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Acneiform Eruption in a Patient Receiving Bevacizumab for Glioblastoma Multiforme

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Bevacizumab, a humanized monoclonal antibody targeting vascular endothelial growth factor (VEGF), is used in the treatment of several cancers, macular degeneration, and proliferative diabetic retinopathy as a means of limiting angiogenesis, a hallmark feature of these diseases. Nonspecific skin eruption has been reported in some patients receiving bevacizumab, and recently, bevacizumab-associated acneiform eruption was reported in the treatment of colon cancer (systemic administration) and macular degeneration (intravitreal administration).¹⁻³ The eruption in these patients was strikingly similar to that characterized in patients treated with epidermal growth factor receptor (EGFR) inhibitors.¹⁻⁴ We report a case of bevacizumab-induced acneiform eruption in a patient with glioblastoma multiforme.

Report of a Case

We describe a 39-year-old white man with glioblastoma multiforme that recurred despite treatment with surgical excision, temozolomide, and irradiation. Bevacizumab was administered as salvage therapy. Ten days after the initial intravenous infusion of bevacizumab, 1000 mg, the patient developed an asymptomatic eruption of 2- to 5-mm follicular-based erythematous papules and pustules on the chest and back (**Figure**). Coincidentally, the patient was receiving treatment with rituximab and radiation therapy for B-cell lymphoma of the mediastinum. The patient had been treated with systemic corticosteroids for longer than 2 years and had never reported any skin eruption. Other medical history and medications were noncontributory.

Comment

Reports suggest that the bevacizumab-associated eruption strongly resembles the characteristic acneiform eruption seen in patients treated with EGFR inhibitors.¹⁻³ However, in the case of bevacizumab, the pathophysiologic characteristics of this cutaneous reaction are poorly understood. Current theories speculate that a blockade of EGFR signaling in the skin and hair follicles results in subsequent abnormal differentiation and proliferation (EGFR is a growth factor for the epidermis and epidermal appendages).⁴ Recently, it has been shown that VEGF is a growth factor for follicular cells and keratinocytes as well as endothelial cells; therefore, it is possible that the skin eruption associated with bevacizumab may occur by a similar mechanism to that of the EGFR inhibitor-associated eruption.⁵

The association between increased overall survival and acneiform eruption in patients receiving EGFR inhibitors is well documented, leading to the proposal that the eruption is an

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indication of response to the drug.⁴ Interestingly, it has been proposed that as with the EGFR inhibitors, a correlation may also exist in the case of VEGF inhibitors. In the 3 reported cases of follicular eruption associated with bevacizumab that we found in the literature, the authors proposed that improvement of the patients' disease was related to the development of the eruption.¹⁻³

Accounts of cutaneous reactions to VEGF inhibitors are limited; nonetheless, reports describe an acneiform eruption that bears remarkable similarity to that seen with EGFR inhibitors. In the present case of bevacizumab-associated acneiform eruption, the patient was receiving treatment for glioblastoma multiforme. Future studies evaluating the incidence of acneiform eruption, the presence of an association with response to treatment and prognosis, and mechanisms underlying the development of the eruption should provide us with clinically significant information in the treatment of cancer with this relatively novel therapeutic agent.

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Figure.
Follicular-based erythematous papules and pustules concentrated on the patient's shoulder.