

Gefitinib-induced Paronychia Treated by Cryosurgery

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Gefitinib (Iressa, ZD1839) is one of the epidermal growth factor receptor (EGFR) inhibitors approved for the treatment of advanced non-small cell lung cancer. The cutaneous reactions to EGFR inhibitors manifest as a follicular eruption, nail toxicity, xerosis, or desquamation. These adverse events, if not properly managed, can interfere with activities of daily living. We report a case of paronychia induced by gefitinib successfully treated with cryosurgery which is a simple and safe treatment. (Ann Dermatol (Seoul) 19(4) 173~175, 2007)

Key Words: Cryosurgery, Gefitinib, Paronychia

INTRODUCTION

Gefitinib (Iressa, ZD1839) is one of the epidermal growth factor receptor (EGFR) inhibitors, approved by the United States Food and Drug Administration (FDA) for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of both platinum-based and docetaxel chemotherapies. A variety of dermatologic adverse reactions with the treatment of epidermal growth factor (EGFR) inhibitors have been reported in literature, such as acneiform eruption, paronychia, hair changes, dry skin, hypersensitivity reaction, and mucositis¹. Of these side effects, painful paronychial inflammation of the fingers and toes often leads to significant functional impairment, with decreasing therapeutic compliance. Although symptomatic relief can be achieved with soaks and splinting and/or treatment with topical or systemic antibiotics for the paronychia, discontinuation of EGFR inhibitor can be considered depending on the severity of paronychial inflammation². We report a case of gefitinib-induced paronychia that has been suc-

cessfully treated by cryosurgery.

CASE REPORT

A 31-year-old Korean woman with advanced non-small cell lung cancer was referred to our dermatology clinic with periungual granulation, acute paronychia and swelling of lateral nailfolds of both big toes with severe pain (Fig. 1). It was hard for her to walk because of the pain. She has been receiving gefitinib 250 mg daily for the treatment of the lung cancer and her skin symptoms developed 6 months after initiation of the chemotherapy. The patient denied any history of previous trauma or nail dystrophy and cultures for bacteria were negative. As paronychia of fingers and/or toes are often reported 2 to 4 months after gefitinib treatment and, as there was no specific trauma or infection history of the patient, we diagnosed her case as paronychia induced by gefitinib. As the patient wanted to continue her chemotherapy, we tried oral minocycline 50 mg twice daily with topical mupirocin twice a day. Even though her symptoms slightly improved after 4 weeks of treatment, we had to stop minocycline because of severe headache and dizziness. She also refused to use the topical application. Therefore, we tried liquid nitrogen cryotherapy using a Cryosurg[®]-Frigitonics spray gun with a two freeze-thaw cycles; 5-second spray and complete

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Fig. 1. Paronychia with nailfold swelling of both big toes during the treatment with gefitinib.



Fig. 2. Almost complete resolution of paronychia after cryosurgery.

thawing between the cycles. Paronychia of the nail folds and swelling significantly decreased without any complication after 6 cryosurgery treatments (every 2 weeks for 3 months, Fig. 2).

DISCUSSION

Nail changes have been observed in 10-15% of cancer patients treated with EGFR inhibitors and reported as a late complication (starting usually not earlier than 4-8 weeks) during the treatment course³. Inflammation of nail fold, periungual granulation tissue, pyogenic granuloma-like changes, brittle nail, and onycholysis have been reported^{4,5}. Sometimes, superinfection with *Staphylococcus*

aureus is observed with recalcitrant paronychia⁴.

Recognized cutaneous loci of EGFR expression are basal keratinocytes, outer root sheath cells, sebocyte, and occasional endothelial cells. EGFR activation serves essential function in the skin such as promotion of the keratinocytes proliferation, regulation of the differentiation and keratinization. Although the exact pathogenesis remains obscure, it is assumed that paronychia may result from the effect of EGFR inhibition on nail matrix and epidermal keratinocytes⁶. Paronychia with pyogenic granuloma of the nail fold is also one of the well-known side effects associated with systemic retinoids and HIV-1 protease inhibitors, which show homologies of the amino acid sequences⁷. These partly overlapping side effects may be due to the downregulating effects of retinoids on the EGFR systems. Similar to that occurring with retinoids, thinning of the stratum corneum and reduced keratinocyte proliferation rates are observed in patients receiving cetuximab (Erbix, IMC-225), another form of EGFR inhibitors approved by FDA for the treatment of metastatic colon cancer⁸.

Cryotherapy has been used in the treatment of pyogenic granuloma and other vascular lesions without any significant scarring. The endothelial cells may be more vulnerable to cryotherapy than collagen fibers⁹. It is a simple, easy to perform, cheap and safe treatment. Recent report recommends this modality as one of several possible treatment options for nail toxicity associated with EGFR inhibitor therapy based on the experiences of successfully treated paronychia induced by antiretroviral therapy¹⁰. In our patient, pyogenic granuloma-like lesion with other paronychia inflammation was almost completely resolved after cryotherapy. Therefore, it can be used for patients who cannot tolerate oral medications, or in cases of recalcitrant paronychia to previous treatments without discontinuing EGFR inhibitor treatment.

With expanding clinical use of EGFR inhibitors, it is important for the dermatologists to properly diagnose and treat the associated cutaneous side effects. To improve patients' compliance and to maintain satisfactory quality of life of the patients during the treatment with EGFR inhibitors, we, dermatologists, can choose the most appropriate individualized treatments according to the type of skin lesions and patients' condition. In this sense, we suggest that cryotherapy can be a good option

or an alternative for the treatment of paronychia induced by EGFR inhibitors, including gefitinib.

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