

Chemical Leucoderma of Oral and Labial Mucosal Surfaces from Neem [*Azadirachta indica*]. A Case Series

Sir,
Acquired vitiligo like depigmentation due to repetitive insults by chemicals is known as chemical leucoderma. Apart from aromatic and aliphatic compounds of phenols and catechols, there are other culprits, such as *p*-phenylenediamine, cinnamic aldehyde, etc., which may induce leukoderma.^[1] These chemicals are toxic to melanocyte in genetically susceptible individuals. The leucoderma is limited to the site of contact with these chemicals. In India, household objects are more prevalent than industrial chemicals to cause chemical leucoderma. The neem [*Azadirachta indica*] may uncommonly cause depigmentation. There is only one case series which reports of lip depigmentation due to neem.^[2]

Fourteen patients, nine males and five females, presented with progressive lip depigmentation. They sought consultation for aesthetic reason and for fear of vitiligo. There was no past history of any eruption, application, reverse smoking, or similar lesion.

Out of 14 patients, 10 were using neem twigs daily for brushing teeth. The remaining four patients were chewing and spitting out, four to five neem leaves daily.

On examination there was depigmentation on labial mucosae of both lips [Figure 1a]. It extended to the vermilion border and lateral aspect of lips near the oral commissures and buccal mucosa. Diascopy on buccal mucosa was done taking utmost care to avoid trauma. It revealed patchy involvement with clear-cut demarcation [Figure 1b]. The patchy involvement was also noted on gums and palate [Figure 1c and d]. Only two patients had peri-oral involvement bilaterally.

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The intraoral depigmentation showed prominence on woods lamp examination. The oral and lip depigmentation raised possibility of vitiligo and chemical leucoderma. We advised patch testing and blood investigations.

The blood investigations reconfirmed four known diabetic patients. The patch testing and photographic recording was done after taking written consent. Patch testing was done in six patients using powder of fresh neem leaves and scrapings from neem twig bark. The moist empty chamber served as control [Figure 2a]. Saline was used as vehicle. Readings were taken for early reaction on day 2, 4 and 7. Reading for delayed reaction was taken at 6–8 weeks. Patient's patch test results, demographic and other characteristics are summarized in Table 1.

Patients were treated with topical tacrolimus ointment 0.1% twice daily and advised to stop neem usage totally. On one year follow-up, there was no progression of depigmentation in all patients. The peri-oral area started responding earlier and had near complete repigmentation [Figure 3a and b]. Repigmentation on labial mucosa was seen extending from mucocutaneous junction of lip [Figure 3c and d]. The patch test site also started repigmenting. The intraoral depigmentation showed no signs of any repigmentation but was stable.

Oral mucosal depigmentation can occur as a part of vitiligo vulgaris, part of acrofacial vitiligo or as pure mucosal vitiligo.^[3] Chemical leucoderma exactly mimics vitiligo. This is true for mucosal depigmentation also. Mathais *et al.* were first to report toothpaste-induced leucoderma.^[4] Later on Indian researcher Ghosh, Alam, and Mukhopadhyay^[1,5] reported many cases with leucoderma

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Figure 1: (a) Depigmentation on labial mucosae of lower lip. (b) Depigmentation of buccal mucosa with clear-cut demarcation on diascopy. (c) Depigmentation on gums. (d) Patchy Depigmentation on palate

on lips due to cinnamic aldehyde. In our case series, depigmentation was seen not only on lips but also on oral mucosal surfaces.

Our patients presented with lip depigmentation. They did not report of burning sensation in oral cavity. Patients were unaware of the oral involvement. There were no features suggestive of any irritant or allergic contact stomatitis. All patients had more involvement of mucosal aspect as compared to the cutaneous aspect. This indicates inside out progression of leucoderma in these cases. This localization of acquired vitiligo like depigmentation and continuous exposure to neem

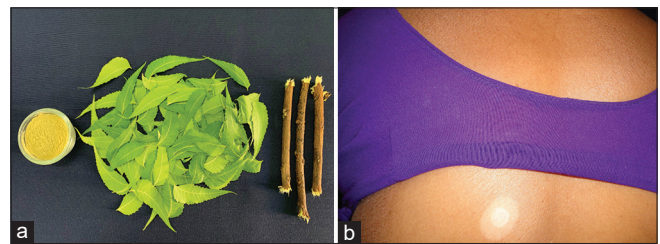


Figure 2: (a) Neem powder, leaves, and twigs. (b) Depigmentation at neem patch test site

Table 1: Patients demographic and other characteristics

Age (years)	Sex	Neem usage, duration	Duration of depigmentation	Patch test results	Follow-up 1 year
36	Female	Twig, 10 years	7 months	Not done	Excellent repigmentation on lip
65	Male	Twig, 8 months	5 months	Not done	Partial repigmentation on lip
37	Male	Twig, 6 months	2 months	No reaction on day 2, 4, and 7. Depigmentation after 2 months	Partial repigmentation on lip
32	Male	Twig, 5 years	3 months	No reactions on day 2, 4, 7, and 2 months	Stable depigmentation
65	Male	Twig, 2 months	1 month	Not done	Stable depigmentation
48	Female	Twig, 1 year	6 months	No reactions on day 2, 4, 7, and 2 months.	Minimal repigmentation on lip
58	Male	Twig, 6 months	1 month	No reaction on day 2, 4, and 7. Depigmentation after 2 months	Few areas repigmentation on lip
55	Female	Twig, 2 months	1 month	Not done	Stable depigmentation
53	Male	Twig, 2 years	3 months	Not done	Minimal repigmentation on lip
60	Female	Twig, 3 months	1 month	No reaction on day 2, 4, and 7. Depigmentation after 2 months [Figure 2b].	Complete repigmentation of Para oral areas. Repigmentation started on lips
54	Male	Leaves, 4 years	24 months	Erythematous papule on day 2 [ICDRG 1+] subsided in a week after topical steroid. No depigmentation.	Stable depigmentation
69	Female	Leaves, 5 years	3 months	Not done	Near complete repigmentation of paraoral areas.
70	Male	Leaves, 8 months	1 month	Not done	Stable depigmentation
52	Male	Leaves, 3 months	2 months	Not done	Stable depigmentation

ICDRG=International Contact Dermatitis Research Group



Figure 3: (a) Lip and paraoral depigmentation. (b) Repigmentation on lip and paraoral area. (c) Depigmentation on lower labial mucosa. (d) Extension of repigmentation on lower labial mucosa

fulfilled clinical diagnostic criteria for chemical leucoderma laid by Ghosh and Mukhopadhyay.^[1] Patch testing was done in six patients.

Indian standard battery does not contain any allergen related to our cases. Hence, we performed patch testing with fresh neem leaves and bark as is.

Though the validity of patch test is limited due to nonstandardized antigen, it proved the culprit as neem. Neems phytochemical constituents are limonoids azadirachtin of class tetranortriterpenes. In genetically susceptible individuals, the direct melanocytotoxicity of these limonoids in neem could be responsible for causing oral mucosal leucoderma.^[6] Due to unavailability of kit and widespread mucosal involvement, mucosal patch test could not be done.

The fulfillment of clinical diagnostic criteria, patch test results and favorable outcome after avoiding neem confirms neem as causative agent in our cases.

Large population is at risk of getting oral leucoderma using neem. Awareness of “Neem leucoderma” in doctors and public is needed for prevention and treatment of this condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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