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Case Report

Afatinib-Induced Acneiform Eruption in EGFR Exon 21 L858R-Mutant Stage IVA Lung Adenosquamous Carcinoma: Dermoscopy-Supported Diagnosis and Complete Resolution Fifteen Days After Drug Withdrawal

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ABSTRACT

Background: Acneiform eruption is a monomorphic inflammatory disorder of the pilosebaceous unit that resembles acne vulgaris but characteristically lacks comedones; drug reactions, particularly to epidermal growth factor receptor (EGFR) inhibitors, are its commonest trigger.

Objective: To describe the clinical course, bedside diagnostic reasoning and outcome of an afatinib-induced acneiform eruption documented by serial photography, dermoscopy and potassium hydroxide microscopy.

Case Presentation: A 59-year-old man with stage IVA adenosquamous carcinoma of the left lung harbouring an EGFR exon 21 leucine 858 to arginine (L858R) mutation developed erythematous papules and pustules on the face, neck, chest and back three days after his first dose of oral afatinib 40 mg daily, and was referred on day 21 with intense pruritus, burning and adherent nasal crusting. Examination showed discrete follicular papules and pustules with crusting and no comedones at any site. Dermoscopy demonstrated folliculocentric papules without comedonal plugging, and 10% potassium hydroxide microscopy showed no hyphae, mites or lice, excluding *Malassezia* folliculitis and demodicosis. Naranjo scoring yielded 7 points, indicating a probable adverse drug reaction. Afatinib was withdrawn and oral doxycycline 100 mg twice daily for two weeks, as-required cetirizine, saline compresses followed by clindamycin 1% lotion, hydrocortisone 2.5% cream, emollient and photoprotection were given. Pustules and crusts cleared by day nine and the eruption resolved completely fifteen days after withdrawal, leaving post-inflammatory hyperpigmentation.

Conclusion: Recognising the monomorphic, comedone-free morphology and its temporal link to the drug permits accurate bedside diagnosis, while prophylaxis begun with the inhibitor may avert withdrawal of effective targeted therapy.

All authors have reviewed and approved the final version of the manuscript.

1. Introduction

Acneiform eruption is the collective term for a group of inflammatory disorders of the pilosebaceous unit whose clinical appearance superficially resembles acne vulgaris but whose pathogenesis, natural history and management are fundamentally different. The resemblance is limited to the presence of follicular papules and pustules. What separates the two entities at the bedside is the absence of the comedo, the obligatory precursor lesion of acne vulgaris, together with an abrupt onset, a strikingly uniform lesional morphology and a distribution that frequently extends beyond the classical seborrhoeic territories. The distinction is not semantic. Acne vulgaris is a chronic disorder of adolescence and early adulthood in which follicular hyperkeratinisation, sebaceous hyperactivity and a characteristic shift in the cutaneous bacterial community act together over months; a large population-based cross-sectional study using 16S ribosomal RNA sequencing in 399 adolescents with physician-evaluated acne and 527 healthy controls, of median age 13 years, confirmed that a distinct facial bacterial microbiota composition accompanies the disease.[1] An acneiform eruption has none of these features. It is a reaction pattern rather than a disease, and the diagnosis therefore immediately demands an aetiological question rather than a therapeutic one.

The list of recognised triggers is broad and includes fungal and bacterial folliculitides, occupational exposure to halogenated hydrocarbons and mineral oils, comedogenic cosmetics, and a very large number of systemic drugs. Among these, systemic medication has become the dominant cause in contemporary practice, and within the drug category the molecularly targeted anticancer agents now occupy first place in oncology and dermato-oncology settings. The breadth of the drug

list continues to widen. Acneiform eruptions have been documented after the tyrosine kinase 2 inhibitor deucravacitinib prescribed for chronic plaque psoriasis,[2] after high-dose parenteral vitamin B12,[3] after the serotonin-noradrenaline reuptake inhibitor desvenlafaxine,[4] after mitogen-activated protein kinase kinase inhibition in a child treated for a low-grade glioma,[5] after the cystic fibrosis transmembrane conductance regulator modulator combination elexacaftor, tezacaftor and ivacaftor,[6] and, in biopsy-confirmed form, after ciclosporin prescribed for severe atopic dermatitis.[7] This diversity of culprits sharing a single clinical phenotype is itself informative: it indicates that the pilosebaceous unit possesses a limited repertoire of inflammatory responses, and that arriving at the correct culprit depends far more on a disciplined drug history than on the appearance of the lesions themselves.

