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.
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. 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. 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. Additionally, EGFR inhibition induces altered chemokine expression on keratinocytes resulting in increased skin inflammation. On histology, the stratum corneum decreases in thickness, loses the basket weave appearance, and in some cases may reveal parakeratosis. Pustule formation can also be seen within sweat glands and hair follicles, which might be infectious or sterile.

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.
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. 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. The pathogenesis has been related to blockage of the sweat duct causing dilation of the cystic excretory eccrine glands and retention of sweat.

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.

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:
Nicole Nagrani, BS
Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery
University of Miami Miller School of Medicine
1600 NW 10th Ave
RMSB 2023A, Miami, FL 33136
Email: nanagranin@upstate.edu

References: