

Case Report

Erosive pustular dermatosis of the scalp following cetuximab

使用西妥昔單抗後，出現糜爛膿皰性頭皮皮膚病一例

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Cetuximab is a monoclonal antibody that directly inhibits the epidermal growth factor receptor and thus inhibits cell proliferation, angiogenesis and potential metastases whilst promoting apoptosis. Cutaneous reactions are a well documented side effect from the use of epidermal growth factor receptor inhibitors, with a positive relationship established between the severity of the cutaneous adverse reaction and the efficacy of cetuximab. We present a case of 51-year-old male who, after three months use of cetuximab for metastatic colon cancer, presenting with erosive pustular dermatosis of the scalp (EPDS) that improved with the combination of potent topical steroids and oral antibiotics. This is the first recorded presentation of EPDS in association with cetuximab.

西妥昔單抗是一種單克隆抗體，直接抑制表皮生長因子受體，從而抑制細胞增殖、血管生成及轉移的潛力，同時促進細胞凋亡。皮膚反應是使用表皮生長因子受體抑制劑的公認副作用，而西妥昔單抗的功效和皮膚不良反應的嚴重程度有著正相關關係。我們詳述一個五十一歲的男病人，在使用西妥昔單抗治療轉移性結腸癌三個月後，出現糜爛膿皰性頭皮皮膚病，隨著使用強效外用類固醇和口服抗生素組合後，情況得到改善。這是第一次紀錄到糜爛膿皰性頭皮皮膚病與使用西妥昔單抗的關聯。

Keywords: Cetuximab, erosive pustular dermatosis of the scalp

關鍵詞：西妥昔單抗、糜爛膿皰性頭皮皮膚病

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Case report

Cutaneous reactions are well-documented side effects of the epidermal growth factor receptor (EGFR) inhibitors. We present a case of 51-year-old male who was reviewed in the dermatology department after referral from the medical oncology team. The patient was being treated for metastatic colorectal carcinoma (Stage IV sigmoid colon cancer) and had previously undergone surgical resection and subsequently yttrium microsphere implantation for liver metastasis. Cetuximab had been commenced for three

months to control his disease progression recently. Following commencement of cetuximab, he developed an acneiform reaction on his face which responded well to oral minocycline. However, some crusted lesions began to develop on his scalp which oozed or bled with mild trauma. The lesions were first noticed one month after commencement of cetuximab.

On examination, the patient, with pre-existing Hamilton type IV male pattern baldness, had widespread grey crusts with underlying pus over the frontal and vertical aspects of his scalp (Figure 1). The presentation of the lesions was consistent with a clinical diagnosis of erosive pustular dermatosis of the scalp (EPDS). A biopsy revealed that most of the epidermis was absent and had been replaced by a thick inflammatory crust composed of fibrin and large numbers of neutrophils. Many pityrosporum-like spores were present and mixed with the inflammatory debris. The underlying dermis showed inflamed and ruptured hair follicles associated with formation of a superficial abscess (Figures 2 & 3). Swabs of the pus revealed *Staphylococcus aureus*. The scalp was gently debrided revealing a raw, erythematous base which oozed blood-stained exudate.



Figure 1. Patient with erosive pustular dermatosis of the scalp on initial presentation.

The patient was treated with Diprosone OV cream® (betamethasone dipropionate 0.05% cream) and oral cephalexin with continuation of his oral minocycline (100 mg BD) and daily dressing changes. After two weeks of therapy, the patient continued to improve (Figure 4). In association with the medical oncology team, the decision was made to continue with cetuximab therapy, with further debridement of his scalp for the remaining

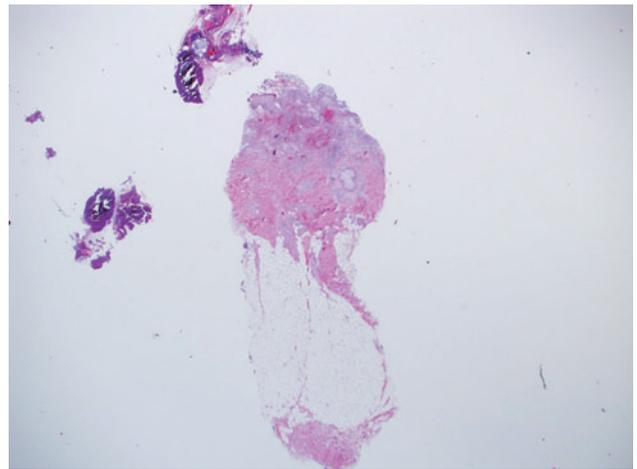


Figure 2. Low power view of a punch biopsy showing an ulceration (or ulcerations) and underlying inflammation, and separate fragments of inflammatory scale crust.

