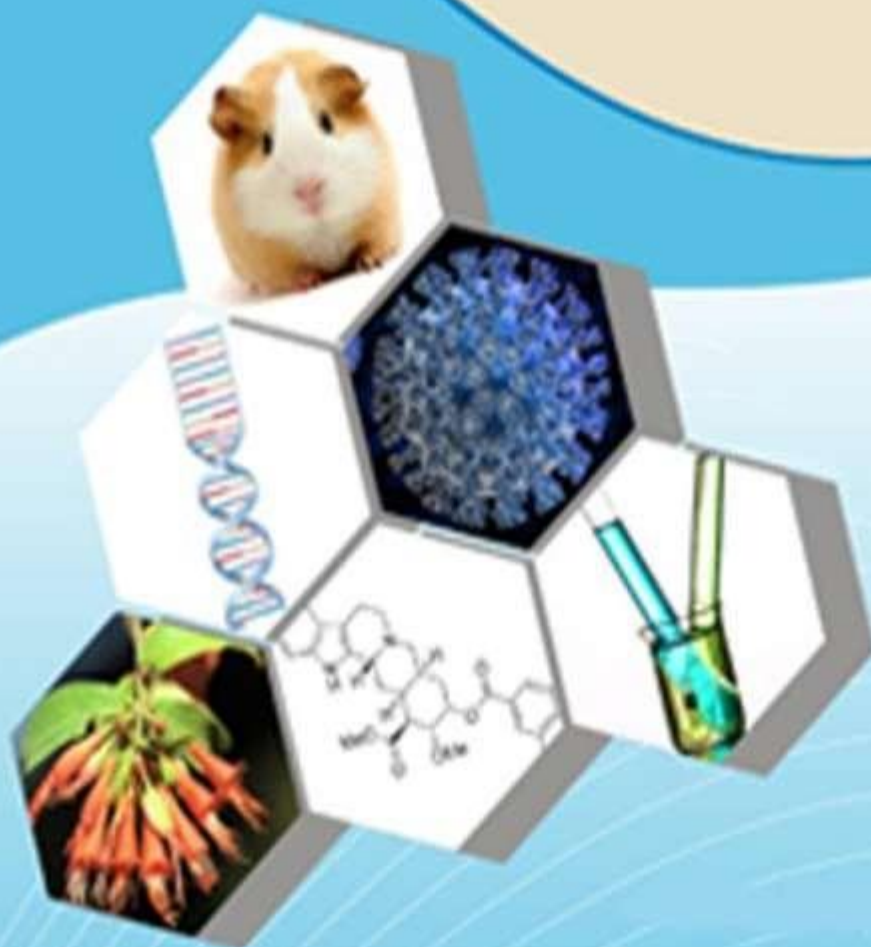




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Skin cancer patients undergoing etoposide, prednisolone, vincristine, and cyclophosphamide therapy may have hyperpigmentation of the teeth and tongue.

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Abstract

Chemotherapeutic medicines such as etoposide, vincristine, and cyclophosphamide are often used to treat the uncommon malignancy known as cutaneous extranodal non-Hodgkin lymphoma. These drugs very infrequently produce hyperpigmentation in the skin and nails. Here, however, we report an instance of hyperpigmentation that spread to the teeth and tongue. It wasn't long after chemotherapy started that the tongue and teeth began to hyperpigment. No pharmaceutical, surgical, or lifestyle therapies were necessary for the hyperpigmentation to resolve itself within a week.

Search Terms: Hyperpigmentation, cyclophosphamide, teeth, and tongue

Malignant T cells infiltrating the skin is a hallmark of cutaneous T-cell lymphomas, a diverse category of non-Hodgkin lymphomas that do not originate in the lymph nodes. In addition, most of these cases fall within the categories of mycosis fungoides and Sezary syndrome, which are defined by skin lumps. Due to the paucity of diagnostic signs in early lesions and the lack of particular presentations in early stages of T cell lymphoma, early diagnosis may be challenging [2]. Although the specific mechanisms by which cutaneous T cell lymphoma develops remain a mystery, they may include signaling, skin lesions, and their precise locations. Accurate histological

examinations, supplementary testing (such as CD4 cell identification), and other criteria are required for a cutaneous T cell lymphoma diagnosis [4].