The epidermal growth factor receptor (EGFR) inhibitors are the most consistently dermatotoxic of all the targeted agents. In a retrospective series of 288 patients with non-small cell lung cancer treated with first-, second- or third-generation EGFR tyrosine kinase inhibitors, papulopustular rash was the single most common cutaneous adverse event, affecting 74.3% of patients, followed by pruritus in 61.1%, xerosis in 52.4% and paronychia in 39.6%.[8] The burden is not merely cosmetic. In the same cohort, the severity of the papulopustular eruption was a determinant of oncological treatment adjustment, including dose reduction and discontinuation.[8] A prospective single-centre study of 62 patients referred to a dedicated skin-toxicity outpatient clinic found that conventional chemotherapy accounted for 24 cases (38.7%) of cutaneous toxicity and targeted therapy for 18 (29.0%), and framed the purpose of such a clinic explicitly as the preservation of therapeutic adherence.[9] A multicentre prospective observational study of treatment-naive patients with advanced EGFR-mutated non-small cell lung cancer, using the European Organisation for Research and Treatment of Cancer quality-of-life questionnaire and the Dermatology Life Quality Index, confirmed that drug-related cutaneous toxicity is one of the principal determinants of impaired quality of life during EGFR-directed therapy.[10] A questionnaire-based cross-sectional survey of 1,004 cancer patients found that 599 reported cutaneous adverse events after targeted therapy, with measurable effects on social participation and on adherence to skin care.[11] Physician grading systematically underestimates this burden; when the patient-reported outcomes version of the Common Terminology Criteria for Adverse Events was applied to hospitalised cancer patients, the symptom severity reported by patients consistently exceeded that recorded by their treating oncologists and dermatologists.[12] The problem is compounding rather than static, since retrospective review of patients receiving EGFR inhibitors combined with immune checkpoint inhibitors shows overlapping and potentially additive cutaneous toxicity profiles.[13]

Afatinib is a second-generation, irreversible inhibitor of the ErbB receptor family, binding covalently to EGFR (ErbB1), HER2 (ErbB2) and HER4 (ErbB4). Its irreversible binding and its activity across three family members give it greater target coverage than the reversible first-generation agents, and also greater off-target epithelial toxicity. In the pivotal randomised programme, between 28% and 53% of patients receiving the standard 40 mg daily dose required dose reduction for adverse events that were predominantly cutaneous and gastrointestinal.[14] Real-world data reproduce this pattern. A Malaysian analysis of 133 patients drawn from a national database examined whether starting afatinib below the recommended 40 mg daily dose compromised outcomes, a question that arises almost exclusively because of toxicity.[15] A prospective non-interventional German study of older patients with EGFR mutation-positive disease reached similar conclusions about the interplay between tolerability and dose intensity.[16] A multicentre single-arm phase II study of a reduced 30 mg starting dose was designed explicitly to test whether tolerability could be improved without loss of efficacy.[14]

These considerations carry particular weight in Indonesia. A multicentre retrospective cohort drawn from 14 Indonesian centres screened 1,008 patients with EGFR-positive non-small cell lung cancer between 2019 and 2023; 215 received afatinib and 105 met the eligibility criteria for the progression-free survival analysis, with a median age of 59 years.[17] An eight-year cross-sectional analysis of 4,778 Indonesian patients with lung adenocarcinoma confirmed both the high prevalence of EGFR mutations in this population and the clinical importance of correctly characterising the specific variant, because sensitivity to first- and second-generation inhibitors differs substantially between common and uncommon mutations.[18] Afatinib is therefore prescribed frequently in Indonesian thoracic oncology practice, and the dermatologist who receives these referrals must be able to distinguish a predictable pharmacological effect from an infection, from an idiosyncratic hypersensitivity reaction and from an unrelated primary dermatosis.

The tumour in the present case is itself uncommon. Adenosquamous carcinoma is a rare subtype of non-small cell lung cancer that, by definition, contains both glandular and squamous components. In a single-centre review of 66 patients diagnosed over 27 years, median overall survival was 41.7 months overall but only 15.3 months in those managed palliatively, underlining the aggressive behaviour of the subtype.[19] Evidence for EGFR-directed therapy in adenosquamous carcinoma is correspondingly thin. A retrospective study of 44 patients supplemented by a pooled analysis of 74 patients reported an objective response rate of 54.5% and a median progression-free survival of 8.8 months in the retrospective cohort, with pooled figures of 63.4% and 10.0 months respectively, values that are lower than those customarily achieved in pure adenocarcinoma.[20] A patient with EGFR-mutant adenosquamous carcinoma therefore stands to gain from every day of tyrosine kinase inhibitor exposure that can be tolerated, which makes the dermatological

decision to withdraw or to continue the drug consequential rather than routine.