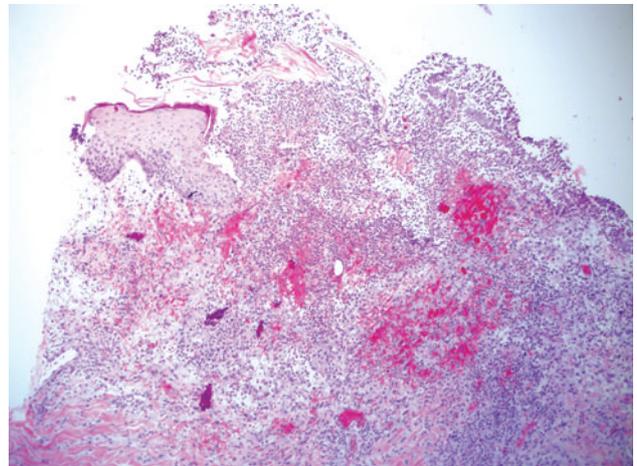


Figure 3. High power view showing an area of relatively discrete ulceration with dense mixed inflammatory infiltrate extending into the dermis.

regions. However, after four months of treatment and debridement, the patient relapsed with recurrence of pustules and crusted lesions (Figure 5). A regime of gentle soaking with mechanical debridement was continued with the addition of topical clindamycin and oral rifampicin. A better outcome (Figure 6) was observed.

Discussion

Cetuximab is a recombinant immunoglobulin G1 (IgG1) monoclonal antibody to the ligand binding domain of EGFR. It inhibits the proliferation of cells that depend on EGFR for growth.¹ Binding to the EGFR blocks phosphorylation and activation of receptor-associated kinase which results in a decreased number of receptor target and thus inhibits cell proliferation, angiogenesis and metastasis whilst promoting apoptosis.² EGFR inhibitors are especially effective against tumours that overexpress EGFR including colorectal, breast, pancreatic, non-small cell lung cancer and squamous cell carcinoma of the head and neck.³

Skin reactions are very common side effects of cetuximab therapy with rates of up to 86% for patients in some series developing an acneiform rash.⁴ A small phase II trial (n=10) for the use of cetuximab as monotherapy for renal cell carcinoma gave an even higher response of 100% for a pustular acneiform reaction.⁵ Such is the significance of the skin reaction to cetuximab, it was observed in a multicentre phase II trial which indicated that the more pronounced the skin reaction (CTCAE V3.0 Grade 2 and 3), the greater response to treatment, when compared to Grade 1. Of note, nil response to EGFR inhibition was noted in those without a skin reaction.⁶

Similar presentations have been reported in other EGFR inhibitors (gefitinib, lapatinib, and erlotinib). In a comprehensive review, Toda et al⁷ found 11 other cases of alopecia associated with EGFR inhibitors with various presentations including two EPDS-like cases due to gefitinib.^{7,8} These two cases, in Toda's series,⁷ had EPDS with concomitant



Figure 4. Patient's scalp – 2 weeks post gentle debridement and application of potent topical steroid cream.



Figure 5. Presentation following relapse.



Figure 6. Patient's scalp after treatment with Diprosone OV ointment, topical clindamycin and rifampicin.

S. aureus colonisation whilst Wu et al did not find any *S. aureus* colonisation in their patient who had previous radiotherapy to the scalp.⁸

EPDS is a condition that is normally associated with areas of scarring alopecia which are either actinically damaged, atrophic, associated with trauma,⁹ or a combination of the above with the development of sterile pustules, erosions and crusted lesions on the scalp. It has also been reported in association with a wide range of conditions such as herpes zoster,¹⁰ myasthenia gravis¹¹ and Klippel-Feil syndrome,¹² although the actual mechanism is still unclear. The histology of classic EPDS depends on the structure of the epidermis and whether it is ulcerated. Any remaining epidermis is likely to be atrophic. A mixed dermal infiltrate consisting of lymphocytes, plasma cells and neutrophils can be present. In areas of follicular destruction, foreign body giant cells may be present.¹³ Whilst EGFR is expressed within the basal keratinocytes and outer root sheath of the hair and is turned on and off during the hair cycle,⁷ this mechanism would not lead to the inflammatory changes noted. It would therefore need to be considered that the administration of cetuximab has caused some disruption to the scalp and follicular unit combined with existing photo-damage/ageing that may have allowed the erosive changes due to *S. aureus* infection to occur.

Conclusion

This is believed to be the first report of erosive pustular dermatosis of the scalp as a reaction to the use of cetuximab as monotherapy although it has previously been reported in other EGFR inhibitors, either as monotherapy or used in conjunction with radiotherapy. Due to the high prevalence of skin reaction resulting from EGFR inhibitors where cutaneous toxicity appears to reflect efficacy, the ability to appropriately treat and thus manage cutaneous side effects should not preclude their use, but

instead should ensure a prompt referral for dermatology intervention as part of a multidisciplinary management.

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