**International Journal of Clinical and Experimental Human Medicine**

https://www.harrisonacademicpress.com/index.php/IJCEHM

**Vol 1, Issue 1, 2026**

# Hyperpigmentation of the teeth and tongue may occur in skin cancer patients receiving etoposide, prednisolone, vincristine, and cyclophosphamide treatment

[1] **Dr. M. SREENIVASULU*** PRINCIPAL AND PROFESSOR, DEPT OF PHARMACEUTICAL CHEMISTRY,

[2.] **Dr. LALITHA CHEMBETI,** PROFESSOR, DEPT OF PHARMACEUTICAL CHEMISTRY

[3.]**Dr. S. Niveditha,** professor &principal, DEPT OF PHARMACOGNOSY, SWATHI COLLEGE OF PHARMACY, NELLORE.

[4] **Ms.Sk.Salma Sultana,** Asso Professor, DEPT OF Pharmacology,

[5] **A. RANI**, Asso. Professor, DEPT OF PHARMACEUTICS

[1,2,4,5] NARAYANA PHARMACY COLLEGE, CHINTHA REDDY PALEM, NELLORE

## Abstract

Cutaneous extranodal non-Hodgkin lymphoma is an unusual cancer that often responds to chemotherapeutic drugs including cyclophosphamide, vincristine, and etoposide. Hyperpigmentation of the nails and skin is an extremely rare side effect of these medications. A case of hyperpigmentation that extended to the tongue and teeth is shown here, however. Teeth and the tongue started to hyperpigment soon after chemotherapy began. Within a week, the hyperpigmentation cleared up without the need for any medication, surgery, or changes to one's way of life.

**Search Terms:** Hyperpigmentation, cyclophosphamide, teeth, and tongue

Utaneous T-cell lymphomas are characterised by the invasion of skin by malignant T cells; these lymphomas do not begin in the lymph nodes and belong to a broad range of non-Hodgkin lymphomas.Furthermore, the majority of these instances are classified as mycosis fungoid or Sezary syndrome, both of which are characterised by the presence of lumps on the skin.Early diagnosis may be difficult since there are few diagnostic indicators in early lesions and no specific manifestations in early stages of T cell lymphoma [2].the subsequent While the exact processes that lead to the development of cutaneous T cell lymphoma are yet unknown, they can include signalling, skin lesions, and their particular sites.To diagnose cutaneous T cell lymphoma, one must meet certain criteria, including an accurate histological examination and further tests (such as CD4 cell identification) [4].

Articles published in this open-access journal are licensed under the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License. So, without paying for it, anybody may use the articles whatever they like, including modifying and remixing them. Just make sure they give credit where credit is due and license their own works in the same way.

issues with the immune system, alterations to the T cell receptors, skin lesions, and peripheral blood work.[5] A combination of etoposide, prednisolone, vincristine, cyclophosphamide, and doxorubicin is known as the EPOCH regimen, and it is the gold standard for treating cutaneous T cell lymphoma.[6] Some unintended repercussions and side effects of the regimen are more

common than others, however. Heart failure, anorexia, neutropenia, anaemia, vomiting, and nausea are the most common adverse effects.11 times seven Due to the patient's history of cardiomyopathy, doxorubicin is not administered during EPOCH therapy. Therefore, the cyclophosphamide therapy was the only reason the patient's teeth and tongue become darker.

**Reported Case**

The presence of a malignant tumour of the left forearm was confirmed after examining a 67-year-old male patient who had lost weight and complained of a rash, eruption, and scaly areas on his left arm. Immunohistochemistry findings that were positive for CD30, CD45, and CD4 provided further evidence that this diagnosis was correct. Last but not least, a PET/CT scan of the left forearm verified the existence of cutaneous T cell lymphoma. Radiation chemotherapy was the next phase in the patient's treatment regimen. After the patient had two 40 Gy radiation cycles in February and March at a different hospital, they were referred for further chemotherapy with a dose-adjusted EPOCH regimen. While lactic dehydrogenase was greater at 339 U/L, the results of the standard blood test indicated decreased protein levels with albumin - 2.1 g/dL and globulin 3.8 g/dL. This patient should not have received doxorubicin because of their history of cardiomyopathy, which the drug has the ability to worsen.The patient was administered a regimen consisting of cyclophosphamide 750 mg/m2, vincristine 1.4 mg/m2, Etoposide 50 mg/m2, and prednisolone 10 mg for a duration of six cycles. On the second day after the first round of chemotherapy, the patient noticed that her teeth and tongue had become discoloured. She was receiving treatment in the day care unit. As a typical adverse effect of several medications, she also mentioned a change in her taste. The good news is that the patient's symptoms cleared up after seven days of non-medical care. Day 2 of the second round of chemotherapy brought the same discolouration that the patient had experienced during all six cycles of treatment.
The exact pathophysiology of the discolouration caused by the aforementioned regimen remains unknown. On the other hand, interactions with melanocyte stimulating hormone might be to blame for the discolouration.
Hyperpigmentation may be caused by a variation in the gene coding for normal melanin, which modifies the synthesis of normal melanin. The gradual discolouration or hyperpigmentation of the tongue that results from the accumulation of dead papillae is another potential reason.[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 discolouration. The current instance is the first to be linked to cyclophosphamide-induced tooth and tongue discolouration, 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 discolouration 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 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 1:** Discoloration of the tongue following chemotherapy



**Figure 2:** Discoloration of the teeth following chemotherapy

**Statement of the patient's agreement**

By their signatures hereon, the authors confirm that they have obtained all required patient consent forms. With his signature, the patient gives his consent for the journal to publish his images and other clinical data. Although every care will be taken to ensure the patient's identity, we cannot promise that they will stay completely anonymous. Rest assured that their name and initials will be kept secret.

**References**

1.Cutaneous T-cell lymphoma is the subject of Pulitzer M. Clinical laboratory medicine 2017;37:527–46.

2.The 2016 update on the diagnosis, risk-stratification, and treatment of cutaneous T-cell lymphoma was published by Wilcox RA. Published in 2016 in the American Journal of Hematology, volume 91, pages 151–165.

3.Kotz EA, Thiers BH, Anderson D. Skin T-cell lymphoma. Johns Hopkins University Journal of Dermatology and Venereology, 2003, 17(1), 131–137.

4. Latkowski JA, Lo Sicco K, Weed J, and Peterson E. Skin T cell lymphoma: A previously baffling diagnosis unraveled. "Dermatol Clin" published the article in 2019 with the DOI: 37: 455–69.