Establishing the correct diagnosis matters because the therapeutic consequences of error run in opposite directions. Treating a drug-induced sterile folliculitis as an infection exposes the patient to unnecessary antimicrobials and delays the only intervention that reliably works, which is identification of the culprit agent. Conversely, treating a *Malassezia* folliculitis as a drug eruption withholds the antifungal therapy that would resolve it and may lead to the unnecessary discontinuation of an effective anticancer drug. This mimicker is neither rare nor trivial in Indonesia: a multicentre study across seven Indonesian referral teaching hospitals identified 353 cases of *Malassezia* folliculitis between January 2014 and December 2018, 66.3% of them in men, with 44.5% concentrated in the 17 to 25 year age group, pruritus reported by 83.9%, and a lesional distribution dominated by the trunk and chest; being hospital-based, that series describes the population that reaches referral centres rather than the distribution of the disease in the community.[21] A comparable diagnostic trap exists on the parasitic side; a prospective clinical cohort of 89 patients demonstrated that facial *Demodex* overgrowth, defined as a density above 5 mites per square centimetre, coexists with ocular demodicosis and requires targeted treatment rather than empirical antibacterial therapy.[22] Applying the standard acne vulgaris armamentarium is a third error; benzoyl peroxide and topical retinoids are irritant on a barrier that has already been pharmacologically compromised.[23] Two bedside investigations resolve most of this uncertainty within minutes. Dermoscopy discriminates folliculocentric inflammatory papules without comedonal plugging from the comedones of acne vulgaris, from the *Demodex* tails and follicular openings of demodicosis, and from the vascular polygons and persistent background erythema of papulopustular rosacea.[24–26] Direct microscopy of a 10% potassium hydroxide preparation excludes *Malassezia* yeasts, *Demodex* mites and other follicular parasites in a single step.[21]

Reports of EGFR-inhibitor acneiform eruption are numerous, but reports that combine serial, standardised clinical photography at three separate time points with dermoscopic imaging and a documented negative potassium hydroxide preparation remain scarce. We searched PubMed and Crossref on 29 July 2026, combining the terms acneiform eruption, papulopustular rash, afatinib, EGFR inhibitor, dermoscopy and adenosquamous carcinoma without language restriction, and retrieved no report in which such a documented series arose in a patient whose underlying malignancy was a lung adenosquamous carcinoma carrying the exon 21 L858R substitution. We state this as the result of a defined search rather than as a claim of priority, since absence of retrieval is not absence of publication. The aim of this report is fourfold. First, to describe the complete clinical course of an afatinib-induced acneiform eruption from a three-day latency after the first dose through to clinical resolution fifteen days after drug withdrawal, documented photographically at presentation and at two subsequent visits, as presented in Figure 1, Figure 3 and Figure 4 and summarised chronologically in Figure 5. Second, to demonstrate how dermoscopy and potassium hydroxide microscopy, both available at any dermatology outpatient clinic and both shown in Figure 2, allowed the diagnosis to be secured and the principal mimickers, tabulated in Table 4, to be excluded without recourse to biopsy. Third, to apply a structured causality instrument, reported item by item in Table 3, to the drug-eruption relationship rather than asserting it, so that the strength of the attribution can be judged transparently by the reader. Fourth, to set out the therapeutic reasoning behind each component of the regimen that was used, itemised in Table 2, and to discuss the unresolved tension between dermatological control and the preservation of oncological drug exposure in a patient with a rare and aggressive tumour subtype whose baseline profile is given in Table 1.

2. Case Presentation

A 59-year-old Javanese man was referred from the pulmonology service to the outpatient clinic of the Department of Dermatology and Venereology, Dr. Moewardi General Hospital, Surakarta, with red papules and patches involving the face, neck, chest and back, which he estimated to have been present for about two weeks. The lesions were accompanied by intense pruritus and a burning sensation. The eruption had first appeared three days after he took his first dose of oral afatinib, which had been commenced twenty-one days before the dermatological consultation. Lesions began on the face and subsequently spread centrifugally to the neck, the anterior chest and the back. The patient's own estimate of two weeks and the drug-anchored interval are not perfectly concordant: an eruption beginning on the third day of a twenty-one-day course had in fact been present for approximately eighteen days. The discrepancy is best explained by ordinary recall imprecision over a period during which the eruption was evolving continuously. Throughout this report, and in the causality assessment, we have used the drug-anchored chronology, because the first afatinib dose is a fixed and independently documented event whereas the patient's recollection of when the rash began is not. The patient reported that the itching was distinctly aggravated by sun exposure. There was no associated pain and no fever at any stage. In the days preceding referral he had noticed that the lesions were not improving and that thick scale had begun to accumulate over the nose and the surrounding skin, and it was this failure to improve, together with unremitting pruritus over the whole face and trunk, that prompted the pulmonology team to seek a dermatological opinion.

The underlying diagnosis was a left-sided pulmonary adenosquamous carcinoma with a positive EGFR mutation involving exon 21, leucine 858 to arginine (L858R), classified as stage IVA. Targeted therapy with the EGFR inhibitor afatinib had been initiated at a dose of 40 mg orally once every 24 hours and had been taken continuously since. No other new medication had been

introduced in the preceding three months, and the patient had not used any new topical preparation, cosmetic or traditional remedy. Details of any systemic anticancer therapy given before afatinib were not recorded in the dermatological referral and were not available to us.

