Case Report

Erosive Pustular Dermatosis of the Scalp Due to Afatinib: A Rare Case

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Abstract

Afatinib is a tyrosine kinase inhibitor that irreversibly targets the epidermal growth factor receptor and is commonly associated with cutaneous adverse effects such as acneiform eruptions and paronychia. However, scalp involvement has rarely been reported. We present a case of a 57-year-old woman with stage IVA lung cancer who developed thick, yellowish scalp crusts without pain or itch, seven months after initiating afatinib therapy. Clinical, trichoscopic, microbiological, and histopathological examinations confirmed a diagnosis of erosive pustular dermatosis of the scalp (EPDS). Despite treatment with systemic corticosteroids and antibiotics, significant improvement was only observed after dose reduction and eventual discontinuation of afatinib. This case highlights a rare but important adverse effect of afatinib on the scalp, emphasizing the need for clinicians to recognize and manage EPDS early in patients receiving this therapy.

Keywords: Afatinib, scalp, dermatosis, adverse event, EPDS.

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Introduction

Epidermal growth factor receptor (EGFR) inhibitors are commonly used to treat epithelial malignancies.[1] The development of EGFR tyrosine kinase inhibitors (TKIs) has brought new perspectives in managing advanced non-small cell lung carcinoma (NSCLC) with EGFR mutations. While these therapies are better tolerated than traditional chemotherapy, they have distinct side-effect profiles linked to their mode of action. Since the EGFR plays a crucial role in the skin, nails, and hair, dermatologic side effects are frequently observed with EGFR inhibitor usage.[1]

Afatinib is an irreversible second-generation inhibitor of the ErbB receptor family that targets the tyrosine kinase activity of EGFR and its associated dimers. Although being used as first-line treatment for NSCLC, afatinib may cause side effects similar to other EGFR inhibitors, particularly affecting the gastrointestinal tract and skin. This is attributed to the presence of EGFR in basal epidermal cells, hair follicles, sebaceous glands, and the outer root sheath. Inhibition of EGFR causes a cascade of cellular events, promoting cutaneous adverse events such as rash/acne, dry skin, pruritus, and paronychia. Although these adverse events are commonly mild to moderate in severity, they may cause non-compliance and drug discontinuation.[2]

While cutaneous side effects are common afatinib use, to our knowledge, there is lack of discussion about side effects of afatinib on the scalp. Here, we present a case of erosive pustular dermatosis of the scalp (EPDS) induced by afatinib, which immediately resolved after its discontinuation.

Case Report

A 57-year-old woman with adenocarcinoma cell type lung cancer with T4N3M1b staging IVA, positive exon 19 mutation, and bone metastasis

presented with complaints of thick scabs on her scalp for the past 7 months. The patient had been on afatinib 40 mg daily for the past 10 months. The initial complaint appeared as red bumps on the scalp that later burst and became wounds and scabs. This was accompanied by yellowish fluid that dried on the scalp. The symptoms were neither painful nor itchy. The patient also reported hair loss that did not regrow. She also denied any trauma to the scalp, radiation therapy history, and family history of such complaints.

The dermatological examination of the scalp showed erythematous macules with indistinct borders, erosion, and yellow crusts with pus on top. Blood was also seen in some areas (Figure 1).

