BRIEF ARTICLES

Cetuximab Induced Hidrocystomas: A Case Report

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ABSTRACT

Cetuximab is an epidermal growth factor receptor (EGFR) inhibitor that commonly results in follicular-based acneiform eruptions. EGFR is expressed in the epidermis, hair follicle epithelium, sweat gland apparatus, and plays an important role in the differentiation and development of the hair follicle. In this report we describe a 70-year-old man who developed an acneiform eruption on his nose, cheeks, neck, and back when cetuximab was started for metastatic colorectal carcinoma. This initial eruption improved with cessation of cetuximab but left residual cystic papules on his nose and multiple superficial white cysts on his bilateral cheeks, neck and back. Skin biopsy of a representative lesion on the nose revealed a cyst-like cavity lined with epithelium similar to sweat glands within the dermis consistent with a hidrocystoma. In this case, it is plausible that the use of an EGFR inhibitor resulted in a cutaneous inflammatory reaction, that subsequently healed with blockage of the sweat duct apparatus causing the formation of cutaneous cysts, including both hidrocystomas and milia. Alternatively, the blockage of the duct may have resulted from inhibition of basal cell migration and increased cell adhesion within the eccrine gland causing accumulation of eccrine gland secretion, and eventually hidrocystomas. To our knowledge, this is the first case describing the resolution of a typical cetuximab-induced acneiform eruption with residual hidrocystomas and milia.

INTRODUCTION

Cetuximab is an IgG1 chimeric monoclonal antibody targeting epidermal growth factor receptor (EGFR) that is approved to treat several malignancies, including colorectal cancer and squamous cell carcinoma of the head and neck. Cutaneous reactions are the most commonly reported adverse effects, with acneiform eruptions being reported most frequently. We present a case of an elderly woman that developed an acneiform eruption following the start of cetuximab therapy as part of a polychemotherapy regimen for treatment of colorectal cancer. To our knowledge, this is the first case describing the resolution of the typical cetuximab-induced acneiform eruption that resulted in residual hidrocystomas on the nose and milia on the cheeks, neck, and back.

CASE PRESENTATION

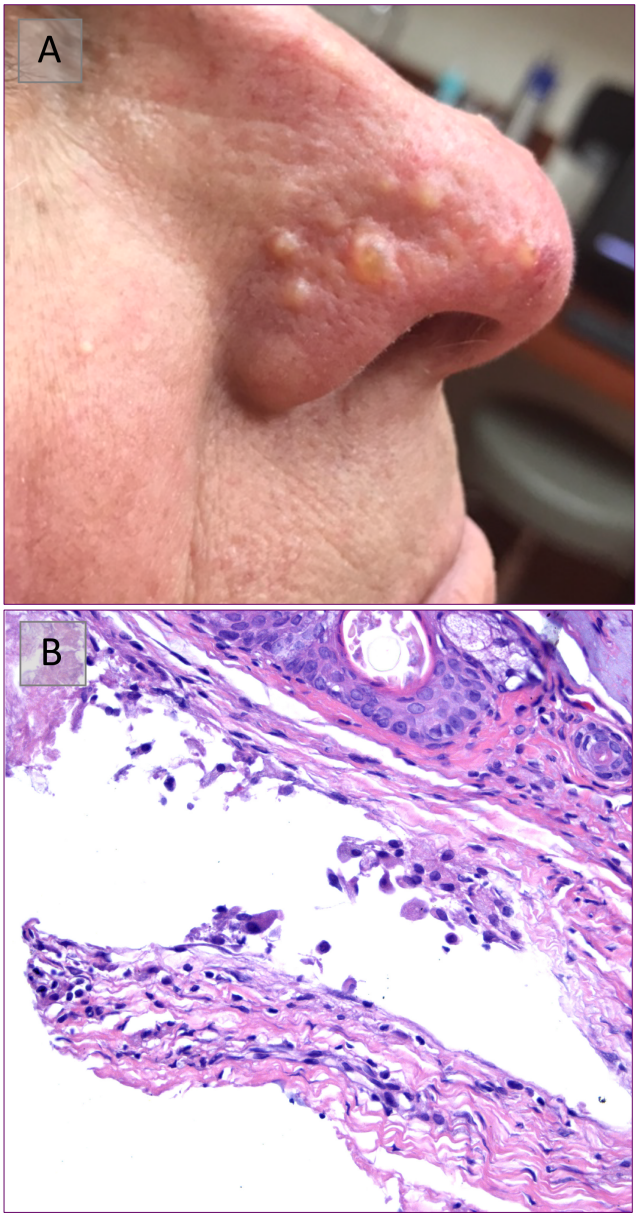
A 70-year-old man presented with an eruption on his nose, cheeks, neck, and back that had been present for one year. His medical history was significant for metastatic

