

## Bevacizumab-associated Sudden Onset of Multiple Monomorphic Comedones on the Scalp Successfully Treated with 30% Salicylic Acid Peels

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**ABSTRACT** Bevacizumab is a humanized monoclonal antibody against vascular endothelial factor (VEGF) that targets tumor cell angiogenesis and proliferation. Although it is usually well tolerated, many side-effects have been reported. These include hypertension, bleeding, and thromboembolic events among others. Drug-associated cutaneous adverse effects are less common and include itching, exfoliative dermatitis, and acneiform eruptions. A man with bevacizumab-associated monomorphic skin eruption successfully was treated with 30% salicylic acid peels. To the author's knowledge, this is the first report of open comedones with no further inflammatory acne lesions that developed in a patient treated with bevacizumab. Complete remission of the rash was achieved after performing 30% salicylic peels, and the patient continued the chemotherapy as planned with no need of either dose reduction or discontinuation of bevacizumab.

**KEY WORDS:** acne, chemical peelings, drug rash

### INTRODUCTION

Bevacizumab is a recombinant humanized monoclonal antibody that targets vascular endothelial growth factor (VEGF). It has been approved for the treatment of advanced non-small cell lung cancer, breast cancer, colorectal cancer, and renal cell carcinoma (1). The most commonly observed adverse events are mucosal bleeding, stomatitis, thromboembolism, and disturbed wound healing (2). Cutaneous reactions are limited and typically include itching, exfoliative dermatitis, skin dryness, and acneiform skin rash resembling that seen after the administration of epidermal growth factor receptor (EGFR) antagonists

(3-5). We report a case of sudden onset of multiple monomorphic open comedones on the scalp in a patient diagnosed with metastatic lung cancer who was recently started on bevacizumab. The patient was consequently treated with repeated 30% salicylic acid (SA) peels until complete disappearance of the skin lesions.

### CASE REPORT

A 56-year-old man with a history of hypertension and hyperlipidemia was diagnosed with lung ad-



**Figure 1.** Initial clinical presentation revealed monomorphic open comedones.

enocarcinoma and supraclavicular and mediastinal lymph nodes metastasis in June 2014. He was started on treatment with carboplatin, pemetrexed, and bevacizumab. After three months in treatment and the third cycle of chemotherapy, the patient developed rapidly progressive lesions on the scalp.

Physical examination revealed multiple monomorphic open comedones on the scalp and forehead (Figure 1). There were no inflammatory nodules, papules, or pustules. Further physical examination was unremarkable.

The patient was treated with 5 sessions of 30% SA peel every 15 days. He continued the chemotherapy with no dose interruption. Clinical photographs were taken to assess the response. Significant improvement was observed even after the first treatment (Figure 2). Complete remission was achieved after the third session, and we performed two more sessions post resolution of the skin lesions (Figure 3). After 3 month follow-up, no recurrence was observed.

## DISCUSSION

Vascular endothelial growth factor is a highly specific mitogen for vascular endothelial cells and the major driver of tumor angiogenesis described to date (6). It induces endothelial proliferation, promotes cell migration, and inhibits apoptosis. Consequently, inhibition of VEGF signaling abrogates the development of a wide variety of tumors through reduction of the number of the endothelial cells and the quantity of micro-capillaries in the tumor tissue (3).

Several therapies that target specific components of the VEGF signaling pathway have been approved for clinical use. Bevacizumab (a humanized VEGF monoclonal antibody) received its first approval in 2004 for combination use with standard chemother-



**Figure 2.** Significant improvement after the first treatment with 30% salicylic acid peel.

apy for metastatic colon cancer and has since then been approved for use in lung, renal, and ovarian cancers (7). Its use has been reported in dermatologic conditions such as metastatic melanoma (8), keratitis-ichthyosis-deafness syndrome, and cutaneous angiomatosis with thrombocytopenia syndrome (9).

Although bevacizumab is generally well tolerated, many side-effects have been reported, such as hypertension, hemorrhage, thromboembolic events, congestive heart failure, impaired wound healing, and infusion-related hypersensitivity reactions (2,10). In comparison with anti-EGFR monoclonal antibodies, bevacizumab causes less frequent and less severe cutaneous side-effects. These include itching, exfoliative dermatitis, skin dryness, and acneiform skin rash. Recently reported cutaneous manifestations include cutaneous lupus erythematosus, hand eruption, scalp ulceration, and perforating dermatosis (11).

There are reports in the literature describing the occurrence of acneiform skin rash after the infusion of bevacizumab, which mainly consisted of papules, pustules, and inflammatory nodules (4,5). Sometimes comedonal lesions were also present. It has been shown that VEGF is a growth factor for follicular cells and keratinocytes in addition to endothelial cells



**Figure 3.** Complete remission after the third 30% salicylic acid peel.

(12). Therefore, we can speculate that the skin eruption described may occur by follicular obstruction and subsequent inflammation through a mechanism similar to that in EGFR inhibitor drug associated rash. This typically acneiform rash was usually treated with topical or oral antibiotics and topical retinoids (13). In the present case, our patient had a unique clinical presentation with multiple monomorphic open comedones on the scalp and forehead, and no further inflammatory acne lesions were observed, as would be expected in rashes after the administration of VEGF or EGFR inhibitor drugs.

Since SA has proven effective in comedonal acne, and no inflammatory lesions were present, we decided that it would be the preferred treatment for our patient. SA is a lipophilic beta-hydroxy acid possessing keratolytic, comedolytic, anti-inflammatory, and antibacterial properties. At concentrations between 20% and 30%, it is used for superficial chemical peels and removes intercellular lipids that are covalently linked to the cornified envelope surrounding cornified epithelioid cells (14). Its indications include acne vulgaris, melasma, post inflammatory hyperpigmentation, and photoaging. There is a recent study that presented repeated SA peels as an alternative treatment for sebaceous hyperplasia (15). The effects of salicylic acid above described may be responsible for the extremely satisfactory results of the 30% SA peels in the successful treatment of the multiple open comedones of our patient without requiring discontinuation of bevacizumab.

## CONCLUSION

To the best of our knowledge, monomorphic open comedones have not been described before as the only cutaneous manifestation in a patient treated with bevacizumab. We propose a successful therapeutic approach with SA peels.

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