EGFR inhibitors and cutaneous toxicities: a systematic literature review and meta-analysis

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Introduction: EGFR inhibitors (EGFRi) have revolutionized cancer treatment, yet their efficacy presents the challenge of cutaneous toxicities. This study synthesizes literature regarding the cutaneous toxicities of EGFRi to offer insights that can inform clinical decision-making and enhance the therapeutic experience for patients undergoing EGFRi treatment.
Methods: A systematic literature search was conducted across major databases such as PubMed and Scopus using PRISMA guidelines to identify studies investigating EGFRi and cutaneous toxicities.
Results: 64 retrospective and prospective cohort studies including 6126 patients were analyzed. The most commonly reported EGFRi were cetuximab (35.6%), erlotinib (33.9%), and gefitinib (15.2%). The predominant cutaneous toxicities were acneiform or papulopustular rash (68.3%), unspecified rash (32.8%), and nail changes such as paronychia (11.8%). Upon examining 116 case reports and case series with a total of 128 patients (mean age 61.5 ±12.0 years). The most common first cutaneous toxicities were acneiform rash (40.6%), unspecified rash (17.2%), and pruritus (15.6%), occurring after an average of 44.0 days. 38.7% of the first cutaneous events were grade 3 or 4. Among 35 patients with a second cutaneous toxicity, unspecified rash (31.4%), acneiform rash (25.7%), and nail changes such as paronychia (20.0%) were most prevalent. Suspension of EGFRi (30.3%) was the most common change in management followed by a single dose reduction (15.7%) and initial suspension and subsequent readministration (15.7%). In 76 cases discussing treatment of cutaneous toxicities, common treatments were systemic antibiotics (46.9%) and topical steroids (42.2%), with complete resolution of cutaneous toxicities in 51.6% of patients. While there was no significant difference in the number of days to the first cutaneous reaction, days to the second reaction were significantly longer for gefitinib (290 days) compared to both erlotinib (62.5 days, $p<0.001$) and cetuximab (74.2 days, $p<0.001$). Also, days from the first to the third cutaneous reaction were significantly longer for gefitinib (362.0 days from first reaction) compared to erlotinib (112.0 days, $p<0.016$) and cetuximab (21.0 days, $p<0.004$).
Conclusion: It is essential to consider cutaneous toxicities in patients undergoing EGFRi therapy. Comprehensive EGFRi management requires awareness of common cutaneous toxicities, varied time-to-reactions, and efficacious treatment options.