | CML |
| Lyne et al.,[6] | 400–600 | 58-year-old Female | Histological diagnosis given | CML |
| Romeo et al.[7] | 400 | 72-year-old Female | Histological diagnosis given | CML |
| Bombeccari et al.[8] | 400 | 63-year-old Male | Histological diagnosis given | CML |
| Dixon and Yassin, | 400 | 57-year-old Male | Clinical diagnosis only | CML |
| Shi et al.[13] | - | - | Histological diagnosis given | CML |
| DiTullio et al., | 400–800 | 47-year-old Male | Histological diagnosis given | CML |
| Tosios et al., | 400 | 61-year-old Male | Histological diagnosis given | CML |
| Mascitti et al., | 400 | 78-year-old Male | Clinical diagnosis only | CML |
| Dani Stanbouly et al.[9] | Unknown | 47-year-old Male | Clinical diagnosis only | CML |

*2.1. Differential diagnosis*

1. Salivary gland neoplasm
2. Drug-Induced melanosis of the hard palate
3. Post-inflammatory melanosis
4. Lichenoid reaction
5. Torus palatinus

## 3. Discussion

The oral mucosa's pigmentation can reveal a variety of lesions or conditions, such as melanoma, blue nevus, racial pigmentation, melanotic macules, and systemic disorders linked to in the event of drug-associated pigmentation, endogenous/exogenous pigment-caused lesions, and oral pigmented lesions.[12]

Melanotic macules are common dark spots seen in the mouth. They happen because of too much melanin in the lower layers of the skin or tissue. These spots usually show up on the gums and lips and are seen more often in females (Buchner et al., 2004; Kaugars et al., 1993). Some medicines can cause pigmentation in the mouth. This can happen due to the drug collecting in the tissues, affecting melanin production, or through other chemical reactions (Meleti et al.[10], 2008). Drugs like minocycline, antimalarials, tetracyclines, and chemotherapy drugs are often linked to this condition (Eisen, 2000; Meleti et al., 2008). Imatinib Mesylate, a medicine used to treat chronic myeloid leukemia, works by blocking certain enzymes like BCR-ABL and C-kit, which are important for pigment cells (Lammie et al., 1994). This drug usually causes lighter skin or mucosa (Valeyrie et al., 2003; Arora et al., 2004), but in rare cases, it can cause dark patches (Lewis, 2009).

## 4. Conclusion

The identification of oral pigmentation associated with imatinib necessitates comprehensive history-taking and meticulous clinical evaluation of melanotic macules. It is essential for both medical and dental professionals to recognize the potential for the patients undergoing therapy with Imatinib mesylate. These hyperpigmented lesions are harmless and don’t need treatment, but it’s a good idea to

have an annual check-up to watch for any changes in size or color.

## 5. Source of Funding

None.

## 6. Conflict of Interest

None.

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**Cite this article:** Tomar N, Das D, Durge ND. Rare oral pigmentation in chronic myeloid leukemia: Melanosis of the hard palate. *J Oral Med, Oral Surg, Oral Pathol, Oral Radiol.* 2025;11(2):87-90.