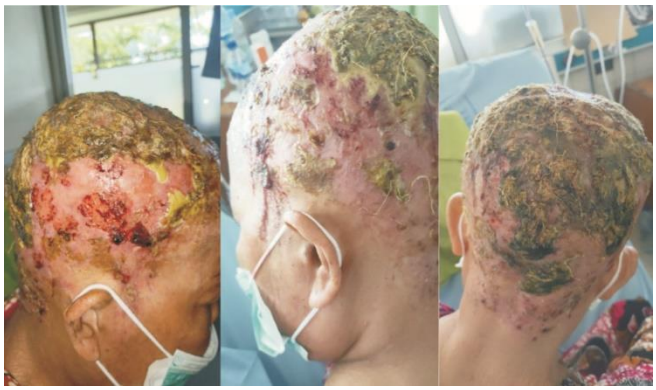

Figure 1: *Clinical manifestation from first visit.*

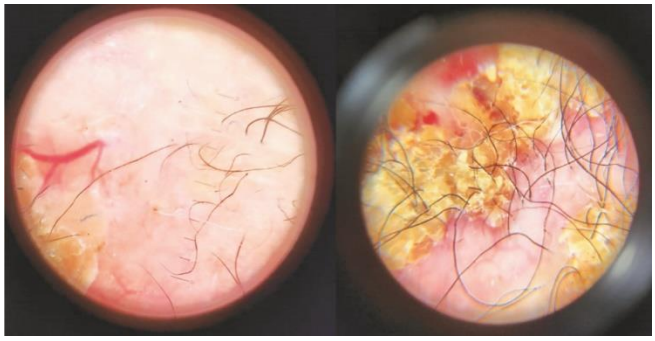

Figure 2: *Trichoscopy examination.*

Laboratory tests revealed low hemoglobin (5.4 g/dl) and elevated leukocytes 19,370 /uL. A Gram examination of the scalp pus showed many leukocytes. Pus culture was positive for *Staphylococcus aureus*. A dermoscopy examination revealed a lack of follicular ostia, thick yellow follicular exudate, and prominent telangiectasis (Figure 2). Histopathological examination showed atrophic epidermis and flattened rete ridges, with no visible subcorneal blisters. The dermis layer was edematous with neutrophil and lymphocyte infiltration (Figure 3).

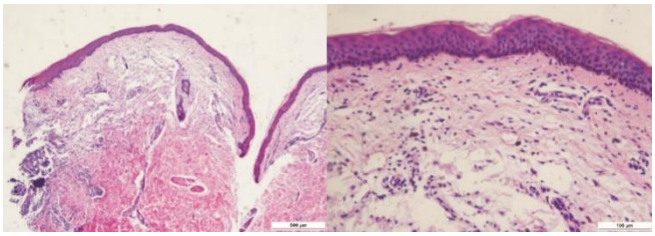

Figure 3: *Histopathology examination*

The patient was then diagnosed with EPDS. The patient was treated with saline compresses, ceftriaxone injection 2x1 gram, fusidic acid cream twice daily, desoximethasone ointment twice daily, and oral 20 mg methylprednisolone. After 2 weeks on this regimen, no improvement was observed, with persistent wounds and thick scabs on the scalp. The afatinib dose was then reduced to 1×20 mg. After one month, there was clinical improvement in the patient's scalp, with thinning of the scabs and no new red nodules (Figure 4A). Eventually, afatinib was discontinued and by the second month, there was a resolution of the scalp symptoms, leaving scarring alopecia (Figure 4B).

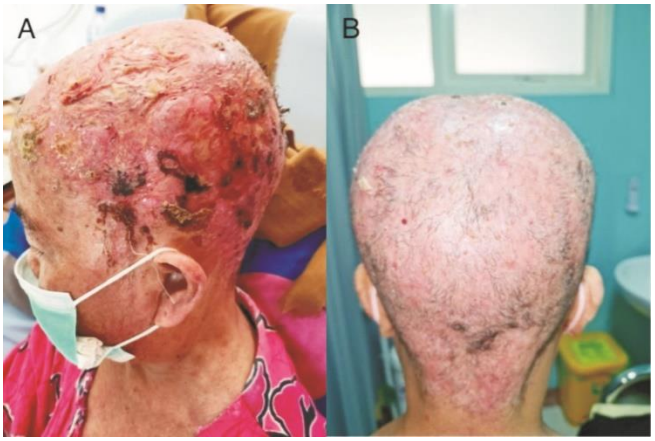

Figure 4: ***A:*** *Clinical features after one month of conventional treatment and afatinib dose reduction.* ***B:*** *complete resolution discontinuation of afatinib.*

