

Two cases of quinine-induced fixed ‘drug’ eruption induced by long drinks

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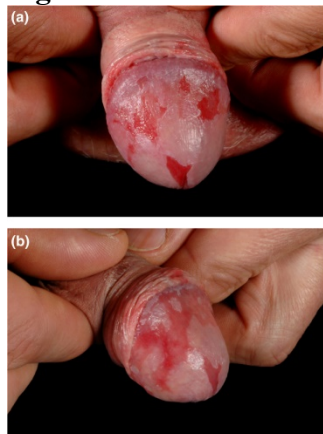
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In 1894, Brocq coined the term ‘fixed drug eruption’ which is characterized by skin changes reoccurring at the same site after ingestion of the triggering drug, preferentially affecting the lips, hands, genitals and the oral mucosa.¹ In 1996, Kelso first described the appearance of a fixed exanthema after strawberry consumption and introduced the term ‘fixed food eruption’.² To date, other foods have been identified as causative agents, including kiwi, peanuts and asparagus.¹

Here, we present two patients with typical clinical features of fixed drug eruption without any associated ingestion of medication. Detailed analysis of the medical history of each patient indicated quinine ingested via long drinks containing tonic water or bitter lemon as the causative agent.

An otherwise healthy 46-year-old male farmer presented with bullous and erosive lesions of the genital and oral mucosa (Fig. [1a](#)) that had been recurring for fourteen years and healed spontaneously each time. The tentative diagnosis was an unspecified autoimmune bullous disease. Histology showed typical features of a fixed drug eruption. The patient did not take any drugs, but had considered a link with alcohol consumption, although he tolerated beer. Thus, we suspected quinine-containing long drinks as the trigger. Oral placebo-controlled exposure was performed separately with alcohol or bitter lemon. Alcohol (ethanol 80%) was well tolerated. Shortly after consuming a cumulative 215 mL dose of bitter lemon, the patient reported tingling paraesthesia of the oral and genital mucosae, which was followed by extensive intraoral and genital blistering (Fig. [1b](#)). Due to the severe eruption induced by bitter lemon, the patient declined further provocation with quinine. The patient now avoids any quinine-containing drinks and is currently symptom-free.

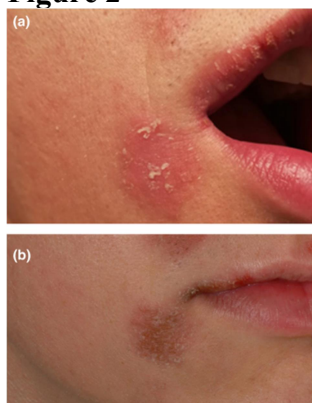
Figure 1



Erosions on the sulcus coronarius and the glans penis (a). Induction of similar lesions upon oral provocation with bitter lemon (b).

Subsequently, an otherwise healthy 26-year-old student presented with similar lesions with additional well-demarcated hyperpigmented facial spots (Fig. 2a). He reported recurrence of lesions every few weeks during the preceding fourteen months. Due to the similarity to the previously described case, the patient was questioned regarding the intake of quinine-containing beverages and reported that he had suspected an association between consuming tonic water and his symptoms. Upon oral exposure with 17 mg quinine hydrochloride (total dose), the patient immediately reported burning sensations on the cheeks, the tongue and oral mucosa. At these sites, discrete erythema appeared and developed into erosions over the subsequent 3 days. The lesions spontaneously healed leaving postinflammatory hyperpigmentation (Fig. 2b).

Figure 2



Erythematous facial lesions that are centrally slightly erosive. These occurred after consumption of long drinks and spontaneously healed resulting in scaly hyperpigmented macules (a). Induction of similar lesions upon oral exposure to quinine (b).

Quinine is known to cause adverse reactions, including vasculitis, haemolytic uremic syndrome, photosensitivity, lupus-like syndrome and thrombocytopenia.³⁻⁵ As the role of quinine as a therapeutic agent has diminished, it is now primarily used by the food industry at low concentrations in tonic water and in bitter lemon. The consumption of tonic water is increasing worldwide. Hence, it is not surprising that recently reported fixed drug eruptions induced by quinine were not due to its intake as a drug but to consumption of quinine-containing drinks.^{3, 6-12} Quinine as a trigger for fixed drug/food eruption can be detected by a patch test *in loco* and by oral provocation.⁶ Since only a few authors report having obtained positive patch test results, the current data available on the reliability of *in loco* patch testing for quinine are contradictory.¹⁰⁻¹² Similar observations have been made regarding *in loco* patch testing with NSAID and antibiotics.¹³ Only 40.4% of performed patch tests were positive when suspecting NSAID as the causative agent for a fixed drug eruption.¹³ Therefore, the causative agent itself seems to play a crucial role in whether or not patch testing will lead to reliable results. Another test method is the lymphocyte transformation test. However, it has rarely been reported to be positive in patients with fixed drug eruption when cultivating lymphocytes with the causative drug only.¹⁴ Surprisingly, Gimenez-Camarasa *et al.*¹⁵ reported in 1975 positive results when combining the lymphocyte culture, the causative drug and patient serum obtained at the acme of fixed drug eruption. For quinine, this has to be investigated further in the future.

Whether these two cases should be considered fixed drug or fixed food eruptions is open to discussion: either are permissible since in both cases, the lesions were induced by a food containing small amounts of a well-known drug. Despite quinine's now diminished therapeutic importance and clinical use, the contribution of dietary quinine to clinical symptoms of a fixed drug eruption should be considered, and adequate testing should be performed.