Panitumumab-Induced Acneiform Rash in a Patient with Metastatic Colon Adenocarcinoma

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Sir,

Human epidermal growth factor receptor (HER1/EGFR) is a transmembrane glycoprotein of the tyrosine kinase growth factor family that is dysregulated in many solid tumors and correlated with increased metastasis, reduced survival, and poor prognosis.[1] Panitumumab is a fully human immunoglobulin G2 monoclonal antibody that binds specifically to the EGFR with promising results for the treatment of metastatic colorectal cancer when used as monotherapy[2] or when added to standard chemotherapeutic regimens.[3]

Despite the favorable toxicity and safety profiles, several adverse events have been reported, including gastrointestinal disorders, metabolism and nutritional disorders, and mild to moderate dermatologic toxicities.[4] In this correspondence, we describe a case of panitumumab-induced acneiform rash in a patient with metastatic colon adenocarcinoma.

A 63-year-old woman was diagnosed with metastatic colon adenocarcinoma carrying wild-type kirsten rat sarcoma 2 viral oncogene homolog (KRAS gene) with elevated serum carcinoembryonic antigen (CEA) level (>130 ng/mL). He was initially treated with oxaliplatin (OX) and bolus 5-fluorouracil/leucovorin (5-FU/LV). Since the patient developed several adverse effects during the fourth cycle, including nausea, vomiting, oral mucositis, unilateral hydronephrosis, splenomegaly, and diarrhea, the protocol was changed to bevacizumab plus irinotecan with poor clinical response (CEA 217 ng/mL). The patient received cetuximab plus FOLFOX-6 (FU, LV, OX), but developed severe neutropenia. Currently, panitumumab is being administered at 6 mg/Kg intravenously every 2 weeks with satisfactory clinical response (CEA 63 ng/mL). During the first cycle of panitumumab, the patient developed tender acneiform rash in the face, scalp, thorax, and abdomen [Figure 1], and is being referred to a dermatologist. The reaction was classified as Grade 3, since papules covering > 30% of body surface area were associated with the symptoms. Xerosis, pruritus, and paronychia were not observed. Tetracycline 500 mg orally for 30 days, clindamycin gel 1% for 60 days, and daily use of a hypoallergenic sunscreen were prescribed with significant improvement in the skin reactions.

A multicenter, randomized, metastatic colorectal cancer clinical trial conducted in 200 US centers indicated that dermatologic toxicities were the most common adverse effects related to the panitumumab, but the incidence of severe reactions was not frequent.[4] Approximately 11% of the patients develop Grade 3-5 dermatitis acneiform usually within the first 2-4 weeks of treatment, which can result in cosmetic and stigmatizing effect as well as in a significant discomfort in the affected areas. In addition to the papulopustular reaction (acneiform rash), some patients may have other cutaneous complications including hair abnormalities, trichomegaly, increase in the length of the eyebrows, pruritus, xerosis, aphthous ulcerations, and urticaria, in a condition known as papulopustules and/or paronychia, regulatory abnormalities of hair growth, itching, dryness due to epidermal growth factor receptor inhibitors syndrome.[5] Therefore, dermatologic toxicities may eventually result in poor patient's compliance, more dose delays, and interruptions or discontinuation of therapy.[6]

EGFR is physiologically expressed in epithelial tissues and hair follicles, stimulating the epidermal proliferation, differentiation, and hair growth. The interference with the follicular and interfollicular epidermal-growth signaling

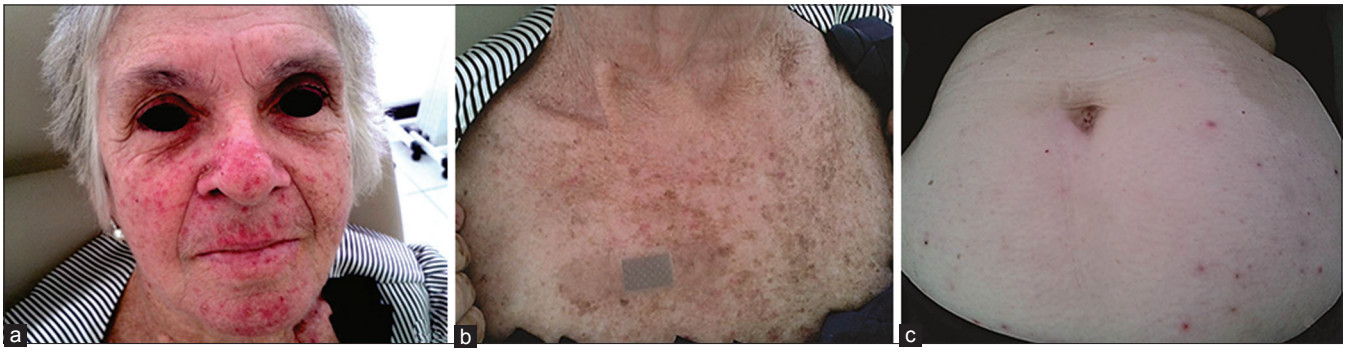

Figure 1: Clinical manifestation of acneiform eruption. (a) Papulopustular eruption on face, (b) thorax, (c) abdomen

pathway is considered critical for the development of cutaneous reactions[7] and may help to explain the papulopustular reaction of the patient in the present case. However, it has been suggested,[8] as in the present case, that skin rash is a suitable surrogate marker for efficacy of anti-EGFR therapy, with a positive association between clinically graded skin toxicity and patient-reported outcome, quality of life, longer progression-free survival, and overall survival.

Appropriate treatment of severe dermatologic toxicities prevents infectious sequelae and septic death,[4] but to the best of our knowledge, only one standard guideline was published so far.[5] As in the present case, topical and systemic treatment with clindamycin and tetracycline, respectively, as well as use of sunscreen in exposed areas, seems to be an effective therapy for Grade 3 panitumumab-induced acneiform rash. Although some authors have indicated reducing the dose of panitumumab in severe dermatologic reactions,[9] it is possible that this type of practice has a negative influence on the treatment outcomes. Reducing the dose of antibodies or discontinuing therapy seems to be the best approach in cases of worsening or no improvement of symptoms or life threatening.[5] In summary, at the first signs of cutaneous reactions, patients should be referred to the dermatologist for a proper diagnosis and management.

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