Oral Presentation of Chronic Hyperplastic Candidiasis in Patient under Imatinib Mesylate: A Rare Case

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Candida albicans is the major human pathogen among Candida species. It is a commensal yeast of the oral, gastrointestinal, and vaginal mucosa in healthy individuals. The genus Candida has about 154 species, and different species show a different level of resistance to antifungal drugs and have a high degree of phenotypic similarity. Oropharyngeal candidiasis is the most common infection in oral cavity both pre- and post-treatment of cancer. Immunocompromised state in a cancer patient induces candidal species which get activated as a pathogen. It is found that in certain high-risk groups antifungal prophylaxis reduces the incidence and severity of infections. This case report discusses the occurrence of hyperplastic candidiasis in the patient under treatment by a chemotherapeutic agent imatinib mesylate for gastric tumor. We have discussed the probable cause for oral candidiasis in patients under imatinib mesylate and treatment advised for the oral hyperplastic candidiasis.

Keywords: Candida, Candidiasis, Chemotherapy, Imatinib mesylate

INTRODUCTION

Imatinib mesylate is a chemotherapeutic drug, which acts as a tyrosine kinase inhibitor and is used in the treatment of acute lymphoblastic leukemia, chronic eosinophilic leukemia, gastrointestinal stromal tumor, myelodysplastic/myeloproliferative neoplasm, systemic mastocytosis, etc.¹² Short-term toxicity of the imatinib mesylate in 1-10% includes pancytopenia, febrile neutropenia, and flushing. Imatinib mesylate inhibition of c-kit and platelet-derived growth factor receptors (PDGF-R), which plays role in normal immune responses, causing altered immune function.² It has been reported that there is a significant hypogammaglobulinemia in patients treated with imatinib mesylate.³ Fungal infections in patients under certain other chemotherapeutic drugs occurs due to suppressed oral/mucosal immunity, salivary gland dysfunction causing xerostomia and alteration in oral flora.¹ Some cases have been reported about the lesion in the oral cavity such as painful erosions with lichenoid reactions in patients under imatinib mesylate.³ Till date, there are no case reports about occurrence of oral candidiasis in patients who are under treatment of imatinib mesylate. The most common form of oral candidiasis in cancer patients are pseudomembranous and erythematous type of candidiasis while the hyperplastic type of candidiasis is rarely reported.⁶ Herein, we report a rare case of oral hyperplastic candidiasis in a patient under the treatment of malignant gastric tumor with imatinib mesylate.

CASE REPORT

A 48-year-old female patient reported to our Department of Oral Medicine and Radiology with a chief complaint of pain in the gums in both right and left side of lower jaw. The pain was moderate, burning type, intermittent, and aggravates while chewing food or drinking water relieves on taking rest. The patient gave medical history of malignant tumor in the hypogastric region on left side for which she had undergone surgery 4 months back. The patient was on the medication, glivac 400 mg tablets (imatinib mesylate 400 mg, Novartis Pharma AG, Switzerland) daily since 4 months. On general examination subconjunctival pallor, pallor, palpable lymph nodes in the neck, and flushing of the nail bed were seen. On extra oral examination,
submandibular lymph nodes were palpable on both right and left side 3 in number on the right side and 1 in number on the left side. Lymph nodes were of dimension 1 cm each in left side and 1.5 cm on right side. Lymph nodes were firm in consistency, tender on palpation, mobile. On intraoral examination white hyperkeratotic patch was seen on gingiva extending from distal of 43 to mesial of 47 and anteriorly in relation to 32, 31, 41, 42 and on left side in relation to 34, 35 and lingual to 47, 48 of the mandibular jaw (Figures 1 and 2). Superiorly hyperkeratotic patch extending from attached gingival to the buccal vestibular region inferiorly. Surface over the hyperkeratotic area was rough and borders were irregular. Gingiva surrounding the hyperkeratotic area was erythematous and tender on palpation. Hyperkeratotic area was non-scrapable on application of pressure with gauze piece at its entire extent. There was the presence of white coating on the tongue.

Superficial layer was forcibly scraped off with blunt end of the BP blade, and the pathological evaluation was advised wherein *Candida albicans* were isolated. On the basis of history, clinical and pathological findings, a final diagnosis of chronic hyperplastic candidiasis was given. Antifungal treatment with clotrimazole 1% mouth paint and chlorhexidine mouthwash of 0.12% were started and followed up after 2 weeks, and there was 30% decrease in the size of the lesion (Figures 3 and 4). Further follow-up of patient was not possible in the event of death of the patient.

**DISCUSSION**

Mutations of c-kit proto-oncogene are reported in 85%, and mutations of PDGF-Rα chain are reported in 35% of gastrointestinal tumors. BCR-ABL tyrosine kinase is the product of Philadelphia chromosome, which is a causative factor for chronic myelogenous leukemia. Imatinib is an inhibitor of the receptor tyrosine kinases for PDGF and stem cell factor (SCF), c-kit, and inhibits PDGF and SCF-mediated cellular events and thereby acts as anti-tumor drug. Therefore, imatinib mesylate is used either as the...
first line of treatment or as an adjuvant in the treatment of gastrointestinal tumors.9

The most common side effect of other chemotherapeutic drugs like methotrexate, cyclophosphamide related to oral cavity is oral mucositis. Mucositis provides favorable conditions for the development of oral candidiasis. Candida, commensal yeast of the digestive tract, is capable of colonizing mucositis lesions and infecting the oral mucosa. Overall, 60-90% of mucositis lesions are infected by Candida.10 For candidiasis to occur particularly in chemotherapeutic patients, there has to be altered local resistance to the infection (e.g., Xerostomia), compromised immune function (e.g., altered functions of inflammatory cells), and generalized debilitation of the patient (e.g., malnutrition and malabsorption).11

Oral lesions associated with imatinib mesylate reported are painful erosions associated with lichenoid reactions.5 The cause for oral candidiasis in patients under treatment with imatinib mesylate is unknown. However, it can be hypothesized that as there will be altered immune function, hypogammaglobulinemia leading to immunocompromised state in patients with imatinib mesylate drug therapy along with the associated poor oral hygiene can aggravate the normal commensal Candida to colonize leading to oral candidiasis, as was reported in the present case (Figure 5). Cases have been reported in which there was reactivation of hepatitis B virus after the therapy with imatinib mesylate.12

In our case, candidiasis was treated with clotrimazole 1% mouth paint, local application 5 times daily. Other treatment options for oral candidiasis include nystatin (available as a suspension of 100,000 U/mL (4-6 mL q.i.d.) or as flavored 200,000 U pastilles (one or two 4-5 times daily) for 7-14 days). Chlorhexidine mouthwash 0.12% used in 1:1 dilution with water, for 3 times a day.

However, most important intervention is to maintain proper oral hygiene, as in most of the cases poor oral hygiene is the main inducing factor for the occurrence of candidiasis.

CONCLUSION

Oral candidiasis is an avoidable complication in chemotherapeutic patients. Educating the patients about the oral hygiene maintenance by referring them to dentist is a piece of advice needed to be provided by the oncologist. As the chances of occurrence of oral candidiasis are high, regular oral hygiene maintenance, regular referral to the dentist is important as to improve the quality of life of the patient.

REFERENCES


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