He had never experienced a similar eruption. There was no history of diabetes mellitus, atopy, drug allergy, food allergy or other chronic disease, and no family history of a similar eruption, drug allergy, food allergy or atopy. Occupationally he was a construction labourer, with a history of cigarette smoking, chronic exposure to wood smoke and residence in an industrial area; the cumulative tobacco exposure was recorded qualitatively and was not quantified in pack-years. These exposures are relevant on two counts: they constitute plausible confounders in the assessment of an acneiform eruption, since occupational contact with mineral oils, tars and halogenated compounds is an established cause of the same reaction pattern, and they also entail sustained ultraviolet exposure in a patient whose skin barrier had been pharmacologically compromised.

On examination he appeared moderately ill and was fully alert. Blood pressure was 120/80 mmHg, pulse rate 82 beats per minute, respiratory rate 20 breaths per minute and axillary temperature 36.8 degrees Celsius. He weighed 54 kg and measured 165 cm in height, giving a body mass index of 19.8 kg/m^2, within the normal range. The complete demographic, oncological and baseline clinical profile is summarised in Table 1.

Table 1. Demographic, oncological and baseline clinical profile of the patient at the first dermatological consultation (24 September 2025, day 21 of afatinib therapy).

Domain	Parameter	Finding
Demographic		
	Age / sex	59 years / male
	Ethnicity	Javanese
	Occupation	Construction labourer (outdoor, unprotected sun exposure)
	Environmental exposure	Cigarette smoking (not quantified in pack-years); chronic wood-smoke exposure; residence in an industrial area
Oncological		
	Primary diagnosis	Adenosquamous carcinoma of the left lung
	Molecular profile	EGFR mutation positive, exon 21 leucine 858 to arginine (L858R)
	Stage	Stage IVA
	Targeted therapy	Afatinib 40 mg orally every 24 h, commenced 21 days before consultation
	Prophylactic skin regimen at initiation	None prescribed
Past and family history		
	Previous similar eruption	None
	Diabetes mellitus, atopy, drug or food allergy, other chronic disease	None
	Family history of similar eruption, allergy or atopy	None
General examination		
	General condition / consciousness	Moderately ill / compos mentis
	Blood pressure	120/80 mmHg (normal)
	Pulse rate	82 beats/min (normal)
	Respiratory rate	20 breaths/min (normal)
	Axillary temperature	36.8 °C (normal)
	Body weight / height	54 kg / 165 cm
	Body mass index	19.8 kg/m^2 (normal weight, 18.5–22.9 kg/m^2)
	Fitzpatrick skin phototype	Not formally documented
Dermatological		
	Sites involved	Face, neck, anterior chest, upper and lower back
	Primary lesions	Multiple discrete erythematous follicular papules and pustules
	Secondary lesions	Adherent yellowish crust over the nasal dorsum and perinasal skin
	Comedones	None identified at any site
	Symptoms	Intense pruritus and burning, aggravated by sun exposure
	Mucosal, palmoplantar, scalp, nail involvement	None
Chronology		
	Latency from first afatinib dose to eruption	3 days
	Duration of exposure after onset of eruption	18 days
Severity		
	NCI-CTCAE v5.0 grade (papulopustular rash)	Grade 2 (moderate) — papules and pustules over 10 to 30% of the body surface area with pruritus and psychosocial impact, limiting instrumental activities of daily living; at the upper boundary of grade 2

Notes: *EGFR, epidermal growth factor receptor; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events. Body surface area involvement was estimated clinically and not measured planimetrically.*

Dermatological examination of the facial region and of the anterior and posterior trunk revealed multiple discrete erythematous papules and pustules, accompanied by crusting in several areas. The morphology was strikingly uniform. Every inflammatory lesion was a papule or a pustule centred on a follicular ostium, and no open or closed comedones were identified anywhere on the face, the neck or the trunk despite careful inspection of the classical comedonal sites over the forehead, the nasal alae and the chin. Thick, adherent, yellowish crust covered the nasal dorsum and the perinasal skin, and finer serous crust was scattered across the malar regions and the mandibular border. On the anterior chest and the upper back the lesions were sparser and predominantly papular, without the confluent crusting seen on the face. The eruption spared the palms, the soles, the scalp and the mucous membranes, and there was no nail-fold involvement at this stage. Figure 1 shows the baseline dermatological status at presentation.

