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Severe Pigmentation of Oral Mucosa, Skin and Nails Due to Breast Cancer Chemotherapy – Case Report

Nasilone zmiany pigmentowe jamy ustnej, skóry i paznokci w następstwie chemioterapii raka piersi – opis przypadku

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
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Abstract

Almost 10–20% of acquired melanocytic pigmentations are drug-induced in origin. Oral mucosa is a common place to develop drug reactions. In a 57-year-old Iranian female, severe pigmentation due to breast cancer chemotherapy with cyclophosphamide, 5-fluorouracil (5-FU) and doxorubicin was noticed during clinical examination. Extra-oral examination revealed linear dark bands on finger- and toenails as well as freckles on the face. Intraoral examination showed asymptomatic diffuse dark-brown pigmentation of the oral mucosa on the tongue, lips, palate, and buccal mucosa. The lesions were of poorly defined borders, various sizes and shape and a heterogeneous coloring to some extent. The tongue was more severely pigmented by dark gray to black patches. The patient was reassured about the etiology and nature of her problem and advised to return two months later. The lesions had almost disappeared by then.

Awareness of chemotherapy complications is mandatory for physicians and dental practitioners to make accurate diagnoses (*Dent. Med. Probl.* 2015, 52, 3, 363–365).

Key words: breast cancer, chemotherapy, pigmentation, oral, skin, nails.

Słowa kluczowe: rak piersi, chemioterapia, zmiany pigmentowe, jama ustna, skóra, paznokcie.

An adverse drug reaction is defined by the World Health Organization (WHO) as ‘a response to a drug which is noxious, unintended, and happens at doses normally used for the prophylaxis, diagnosis, therapy of diseases or modification of physiological functions’ [1]. Although drug-induced skin reactions are frequently accruing and can be quite various in manifestation, only a few adverse drug reactions appear in the oral mucosa. This is attributed to the higher turn-over rate of oral mucosa which allows easy development of obscure clinical changes [2]. Drug-induced oral reactions fall into several categories: salivary gland disorders (xerostomia, ptyalism, salivary gland pain), oral ulceration (non-specific ulceration, aphthous ulceration, fixed drug eruption, mucositis, pem-

phigoid-like reactions, pemphigus, erythema multiform, lupoid reactions), oral malodor, white lesions (lichenoid eruptions, oral candidiasis, hairy tongue), taste alterations, mucosal pigmentation, teeth discoloration and swellings (gingival hyperplasia, mucosal swelling) [1–3]. Medications might stimulate various forms of mucocutaneous pigmentation including melanosis. Approximately 10–20% of acquired melanocytic pigmentations are drug-induced in origin [4]. Medications most commonly implicated in drug-induced melanoses are antimalarials, phenothiazines, oral contraceptives, and cytotoxic agents [4]. The underlying pathogenesis of drug-related pigmentation can be divided into three mechanisms: sedimentation of drug or drug metabolites in the dermis

and epidermis, intensified melanin production with or without increase in the number of active melanocytes and drug-induced post-inflammatory changes of the skin [3].

Drug-induced pigmentation is substantially observed on the gingivae and hard palate, and is typically gray or blue in color [5]. In most cases, discoloration tends to fade within a few months after drug cessation [4].

Other forms of oral pigmentation include: melanotic macule, melanoacanthoma, melanocytic nevus, malignant melanoma, physiologic pigmentation, smoker's melanosis, post-inflammatory hyper-pigmentation, and melanosis associated with systemic or genetic disease [4].

The aim of this study is to report a case of severe pigmentation of oral mucosa, skin and nails due to chemotherapy with cyclophosphamide, 5-fluorouracil (5-FU) and doxorubicin.

Case Report

A 57-year-old female was referred to the Department of Oral and Maxillofacial Medicine of Shahid Beheshti University of Medical Sciences, Tehran, Iran. The patient presented with gray to black tongue hyper-pigmentation since two weeks after the onset of breast cancer chemotherapy. She was prescribed cyclophosphamide, doxorubicin and fluorouracil for breast cancer, and omeprazole, cimetidine, Neurobion®, and vitamin B as well. The patient's family history was not contributory. Extraoral examination revealed linear dark bands on all finger- and toenails, and freckles on the face (Fig. 1). Intraoral examination showed asymptomatic diffuse dark-brown pigmentation of the oral mucosa on the tongue (Fig. 2), lips, palate (Fig. 3) and buccal mucosa. The lesions were of poorly defined borders, various sizes and shape and a heterogeneous coloring to some extent. The tongue was more severely pigmented by dark gray



Fig. 1. Linear dark bands on hand nails



Fig. 2. Severe pigmented patches on the tongue



Fig. 3. Pigmented macules and patches on the palate

to black patches. However, other mucosa showed brown to black discoloration.

Meanwhile, the patient noticed freckles which had appeared on her face simultaneously to the oral lesions. The patient was reassured about the etiology and nature of her problem and advised to return two months later. The lesions had almost disappeared by then.

Discussion

Local and systemic cancer therapy can induce changes in the skin, mucous membranes, hair and nails [6, 7]. Obviously, precise diagnosis and appropriate management of such events requires adequate knowledge about the features of common adverse drug reactions [6].

Chemotherapy-induced hyperpigmentation appears to be independent of adrenocorticotrophic and melanocyte-stimulating hormones. The underlying pathogenesis of hyper-pigmentation is dependent on the chemotherapeutic agents. Increased mela-

nin, post-inflammatory changes due to pruritus (bleomycin), and direct skin toxicity have been proposed as possible mechanisms [8]. Moreover, genetic predisposition, photosensitization, focal stimulation of melanocytes, and skin types has been put forward for the pathogenesis of chemotherapy-induced hyper-pigmentation [9]. That is why hyper-pigmentation following chemotherapy might manifest with a variety of patterns among different patients. Hyper-pigmentation frequently occurs 1–6 months after chemotherapy, and fades 6 months to a year after the medicine has been quit [8]. Hyper-pigmentation can develop following the consumption of cyclophosphamide, hydroxyurea, fluoropyrimidines such as 5-fluorouracil (5-FU), and anthracyclines like doxorubicin and daunorubicin [6]. Our patient reported the onset of her oral lesions to be subsequent to chemotherapy with cyclophosphamide, 5-fluorouracil (5-FU) and doxorubicin. The lesions appeared as multifocal pigmentation of the tongue, lips, palate and bilateral buccal mucosa, as well as face and nails. Blaya and Saba [10] reported a similar case in a 42-year-old woman with breast carcinoma un-

der chemotherapy with doxorubicin, cyclophosphamide, and paclitaxel. After the second cycle of doxorubicin and cyclophosphamide, hyper-pigmentation was noted on the patient's tongue, but unlike our patient, no pigmentation of the palms, soles, dermal creases, or nails was detected. Casamiquela and Cohen [7] reported a case of black hyper-pigmentation of the tongue and blue lunula, caused by combination chemotherapy. Moreover, Abbasi and Wang [11] reported a male patient with HIV infection and Kaposi sarcoma on HAART therapy and doxorubicin with a hyper-pigmentation on his tongue and lips and linear bands on nails. Although our patient manifested the most diffuse pigmentation of oral mucosa in comparison with other reported cases, it had roughly disappeared within two months after chemotherapy. Similarly, Blaya and Saba [10] reported complete disappearance of tongue lesions within 12 weeks.

In conclusion, we reported a patient with severe pigmentation on oral mucosa as a result of cancer therapy. Awareness about the side effects of chemotherapy helps physicians and dental practitioners arrive at a timely, correct diagnosis.

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