Palmoplantar exfoliation due to chloroquine

Pragya Ashok Nair, Trusha Patel

Abstract:
Chloroquine is the drug very frequently used for the treatment of malaria. It is also used in amebiasis, rheumatoid arthritis, and various dermatological conditions. Chloroquine can cause muscle problems, loss of appetite, and diarrhea as a side effect. Cutaneous toxicity includes pruritus, hair loss, photosensitivity, and color changes. Exfoliation of skin over palms and soles is caused by chemotherapeutic drugs such as axitinib, fluorouracil, idarubicin, doxorubicin, sunitinib, sorafenib, and paclitaxel. Here, a case of a 40-year-old female is presented who developed palmoplantar exfoliation with depigmentation after taking chloroquine. Although not life-threatening, this side effect of a commonly used drug may cause anxiety and functional impairment which in turn affects the quality of life of an individual.

Keywords:
Chloroquine, palms and soles, peeling

Introduction
Peeling of skin from palms and soles is a common condition found in dermatological practice. Causes for palmoplantar exfoliation include genetic syndromes such as acral peeling skin syndrome and keratolysis exfoliativa and infections such as tinea pedis and scarlet fever, rashes secondary to chemotherapeutics, epidermal growth factor receptor inhibitors, and tyrosine multikinase inhibitors. In most of these conditions, it is not known why systemic exposures or genes cause only the acral skin to peel. A case of depigmentation with peeling of skin from palms and soles after taking chloroquine is reported here.

Case Report
A 40-year-old female presented with complaint of skin lesions over the palms and soles since 5 days. One week back, she took tablet chloroquine for malaria after which she developed exfoliation of skin with depigmentation over the palms and soles associated with itching. A history of similar complaint thrice in 2 years after ingestion of medications for fever was present. The patient did not remember the medications taken in the past. On examination, exfoliation of skin from both palms mainly over the margin with depigmentation [Figure 1a and b] was seen. Exfoliation was also noted over the soles more toward the margin with depigmentation [Figure 2a and b]. The mucous membranes, hair, and nails were normal. There was no lymphadenopathy in the cervical, axillary, or inguinal chains. Hematological tests such as histogram, liver function test, and renal function test were normal. Chest X-ray, HIV, and urine were also normal.

Severity assessment scores for drug reactions were calculated, which showed WHO-UMC causality care as probable or likely, Naranjo et al. adverse drugs reaction score as 8 or probable and Hartwig’s Severity assessment scale as level 3 or moderate. Although we could not find the drugs taken during the past episode, probability of chloroquine was more as drugs taken were for fever.

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Skin biopsy was advised, but the patient was not willing for the same. A diagnosis of chloroquine-induced palmoplantar exfoliation was made. Topical antibiotics and emollients were given with advice to avoid tablet chloroquine in future.

**Discussion**

Drug sensitivity is a well-known condition found in day-to-day practice of dermatology outpatient department. Generalized exfoliation of skin is common which is due to drugs such as antiepileptics, antimalarials, heavy metals, and certain antibacterials.

Exfoliation of skin over palms and soles is caused by chemotherapeutic drugs such as axitinib, fluorouracil, idarubicin, doxorubicin, sunitinib, sorafenib, and paclitaxel. The underlying mechanism by which sirolimus (rapamycin), an immunosuppressive agent, produces desquamation of the palms and soles is unclear. There are numerous sweat glands on acral sites, and if drugs accumulate in sweat, there will be high concentration of drug in the skin of palms and soles, which damages the epidermis. Rarely, blisters may develop or there may be involvement of knees or elbows. Hand-foot syndrome also called palmar-plantar erythrodysesthesia is redness, swelling, and pain on the palms of the hands and the soles of the feet caused by some cancer treatment.

Chloroquine is the drug used in the treatment of malaria, amebiasis, and rheumatoid arthritis. Its dermatological indications are systemic lupus erythematosus, porphyria cutanea tarda, dermatomyositis, chronic ulcerative stomatitis, sarcoidosis, polymorphic light eruption, generalized granuloma annulare, lichen planus, and lichen sclerosus et atrophicus.

Chloroquine is usually taken orally. It gets well absorbed from the gut and is selectively concentrated in the liver, spleen, lung, adrenals, spinal cord, and skin. The actual peak ultraviolet (UV) absorption spectrum of chloroquine is between 320 and 340 nm which is clinically not significant. However, when chloroquine is irradiated, there is a spectral shift resulting in markedly increased absorption in the UVB range, which is clinically highly significant.

Chloroquine has a very high volume of distribution, as it diffuses into the body’s adipose tissue. It is also a lysosomotropic agent, means it accumulates preferentially in the lysosomes of cells in the body. Side effects of chloroquine include loss of appetite, diarrhea, skin rash, retinal toxicity, muscle damage, seizures, and low blood cell levels. Even though been used in various photodermatitis, it can cause photosensitive dermatitis.

Chloroquine-induced itching is very common among African descent or African descent with dark skin (70%), but much less common in other races. It increases with age and is so severe as to stop compliance with drug therapy. It is increased during malaria fever; severity is correlated with load of malarial parasite in blood. It has a genetic basis and is related to its action with opiate receptors centrally or peripherally.

Rare cutaneous side effects of chloroquine include exfoliative dermatitis, erythema multiforme, toxic epidermal necrolysis, Stevens–Johnson syndrome, and desquamation of skin which is seen in <0.1% patients. Pruritus, rashes, pleomorphic skin eruptions, lichen planus-like eruptions, urticaria, generalized exanthematous pustulosis, exacerbation of psoriasis, hypopigmentation, and hair loss are the side effects, incident of which is not recorded.

Chloroquine can cause bluish black or slate-gray pigmentation of the periorbital, facial, truncal, subungual, and hard palate which is due to the deposition of the drug in the affected tissues. Hypopigmentation of the hair and freckles has also been reported. Vitiligo-like depigmentation as seen in our case is an extremely rare side effect of this medication, with only five cases reported, all of which involved African descent or African descent with dark skin.

Our patient had exfoliation of skin from only palms and soles with depigmentation. Awareness and vigilance...
should be there in practicing physicians about this side effect of commonly used drugs such as chloroquine. Although this condition is not life-threatening, it may cause anxiety and functional impairment.

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Conflicts of interest
There are no conflicts of interest.

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