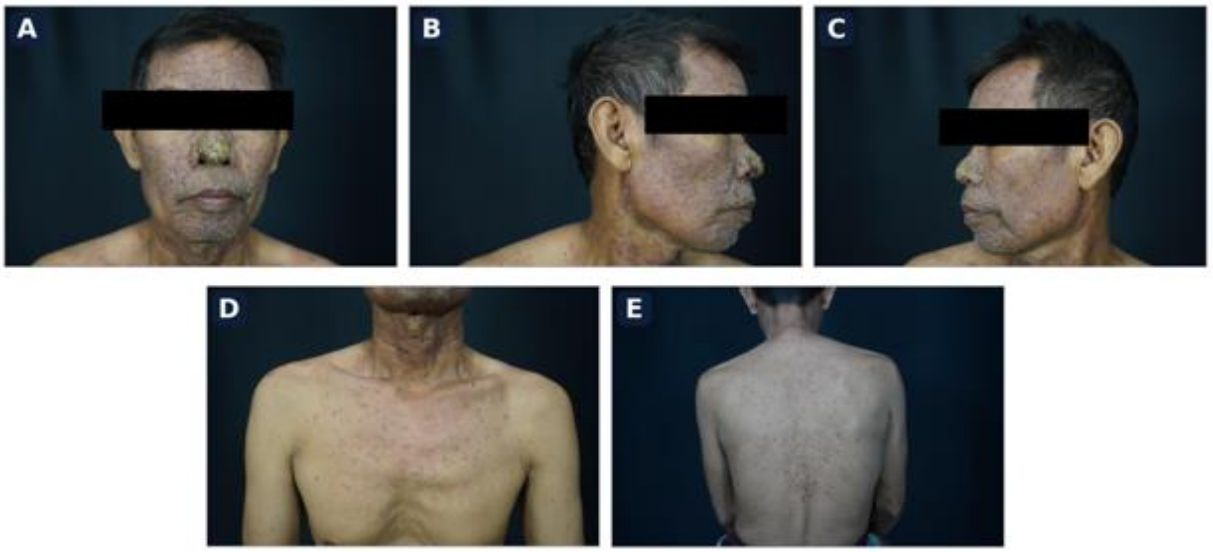

Figure 1. Dermatological status at the first consultation, 21 days after the first dose of afatinib (24 September 2025). *(A)* Frontal view showing multiple discrete erythematous follicular papules and pustules over the entire face with confluent adherent yellowish crust over the nasal dorsum and perinasal skin. *(B)* Right lateral and *(C)* left lateral views demonstrating extension onto the preauricular, mandibular and anterior cervical skin, well beyond the centrofacial territory. *(D)* Anterior trunk with discrete erythematous papules over the upper chest and supraclavicular fossae. *(E)* Posterior trunk with papules scattered over the interscapular and lower dorsal skin. No open or closed comedones were identified at any site. The periocular region has been masked to preserve patient anonymity.

As shown in Figure 1A, the facial involvement was dense and symmetrical, with confluent crusting over the nasal dorsum. The lateral views in Figure 1B and Figure 1C demonstrate that the eruption extended posteriorly onto the preauricular and mandibular skin and inferiorly onto the anterior neck, that is, well beyond the strictly centrofacial territory that characterises papulopustular rosacea. Figure 1D shows the anterior trunk, where discrete erythematous papules were distributed over the upper chest and the supraclavicular fossae, and Figure 1E shows the corresponding involvement of the interscapular and lower dorsal skin. Taken together, the distribution followed the sebaceous-gland-rich territories of the face, the upper chest and the upper back but was not confined to them.

On the basis of the history and the physical examination the working diagnosis was an acneiform drug eruption. The offending drug was identified from the medication history as afatinib, on the strength of the three-day latency between the first dose and the appearance of the first lesions, the absence of any other new drug exposure, and the well-characterised propensity of EGFR inhibitors to produce precisely this reaction pattern.

Two bedside investigations were performed to characterise the lesions further and to exclude the principal mimickers. Dermoscopy was performed on untreated lesional skin of the malar region, and a direct microscopic examination of a 10% potassium hydroxide preparation was made from material expressed from a pustule and from adjacent scale, screened at an original magnification of ten times and examined at forty times. Both dermoscopic panels were acquired from untreated lesional skin of the same malar region before any material was expressed for the potassium hydroxide preparation, and they show two different lesional fields rather than one field at two magnifications. As shown in Figure 2A and Figure 2B, dermoscopy demonstrated multiple erythematous papules arranged around hair follicles, that is, a folliculocentric pattern, on a background of diffuse erythema. Individual follicular ostia were occupied by inflammatory papules and, in Figure 2B, by a discrete pustule with a central follicular opening surrounded by a narrow white halo of perifollicular scale. No comedonal plugging, no keratotic follicular casts of the type seen in acne vulgaris, no *Demodex* tails and no follicular openings occupied by protruding mites were observed in any field. Figure 2C shows the potassium hydroxide preparation, in which no fungal hyphae, no budding yeast cells, no *Demodex* mites and no *Pediculus* were identified; the field contains only keratinocyte debris and amorphous material.

