

## Gefitinib-induced pyogenic granuloma in a patient with lung cancer

Sir,

Gefitinib, a tyrosine kinase inhibitor (TKI), is commonly used as first-line targeted therapy in adenocarcinoma of the lung with epidermal growth factor receptor (EGFR) exon 19 and 21 mutation. It interrupts signaling through the EGFR in the target cells. We report a case of lung cancer treated with gefitinib, who developed a pyogenic granuloma at 4 months.

A 39-year-old nonsmoker male was diagnosed with advanced-stage adenocarcinoma of the lung with EGFR exon 19 deletion mutation. After being started on daily 250 mg gefitinib for 4 months, he achieved a partial response (significant resolution of his lung mass and metastatic lesions). However, he noticed a small friable pinkish painless growth in the nail plate junction and lateral nail beds of fingers and right toe. It was associated with mild pigmentary change and powdery scaling [Figure 1]. The patient denied a history of trauma to the fingers or toes before the development of lesion or in the recent past. There was no history suggestive of invasive procedure in the recent past. Examination of the skin and mucosa did not reveal any other lesions on the body. Based on history and examination, a provisional diagnosis of gefitinib-induced pyogenic granuloma with nail fold dermatitis was made, and the patient was counseled to continue gefitinib as the benefits clearly outweighed the risks. EGFR TKIs are known for their skin adverse effects causing pyogenic granuloma but are very uncommon. Other cutaneous adverse effects due to EGFR TKIs include acneiform eruption, xerosis, hyperpigmentation, dry skin, rash, telangiectasia, and paronychia.<sup>[1]</sup> Gefitinib binds to the adenosine triphosphate-binding site of the EGFR tyrosine kinase enzyme, thereby inhibiting the activation

of antiapoptotic signal transduction cascade, and results in uncontrolled cell proliferation. This effect of the drug may result in pyogenic granuloma. Other drugs documented to cause pyogenic granuloma include systemic retinoids, anti-EGFR monoclonal antibodies such as cetuximab; antineoplastic agents such as capecitabine, docetaxel, and 5-fluorouracil; and antiretroviral agents such as indinavir.<sup>[2]</sup> EGFR positivity is seen in about 40% of Asian population, particularly more common in females and nonsmokers. Hence, the use of gefitinib has been increased in India, and physicians used to encounter such side effect frequently in patients receiving gefitinib. Reported gefitinib-induced pyogenic granuloma from all over the world is about 25 cases. This is probably the first reported case from India.

Granuloma pyogenicum, a polypoid form of capillary hemangioma, is due to tissue reaction seen after repeated insults. Initial inflammation is confined to nail fold, and later, it develops a pyogenic granuloma (i.e., a pedunculated granulomatous tissue) commonly at the great toes. This may get superinfected at the later stages.<sup>[3]</sup> The average time from the starting of gefitinib and the appearance of pyogenic granuloma is 60 days (2 months). Treatment includes cleaning, wet dressings, and protection from trauma and superadded infection. Padding, use of protected shoes used to avoid pressure on affected nail, and topical or systemic antimicrobials may help from infections in such cases.

Although uncommonly reported, appropriate interpretation of the pathogenicity and the case management of the patient is utmost important in such cases. We report this case to bring awareness among the physicians about pyogenic granuloma in patients treated with gefitinib.



**Figure 1:** (a) Pyogenic granulomas with nail fold dermatitis filling up in many of the fingers and toenails. (b and c) Magnified view showing pyogenic granuloma (arrow) along with crusts at the lateral sulcus end of the great toenail and index finger

### 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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