Dermatology Practical & Conceptual

Folliculitis-Decalvans Like Alopecia During Treatment with EGFR Inhibitors for Lung Cancer: A Case Series of 6 Patients

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Introduction

Epidermal growth factor receptor inhibitors (EGFRi) represent a valid therapeutic option for the treatment of cancers caused by EGFR dysregulation. Skin toxicity is the most common adverse event related to EGFRi, and even though rarely life-threatening, it can seriously affect patients quality of life and their compliance to treatment, often leading to treatment modification or discontinuation [1].

Case Presentation

We report 5 patients developing alopecia during treatment with EGFRi for non-small-cell lung carcinoma (NSCLC) (Table 1). The clinical and trichoscopic presentations mimicked Folliculitis Decalvans (FD) in all patients, with 4 of them presenting a more severe, diffuse and debilitating picture showing erythema, pustules, crusts and patches of scarring alopecia (Figure 1A). The other patients had a milder, less defined areas of alopecia not yet scarring, but with a prominent erythema, telangectasia, casts and scales. Trichoscopy confirmed the clinical picture, highlighting findings as erythema, telangiectasia, scales, haemorrhagic and serum crusts, perifollicular hyperkeratosis and pili torti (Figure 1B). Histology showed keratin aggregation and a dilatation of the infundibulum in combination with numerous intraluminal neutrophils. Sebaceous glands are destroyed early in the process. Additionally, an intrafollicular and perifollicular predominately neutrophilic infiltrate could be found (Figure 2) Based on the clinical, trichoscopic, and

Table 1. Data of patients diagnosed with folliculitis decalvans-like alopecia during treatment with EGFR inhibitors.

Sex Age (years)	Neoplasia	Personal or family history	Oncologic treatment (drug and dosages)	Number of EGFRi cycles	Body areas involved	Trichoscopy	Treatment	Outcome	Impact on oncologic treatment	Relapses
M/57	Lung (NSCLC)	No	Erlotinib at 150 mg once daily + bevacizumab (15mg/Kg every 3 weeks)	1	Face	Absence of follicular ostia, pustules, crusts, severe erythema, perifollicular hyperkeratosis, diffuse desquamation, pili torti	Doxycycline 100 mgx2 and clobetasol 1/day for 1 month	PR	No	Yes
M/62	Lung (NSCLC)	No	Erlotinib at 150 mg once daily + ramucirumab (10 mg/kg every 2 weeks)	2	Face and trunk	Absence of follicular ostia, pustules, crusts, mild erythema, perifollicular hyperkeratosis, diffuse desquamation	Doxycycline 100 mgx2 and clobetasol 17day for 1 month	PR	No	Yes
M/58	Lung (NSCLC)	No	Erlotinib at 150 mg once daily + bevacizumab (15mg/Kg every 3 weeks)	2	Face	Absence of follicular ostia, pustules, crusts, severe erythema, perifollicular hyperkeratosis, diffuse desquamation, hair tufted	Doxycycline 100 mg/day and clobetasol 1/day for 2 months	PR	DR	Yes
M/63	Lung (NSCLC)	No	Gefitinib 250 mg once daily	2	Scalp	Absence of follicular ostia, pustules, moderate erythema, perifollicular hyperkeratosis, diffuse desquamation	Doxycycline 100 mg/day and clobetasol 1/day for 2 months	PR	No	Yes
F/76	Lung (NSCLC)	No	Gefitinib 250 mg once daily	2	Scalp	Vascular ectasia, hair casts, mild keratotic plugs	Ketoconazole shampoo 2-3/ week; doxicicline 100 mg/day for 2 months	PR	No	Yes

CR = complete response; DR = dose reduction; DW = dose withholding; EGFRi = epidermal growth factor receptor inhibitor; NSCLC = non-small-cell lung carcinoma; PD = permanent discontinuation; PR = partial response.