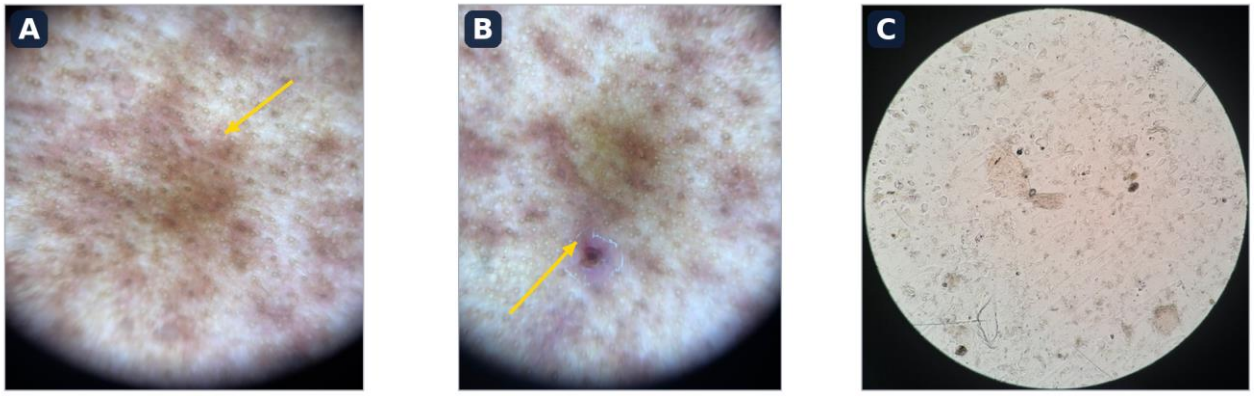

Figure 2. Bedside investigations performed on untreated lesional skin at the first consultation. *(A)* Dermoscopy of the malar region showing multiple erythematous papules centred on follicular ostia (folliculocentric pattern, arrow) on a background of diffus e erythema, with no comedonal plugging. *(B)* Higher-power dermoscopic view showing a discrete follicular pustule with a central follicular opening surrounded by a narrow rim of perifollicular scale (arrow). *(C)* Direct microscopy of a 10% potassium hydroxide preparation of material expressed from a pustule and adjacent scale, screened at original magnification ×10 and examined at ×40, showing keratinocyte debris only, with no fungal hyphae, no budding yeast cells, no *Demodex* mites and no *Pediculus*.

These two investigations converted a morphological impression into a working diagnosis with an explicit differential. The folliculocentric papules without comedonal structures seen in Figure 2A and Figure 2B are the dermoscopic signature of an acneiform eruption rather than of acne vulgaris, and the negative potassium hydroxide preparation shown in Figure 2C excluded *Malassezia* folliculitis and demodicosis, the two mimickers that most often masquerade as a monomorphic pruritic papulopustular eruption. No skin biopsy was performed. The decision not to biopsy was deliberate: the temporal relationship to the drug was unambiguous, the two bedside investigations had excluded the infective and parasitic differentials, and the patient was receiving palliative systemic therapy for a stage IVA malignancy, so an invasive procedure whose result would not have altered management was not justified.

The severity of the eruption was categorised as moderate. Using the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0, the eruption corresponded to grade 2, that is, papules and pustules covering 10 to 30 per cent of the body surface area with associated pruritus and a documented psychosocial impact, limiting instrumental activities of daily living. Body surface area was estimated clinically rather than measured. Although the face, neck, anterior chest and back were all involved, the lesions within those regions were discrete rather than confluent except over the nasal dorsum, so the aggregate area actually occupied by papules and pustules was judged to lie in the upper part of the 10 to 30 per cent band rather than above it. The presence of adherent crusting placed the patient at the upper end of grade 2, close to the boundary with grade 3. We considered whether the crusted areas represented local superinfection requiring oral antibiotics, which would have mandated a grade 3 assignment: there was no tenderness, no purulent discharge, no regional lymphadenopathy and no fever, and the crust had the appearance of dried serous exudate from ruptured follicles rather than of impetiginisation. The oral tetracycline was therefore prescribed for its anti-inflammatory action rather than as treatment of an established infection, and the grade 2 assignment was retained. This reasoning is recorded here so that the reader may judge it independently.

The patient was advised to stop the suspected causative drug, afatinib. In parallel, a combined systemic and topical regimen was instituted. He received oral doxycycline 100 mg every 12 hours for two weeks, oral cetirizine 10 mg every 24 hours to be taken when pruritus was troublesome, compresses of 0.9% sodium chloride applied for 15 minutes followed by clindamycin 1% lotion twice daily in the morning and the evening to the crusted areas, and hydrocortisone 2.5% cream applied twice daily in the morning and the evening to the inflamed lesional skin. The composition of the regimen, the pharmacological rationale for each component and the supporting evidence are set out in Table 2. He was also counselled on gentle cleansing, on the regular use of a non-comedogenic emollient and on strict photoprotection, the last of these being particularly important for two converging reasons: his outdoor occupation combined with a report that pruritus worsened in sunlight, and the fact that doxycycline is itself photosensitising, so that a two-week tetracycline course in a construction labourer with an already photosensitive, barrier-compromised skin required explicit counselling on sun avoidance, protective clothing and broad-spectrum sunscreen rather than a generic instruction. Cetirizine was prescribed on an as-required basis in accordance with local practice; regular rather than intermittent dosing would be expected to give more consistent control of pruritus and is a reasonable alternative. The patient was additionally counselled that the eruption was a recognised, non-infectious and non-contagious consequence of the anticancer drug rather than a sign of infection or of disease progression, that it did not indicate that the cancer was worsening, and that the appearance of the skin would improve once the drug was stopped.