colorectal carcinoma treated with a polychemotherapy regimen, which included cetuximab. When starting therapy with cetuximab, the patient developed an acneiform eruption that improved with cessation of cetuximab but left residual cystic papules on his nose (Figure 1A) and multiple superficial white cysts on his bilateral cheeks, neck and back. A punch biopsy of the nose revealed a cyst-like cavity lined with epithelium similar to sweat glands within the dermis consistent with a hidrocystoma (Figure 1B).

DISCUSSION

Cetuximab is a chimeric IgG1 monoclonal antibody that targets the epidermal growth factor receptor (EGFR) and is indicated for the treatment of various cancers. EGFR is expressed in the epidermis, hair follicle epithelium, sweat gland apparatus, and plays an important role in the normal differentiation and development of the hair follicle.[1] Consequently, EGFR inhibitors commonly result in cutaneous adverse effects, the most frequent being a follicular-based acneiform eruption that commences within a few weeks of initiating treatment and resolves either within 4 weeks after cessation of treatment or at some point during maintenance therapy.[2,3] The acneiform eruption is speculated to be due to inhibition of EGFR on keratinocytes in the basal layer of the epidermis which induces premature cellular differentiation , arrest of cell growth, reduced cell migration, and subsequent apoptosis.[4] Additionally, EGFR inhibition induces altered chemokine expression on keratinocytes resulting in increased skin inflammation.[5] On histology, the stratum corneum decreases in thickness, loses the basket weave appearance, and in some cases may reveal parakeratosis.[3] Pustule formation can also be seen within sweat glands and hair follicles, which might be infectious or sterile.[3]

Figure 1. (A) Multiple yellowish cystic papules on the right nasal ala. **(B)** Cyst-like cavity lined with epithelium within the dermis consistent with a hidrocystoma.



Hidrocystomas are benign cystic lesions of the sweat ducts that can arise in apocrine or eccrine glands. Apocrine hidrocystomas typically present as skin-colored to bluish solitary papules, ranging in size from 3 to 15

mm.[6] These typically have a predilection for the head and neck, but commonly present on the inner canthi. Apocrine hidrocystomas are thought to be caused by benign adenomatous cystic proliferations of the apocrine glands. [1] Conversely, eccrine hidrocystomas can range in size from 1-6 mm and either present as solitary dome-shaped papules with a brownish or bluish hue, or as multiple confluent skin-colored papules confined to the periorbital and malar regions.[6] The pathogenesis has been related to blockage of the sweat duct causing dilation of the cystic excretory eccrine glands and retention of sweat.[6]

In this case, it is plausible that the use of an EGFR inhibitor resulted in a cutaneous inflammatory reaction, that subsequently healed with blockage of the sweat duct apparatus causing the formation of cutaneous cysts, including both hidrocystomas and milia. Alternatively, the blockage of the duct may have developed due to inhibition of basal cell migration and increased cell adhesion within the eccrine gland causing accumulation of eccrine gland secretion, and eventually hidrocystomas.

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