Discussion

Erosive Pustular Dermatosis of the Scalp

EPDS is a rare inflammatory condition of the scalp that predominantly affects mature individuals, with the onset at 60-70 years. It is characterized by erosions, thick yellowish crust, and pustules leading to scarring alopecia. EPDS is an underappreciated mimicker of many cutaneous disorders of the scalp with clinical symptoms frequently mistaken for infection, inflammation, and malignancy. Due to its rarity, the real incidence of EPDS is unclear.[3,4] Scalp, especially the vertex, is the most commonly affected area; although EPDS has also been reported on the face and legs.[5]

Although the etiopathogenesis of EPDS remains unclear, predisposing factors such as actinic damage and epidermal atrophy have been identified.[8] EGFR inhibitors like afatinib, interfere with the normal hair cycle from anagen to telogen phase, and enhance ultraviolet (UV)-induced.[5] This disruption leads to loss of immune privilege within the hair follicle environment, promoting inflammatory responses, cell death, and follicular ducts blockage, which may result in follicular rupture.[5]

EPDS is marked by chronic inflammation involveing a diverse cellular infiltrate composed of neutrophils, lymphocytes, and plasma cells. Neutrophilic spongiosis commonly affects the follicular infundibula, especially in regions surrounding ulcerated areas.[5,6] Unlike other inflammatory dermatoses, EPDS is distinguished by a continuous influx of immune cells into previously damaged scalp tissue, which perpetuates the formation of vesicopustules within hair follicle openings. This persistent process leads to erosion, crust development, granulation tissue, and ultimately scarring alopecia. As the disease progresses, increasing fibrosis contributes to the destruction of hair follicles and sebaceous glands, culminating in epidermal thinning and the complete loss of skin appendages.[7]

Diagnosis

Scalp examination typically reveals multiple extensive erythematous erosions with crusting, surrounded by pustules and serous discharge, primarily in alopecic areas, especially the vertex. Lesions may be covered by exuberant granulation tissue and are often symptomatic, with pain, pruritus, or burning.[4] Lesions will undergo a repeated cycle of healing and recurrences with a fluctuating course over months to years, and without improvement even after topical corticosteroid treatment. Progressive involvement leads to skin atrophy with peripheral extension of pustules and erosions, eventually resulting in cicatricial alopecia if left untreated.[7] This was in line with our case as large erosive, yellowish-crusted patches with pustules occurred in areas around the vertex and extended to parietal and occipital. This had lasted for several months and was unresponsive to treatment, causing cicatrical alopecia.

As EPDS can mimic other scalp diseases, additional examinations are necessary. General serologic tests lack specificity for EPDS. Our patient exhibited low hemoglobin levels, high white blood cells, low albumin levels, and electrolyte imbalances, though their correlation with EPDS severity remains unclear. Mycological and bacterial examinations were performed to exclude infection. KOH examination was negative for fungi, while Gram examination revealed gram-positive cocci. A cutaneous swab for culture confirmed *Staphylococcus aureus*, consistent with previous reports of frequent secondary bacterial colonization in EPDS, especially *Staphylococcus aureus*.[7, 8]

Generally, EPDS may lack specific and pathognomonic histopathological findings. However, a biopsy is essential to rule out differential diagnosis that may mimic EPDS.[6] Histopathological features of EPDS can vary depending on the disease stage. In early lesions, the epidermis may exhibit orthokeratosis and mild psoriasiform hyperplasia, with the dermis showing a mixed inflammatory infiltrate composed of neutrophils, lymphocytes, and plasma cells, accompanied by mild fibrosis. Intermediate-stage lesions often present with parakeratosis, more pronounced psoriasiform hyperplasia, and moderate dermal fibrosis, with a reduction in sebaceous glands and hair follicles. In late-stage EPDS, histology typically reveals compact orthokeratosis, significant epidermal atrophy, sev-

ere dermal fibrosis, and a marked decrease or absence of hair follicles and sebaceous glands. In our patient's scalp biopsy, we observed an atrophic epidermis with flattened rete ridges and an edematous dermis infiltrated by neutrophils and lymphocytes. Although these findings are characteristics of EPDS, the presence of epidermal atrophy in an early-stage lesion is atypical.[8] No subcorneal blisters were observed, and the dermal layer was edematous with neutrophils and lymphocytes infiltration. Although our patient was still in the early stage of the disease, we found epidermal atrophy which commonly occurs in the late stage of the disease. Meanwhile, mixed inflammatory infiltrates were observed in the dermis, which is typical of EPDS although not specific.