Table 2. Therapeutic regimen instituted at the first dermatological consultation, with the pharmacological rationale and the supporting evidence for each component.

Intervention	Dose, route and duration	Pharmacological rationale	Supporting evidence
Withdrawal of afatinib	**Stopped on day 21 of therapy**	**Removal of the causative agent is the only intervention that addresses the mechanism; all other components are adjunctive**	**Dechallenge is the defining step in drug-eruption management and provided the diagnostic confirmation in this case**
Doxycycline	100 mg orally every 12 h for 14 days	Anti-inflammatory action through inhibition of neutrophil chemotaxis and matrix metalloproteinases; incidental cover of secondary staphylococcal colonisation of crusted skin. Doxycycline is photosensitising and requires explicit counselling in an outdoor worker	Systematic review of oral tetracyclines for prevention of EGFR-inhibitor acneiform rash; post hoc analysis of pre-emptive doxycycline in a randomised trial; retrospective association of minocycline with longer progression-free survival
Hydrocortisone 2.5% cream	Topically twice daily to lesional skin	Low-potency topical corticosteroid to suppress perifollicular inflammation with minimal barrier and atrophogenic cost on facial skin	Randomised controlled trial of topical corticosteroid potency strategies for facial acneiform eruption due to EGFR inhibitors
Clindamycin 1% lotion	Topically twice daily to crusted areas, after compresses	Topical anti-inflammatory and antimicrobial activity at sites where barrier disruption is greatest	Standard first-line topical therapy for cancer drug-induced acneiform eruptions
Sodium chloride 0.9% compress	15 minutes before each lotion application	Atraumatic softening and removal of adherent crust, permitting topical penetration	Expert practice rather than trial evidence; standard supportive wound care for crusted inflammatory dermatoses
Cetirizine	10 mg orally every 24 h as required	Symptomatic control of pruritus; does not modify the underlying neutrophilic process	Patient-reported symptom burden of dermatological adverse events consistently exceeds physician grading
Skin-care counselling	Continuous	Gentle non-alkaline cleansing, regular non-comedogenic emollient, avoidance of alcohol-based products, restoration of the pharmacologically disrupted barrier	Barrier restoration is a core component of every published supportive-care protocol
Photoprotection	Continuous, broad spectrum	Mitigation of EGFR-inhibitor photosensitivity and prevention of post-inflammatory hyperpigmentation in an outdoor worker	Prevention of post-inflammatory hyperpigmentation outperforms treatment applied after the event
Deliberately withheld: benzoyl peroxide, topical retinoids, systemic corticosteroids	**—**	**Benzoyl peroxide and retinoids are irritant on an already compromised barrier; systemic corticosteroids may themselves induce an acneiform eruption and add immunosuppression without addressing the mechanism**	**Standard practice in EGFR-inhibitor eruptions; benzoyl peroxide has been trialled only in the prolonged, corticosteroid-refractory phase**

Notes: *EGFR, epidermal growth factor receptor. Full citations for the supporting evidence are given in the accompanying text.*

The patient was reviewed on 3 October 2025, nine days after the withdrawal of afatinib and the commencement of therapy. As shown in Figure 3A, the confluent crusting over the nasal dorsum and the perinasal skin had resolved completely, and no pustules were identifiable on the face. What remained was a background of erythema with early, diffuse hyperpigmentation across the malar regions, the nasal dorsum and the mandibular skin. The lateral views in Figure 3B and Figure 3C show the same pattern over the preauricular, mandibular and cervical skin. Figure 3D demonstrates residual erythema over the upper anterior chest with scattered non-inflammatory macules, and Figure 3E shows sparse residual papules with early hyperpigmented macules over the interscapular region. Pruritus had diminished substantially and the burning sensation had abated.

