

25. Sebaceous glands as the primary target of EGFR-inhibitor in the development of papulopustular eruption

Tomoya Takata¹⁾, Masahito Tarutani¹⁾, Shigetoshi Sano¹⁾

¹⁾Department of Dermatology, Kochi Medical School, Kochi University

Papulopustular eruption (PPE) is an adverse reaction of the skin most commonly seen in cancer patients treated with EGFR inhibitors. Although PPE is distinct from folliculitis/acne by its clinical manifestations, the underlying mechanism is still undefined. We first investigated the histological difference between PPE and unrelated folliculitis. Abundant droplets accumulated within intraepidermal pustules in PPE, and were positive for adipophilin, suggestive of sebum-derived. In PPE, a number of cell infiltrates was found around the sebaceous glands, not around the infundibulum frequently found in folliculitis. Interestingly, histology from lesions at the earlier stage of PPE revealed sebaceous hypertrophy with positive staining for TNF- α . These findings lead us to speculate that sebaceous gland might be the primary target of EGFR inhibitors and plays a major role in the onset of PPE. Next we studied the effects of EGFR inhibitor (cetuximab) on the biology of immortalized human sebaceous gland cell line, SZ95. Stimulation of SZ95 cells with cetuximab resulted in increase of the expression of various proinflammatory cytokines and sebocyte differentiation-related molecules, adipophilin and melanocortin-5 receptor. These results suggested that EGFR-inhibitors targeted sebocytes, which subsequently released proinflammatory cytokines and sebum. L-ascorbyl-2-phosphate (APS) is an anti-oxidant and inhibitor of sebum secretion. APS suppressed the expression of IL-6, IL-8 and TNF- α in cetuximab-treated SZ95 in a dose-dependent manner. These results indicate that APS would be therapeutically effective for the treatment of PPE induced by EGFR inhibitors.