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abnormalities in the immune system, changes in the receptors on T cells, skin lesions, and blood samples taken from patients' periphery.[5] To effectively treat cutaneous T cell lymphoma, the best course of treatment is the EPOCH regimen, which includes etoposide, prednisolone, vincristine, cyclophosphamide, and doxorubicin.[6] On the other hand, there are certain undesirable consequences and side effects associated with the regimen, some of which are more prevalent than others. The most typical side effects are nausea, vomiting, alopecia, neutropenia, anemia, anorexia, and cardiac heart failure. seven times eleven Doxorubicin is known to induce cardiomyopathy; hence, it is avoided in EPOCH treatment in this patient with a history of cardiomyopathy. Thus, the darkening seen on the patient's teeth and tongue was solely caused by the cyclophosphamide treatment.

Reported Case

An investigation into a 67-year-old male patient's history of weight loss and subsequent complaints of a rash, eruption, and scaly patches on his left arm led to the confirmation of a malignant neoplasm of the left forearm. Additional support for this diagnosis came from an immunohistochemistry report that yielded positive results for CD30, CD45, and CD4. Finally, a positron emission tomography computed tomography scan confirmed the presence of cutaneous T cell lymphoma of the left forearm. The next step in the treatment plan was radiation chemotherapy for the patient. The patient was sent for further chemotherapy with a dose-adjusted

EPOCH regimen after receiving two 40 Gy radiation cycles from February to March at a separate facility. Albumin - 2.1 g/dL and globulin 3.8 g/dL were the results of the routine blood test that showed lower protein levels, whereas lactate dehydrogenase was higher at 339 U/L. Doxorubicin has the potential to exacerbate preexisting cardiomyopathy, hence it was not recommended for this patient due to their history of cardiomyopathy.[7] Cyclophosphamide 750 mg/m², vincristine 1.4 mg/m², Etoposide 50 mg/m², and prednisolone 10 mg were the components of the regimen that the patient underwent for six cycles. During the patient's chemotherapy treatment at the day care unit, she began to notice discoloration of her tongue and teeth on day 2 after the first cycle. She also complained of taste disturbances, which are a common side effect of many drugs. Fortunately, the patient's symptoms went away after a week without any treatment. The patient complained of the same discoloration on day 2 of his second round of chemotherapy as he did throughout all six cycles of the aforementioned treatment.

No one knows the specific pathophysiology of the discoloration that occurs with the aforementioned regimen. The discoloration might be caused by interactions with melanocyte stimulating hormone, however.

one possible cause is a change in the gene code for normal melanin, which in turn changes the production of normal melanin and causes hyperpigmentation. Another possible cause is the buildup of dead papillae on the tongue, which causes



discoloration or hyperpigmentation over time.[12]

Subject for debate

A small number of case reports have mentioned hyperpigmentation of the skin as a side effect of EPOCH treatment.8–11, 13 But there hasn't been a single incidence of EPOCH-related tooth or tongue discoloration. The current instance is the first to be linked to cyclophosphamide-induced tooth and tongue discoloration, as established by thorough examination and documentation. While factors including neglecting to properly clean the mouth might explain why some people get dental hyperpigmentation. However, the pigmentation disappeared on its own within a week, which provides further evidence that the discoloration was caused by cyclophosphamide's negative side effects. Consistent with earlier findings by Santosh Kumar et al., the Naranjo likelihood score further demonstrated the likely relationship



Figure 1: Discoloration of the tongue following chemotherapy following chemotherapy

Statement of the patient's agreement

By signing this document, the writers attest that they have collected the necessary patient permission paperwork. The patient has indicated his approval for the publication of his photos and other clinical data in the journal by signing the form. The

between cyclophosphamide and hyperpigmentation.[14]

In summary

Patients receiving cytotoxic drugs often experience hyperpigmentation of the skin. However, in this case, we observed an extremely rare occurrence of hyperpigmentation involving the tongue and teeth. After conducting a thorough investigation and reviewing the relevant literature, we determined that the possible agent could be cyclophosphamide. Additionally, our patient experienced bluish discoloration of the teeth after receiving her regimen. Since this is the first reported incident of cyclophosphamide-induced darkening of the teeth and tongue, we urge the therapeutic team, including doctors, pharmacists, and nurses, to be more vigilant in the event that other cases like this one occur.



Figure 2: Discoloration of the teeth

patient is informed that their name and initials will remain confidential and that every effort would be taken to protect their identity, but that complete anonymity cannot be guaranteed.



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