

Views and Practice

How I treat epidermal growth factor receptor inhibitor-induced paronychia

KH Yeung 楊國鴻

The epidermal growth factor receptor (EGFR) is a member of the type one receptor tyrosine kinase family. The EGFR is related to epidermal proliferation, differentiation, and hair growth and is expressed in hair follicles and epithelial tissues physiologically. It is interesting that EGFR is overexpressed in various solid tumours, where it is involved in apoptosis, angiogenesis, cell proliferation, tumor growth and metastasis.¹ Many clinical studies have shown that inhibition of EGFR is a convincing strategy in anticancer treatment for these types of tumours.^{2,3} However, EGFR inhibitors can induce many side-effects. Cutaneous toxicity is one of the most common adverse reactions that may significantly affect the tolerability of EGFR inhibitors.^{4,5} Among the EGFR inhibitor-induced cutaneous side-effects, paronychia is seen in about 10% to 15% of all treated patients. Precedent trauma is not believed to be the cause but rather an aggravating factor. Morbidity due to associated pain is high which leads to functional limitation, thus adversely affecting the quality of life of the patient.⁶ In one

recent study in a Hong Kong regional hospital, the incidence is 17/135 (12.6%, unpublished data) which is comparable with other studies in Western countries (Table 1). It generally does not develop during the first 4-8 weeks of treatment.

Involvement of the big toenail is common but fingernail involvement may lead to significant functional impairment in daily activities. Pyogenic granuloma and periungual abscesses may develop in some cases.^{4,5,7} A recent study showed that 20 different species of microbes may be cultured from the nail lesions, among these 72% Gram-positive bacteria, 23% Gram-negative bacteria and 5% *Candida* species.⁷ So culturing of perilesional skin to determine if super-infection is present is recommended so that antimicrobials can be administered accordingly.

The mechanism for these vascular overgrowths is still unclear, but it is hypothesized to be related to EGFR interruption of retinoic acid metabolism.⁸ As there are no randomized controlled studies to evaluate therapies for paronychia in these cases, the following recommendations are based on anecdotal reports and expert opinion (level of evidence 5).

General advice to patients to minimize periungual trauma:

1. Avoid trauma or any manipulation of the nail, such as manicuring, finger sucking.

**Social Hygiene Service, Centre for Health Protection,
Department of Health, Hong Kong**

KH Yeung, FRCP, FHKAM(Medicine)

Correspondence to: Dr. KH Yeung

Tuen Mun Social Hygiene Clinic, 5/F, 4 Tuen Lee Street,
Tuen Mun, New Territories

Table 1. Pattern of nail involvement in EGFR induced nail changes in one local regional hospital

Nail changes include: discoloration, ridging (koilonychia), pitting, paronychia, symptomatic separation of the nail bed from the nail plate or nail loss

Area involved	Toes only	7	41.2%
	Toes and fingers	6	35.3%
	Fingers	4	23.5%
Grading	Grade 1	6	35.3%
	Grade 2	11	64.7%

2. Keep the fingernails clean and dry by wearing gloves while cleaning (e.g., household, dishes).
3. Trim the nails regularly. For the toe nails, they should be cut short and straight.
4. Proper choice of footwear (not too tight)

In the initial stages, topical antiseptic measures and application of antiseptic or antibiotic ointments may be used. Most mild cases respond well to such conservative treatment. Examples of such topical treatment include 15% sulphacetamide in spirit, 1% clotrimazole lotion, Castellani's paint (a topical disinfectant in our service which is active against Gram positive bacteria and some fungi) and Neosporin solution (which contains neomycin sulfate, polymyxin B and gramicidin). Antiseptic treatment should be continued after systemic therapy has been initiated.

Other adjuvant therapies include potassium permanganate (KMnO₄) 1:8000 soaking as astringent. The clinician should warn the patient that it may stain the skin and clothing brown but the discoloration will fade away after it is stopped.

I have found that local application of 10% silver nitrate as a form of chemical cauterization on a weekly basis to be very effective in resistant

cases that have developed pyogenic granuloma-like periungual lesions. In my experience, I have had six patients in which topical antiseptics were not effective, five of which later responded to this treatment (Figures 1 & 2). Finger nail lesions responded faster and better than toe nail lesions. Ten percent silver nitrate has antiseptic properties and is mainly

**Figure 1.** Bilateral pyogenic granuloma-like lesions at the middle finger.**Figure 2.** The granuloma disappeared after 2 applications of silver nitrate; there is some black stain on the nail by the silver nitrate solution.

used as a cauterizing agent to remove granulation tissue in these patients. However, high concentrations can be corrosive and as it is an oxidant, organic compounds/tissue may be stained black. Long-term exposure may cause irritation (especially the skin and eye). It is therefore to be used under medical supervision in the clinic. Some clinicians put the silver nitrate in a pen form for easy application and carriage.

If the periungual culture is negative, topical corticosteroid and anti-inflammatory dose of tetracycline can be useful in decreasing periungual inflammation. Systemic antibiotic treatment of paronychia is recommended for painful or infected lesions, as there is a risk for the development of complications such as erysipelas, deep paronychia and tendon sheath phlegmon. Oral cephalosporins are recommended, and oral fluoroquinolones may also be used, especially if Gram-negative infection is suspected. Surgical intervention such as electrocauterisation under local anesthesia may be necessary in selected cases.^{4,5,7} Withdrawal of EGFR inhibitor therapy should only be considered if all the active treatments fail.

References

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