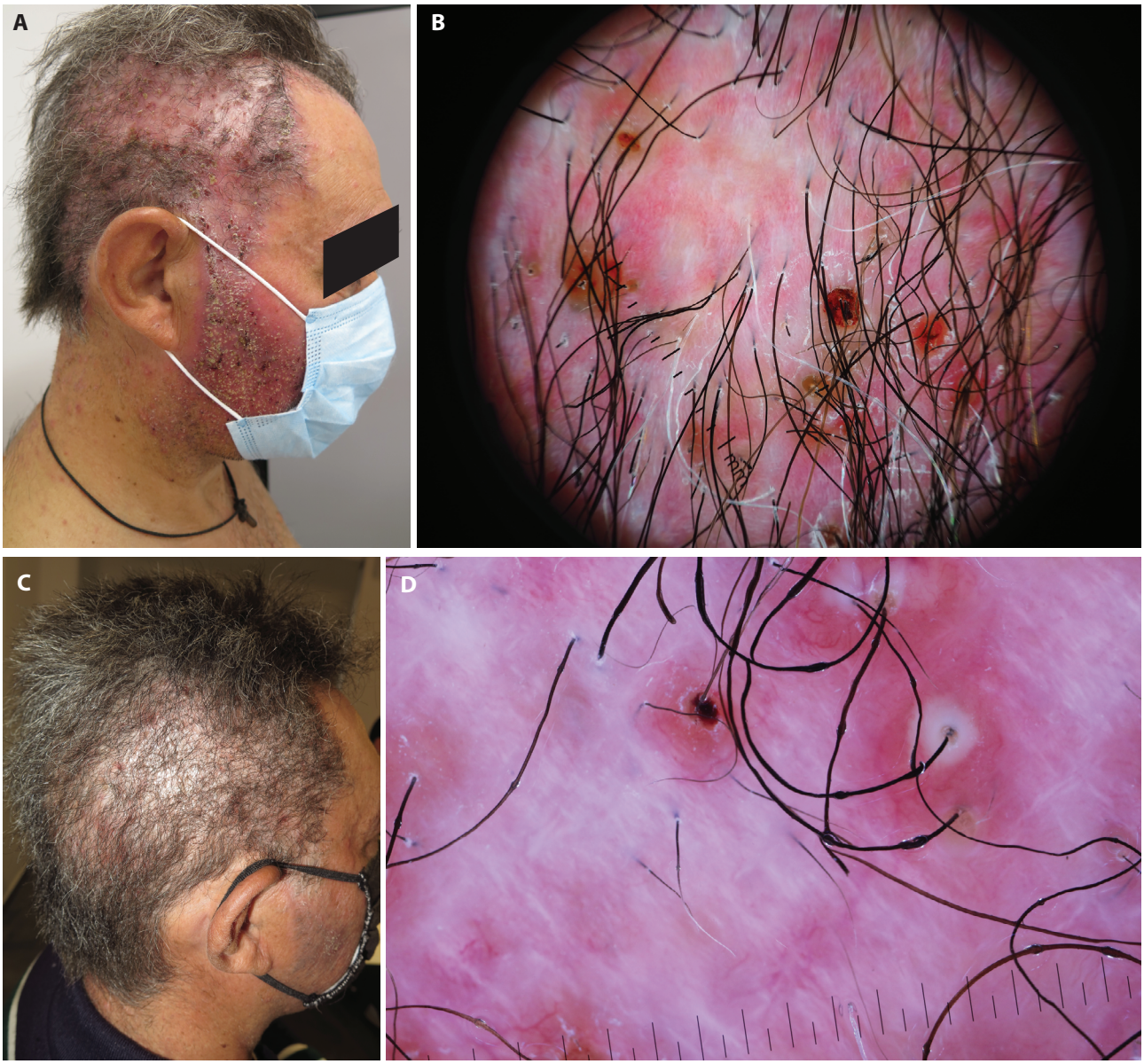

Figure 1. (A) Scarring alopecia with erythema, pustules, crusts, and pili torti in a 57-years-old patient. A similar dermatitis was present also on the face, especially in the beard area. (B) Trichoscopy of the same patient, showing lack of follicular ostia, yellowish serum crusts and reddish hemorrhagic crusts. (C) Clinical picture of the same patient after one month of treatment showing a good improvement of the inflammation. (D) Trichoscopy of the same patient, showing absence of inflammatory signs.

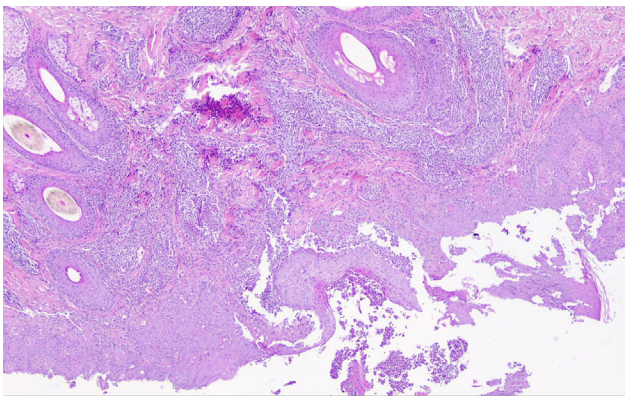

Figure 2. H&E stain showed destructive suppurative folliculitis, with dense neutrophilic infiltrate and tufted hairs, confirming the diagnosis of folliculitis decalvans.

histopathological features we established the diagnosis of folliculitis decalvans-like, scarring alopecia.

In collaboration with the oncologists, the anticancer treatment was continued without modification in all individuals, except for a patient who required a dose reduction. Management included systemic doxycycline in combination with topical clobetasol in 4 individuals, doxycycline alone and clobetasol shampoo alone in the patient with milder involvement. Follow-up period of patients included three visits, respectively after one month, six months and one year. We observed that all patients showed satisfactory response after one month (Figure 1, C and D), except of one who showed only mild improvement and experienced frequent relapses, too, but with remission at the one year follow up visit.

Conclusions

FD is a primary form of cicatricial alopecia, clinically starting as a painful purulent folliculitis with tufts of hairs and perifollicular crusts that eventually evolve in an irreversible scarring process, initially boggy and then atrophic [2]. The main dermoscopic findings are characterized by lack of follicular ostia, erythema, pustules, tuft of hairs emerging from the same ostium, yellowish serum crusts, reddish hemorrhagic crusts [3].

In the 4 cases of FD induced by anti-EGFR reported in literature, the management was similar to our cases, with the prescription of oral antibiotic therapy in combination with topical steroids, and with a marked improvement reported after 3-4 weeks [4].

The most important adverse events caused by the EGFRi are represented by cutaneous toxicity that can sometimes severely impact the quality of life and the compliance to treatment. The most frequent adverse effects include acneiform rash, xerosis, erythema, photosensitivity, paronychia and can be correlated with efficacy of the therapy [1]. Among them, follicular acneiform rash occur in 60%-80% of case, resulting from abnormal keratinization, follicular retention and subsequent rupturing of affected hair follicles [5].

FD-like scalp reaction is a rare, but possible, adverse event induced by EGFRi. Therefore, it is important to early recognize it and promptly start the treatment in order to prevent the scarring evolution. Unless no response to treatment is evident, we discourage the discontinuation of the anticancer treatment. Multidisciplinary management, dermatologic and oncologic in this case, is always advisable in presence of skin toxicities from anticancer drugs.

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