In trichoscopic evaluation, EPDS typically presents with follicular keratotic plugs, milky red zones, white patches, twisted hair shafts, and lack of visible follicular openings. The presence of follicular plugging and absent follicular ostia are characteristics of scarring alopecia. White areas and milky red zones are thought to reflect underlying inflammation and fibrotic changes in the scalp. A distinct trichoscopic sign of EPDS is the visible anagen hair bulbs through the thinned, atrophic epidermis. The presence of clear telangiectasis, particularly after detachment of the crust may also indicate EPDS.[6] In line with these findings, this case demonstrated scarce follicular ostia, follicular yellow thick exudate, and prominent telangiectasis.

EPDS and Afatinib

EGFR is notably expressed in hair follicles, especially within the outer root sheath. EGFR activation is essential for promoting cell cycle progression from the G1 to the S phase. Disruption of EGFR signaling hinders the hair follicles transition from anagen to telogen phase. Additionally, EGFR inhibition amplifies UV-induced apoptosis in keratinocytes, as evidenced by higher levels of keratinization markers and the breakdown of intercellular connections, which indicate a compromised barrier. This leads to the loss of immune privilege in hair follicles, triggering inflammatory cascades, apoptosis, ductal blockage, and eventually causing their rupture. Some literature reported EPDS induced by EGFR. A study by Nazzaro et al, and Toda et al, revealed cases of EPDS in lung cancer patients treated with Gefitinib, the first generation of EGFR TKIs.[9] Moreover, Suarez-Valle et al, documented a case of EPDS that developed after 24 months of afatinib therapy. However, the patient was also treated with radiotherapy for 20 months before the onset of the scalp lesions.[10]

Therapy

After initiation of afatinib therapy, patients should be advised to take precautions against cutaneous adverse events. Due to its rarity, there are no established treatment guidelines for afatinib-induced EPDS. For acneiform eruption induced by afatinib, the treatment depends on the severity. Patients presenting with grade 3 or severe grade 2 dermatologic adverse events may undergo a temporary interruption of afatinib therapy. Meanwhile, management of EPDS primarily aims to control inflammation, promote healing of erosive lesions, and prevent the advancement of scarring alopecia. Early initiation of therapy is crucial to reduce the risk of irreversible hair loss. Treatment options may involve systemic or topical corticosteroids, topical tacrolimus, oral or topical retinoids, topical calcipotriol, and silicone gel. In our case, the patient had no improvement after conventional therapies.[4] In treating adverse events with high grades, discontinuation of afatinib may be an option. As in this case, we observed complete resolution after discontinuation of afatinib. This finding is consistent with previous reports of afatinib-induced EPDS, as after afatinib was discontinued, pustules, erythema, and crusts were improved, leaving scarring alopecia.[10]

Conclusion

Herein, we report a rare case of EPDS associated with afatinib therapy. EGFR inhibitor-associated alopecia and EPDS can cause irreversible damage to the hair bulge. In this case, treatment was ineffective until afatinib was discontinued. Early recognition is critical to initiate timely intervention and prevent progressive scalp damage.

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Disclaimer

This case report is not intended to substitute for professional medical advice, diagnosis, or treatment. The authors have obtained patient consent and have taken steps to ensure patient anonymity. Any identifiable information has been omitted or anonymized to protect patient privacy.

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Author's Contribution:

JS: Conceived, designed, edited the manuscript, given final approval of the version to be published, critical revisions.

AA: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

NAP: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

CDR: Manuscript writing, final approval of the version to be published.

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