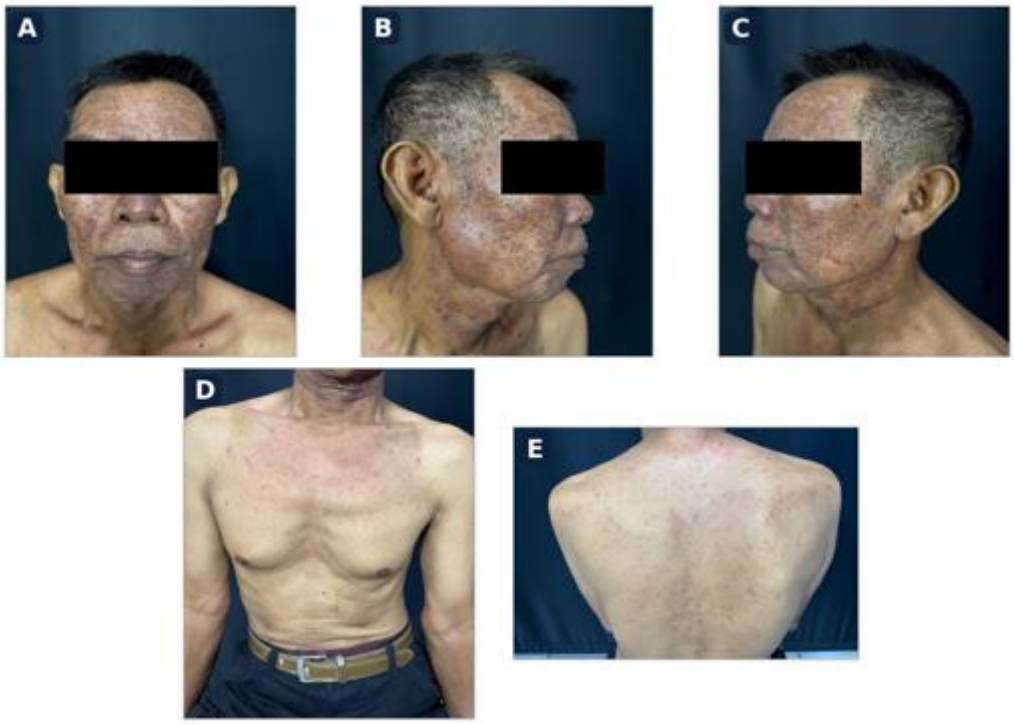

Figure 3. First follow-up visit on 3 October 2025, nine days after withdrawal of afatinib. *(A)* Frontal, *(B)* right lateral and *(C)* left lateral views showing complete resolution of the nasal and perinasal crusting and disappearance of pustules, leaving background eryth ema with early diffuse hyperpigmentation. *(D)* Anterior trunk with residual erythema and scattered non-inflammatory macules. *(E)* Posterior trunk with sparse residual papules and early hyperpigmented macules. These images were acquired under different ligh ting conditions and against a different background from those in Figures 1 and 4; comparison of lesion type and distribution across figures is va lid, but direct comparison of colour should be made with caution. The periocular region has been masked to pres erve patient anonymity.

He returned for a second review on 9 October 2025, fifteen days after the withdrawal of afatinib, and the eruption had resolved. As shown in Figure 4A, the face was free of inflammatory papules, pustules and crust; the red papules were, in the patient's own description, no longer covered by scabs. What persisted was multiple discrete hyperpigmented macules distributed over the previously affected sites, that is, post-inflammatory hyperpigmentation. The lateral views in Figure 4B and Figure 4C confirm the same finding over the lateral face and neck, and Figure 4D and Figure 4E demonstrate that the anterior and posterior trunk had likewise cleared, leaving only discrete hyperpigmented macules and a small number of residual non-inflammatory papular remnants at the shoulders. The fourteen-day course of doxycycline had been completed the previous day. No new lesions had appeared at any site after drug withdrawal.

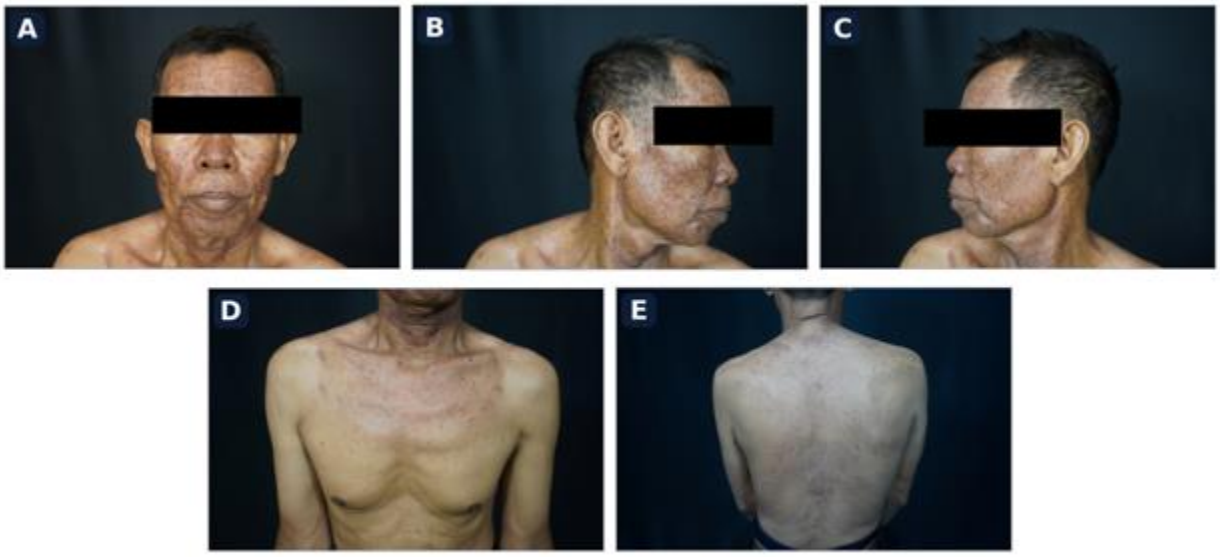

Figure 4. Second follow-up visit on 9 October 2025, fifteen days after withdrawal of afatinib. *(A)* Frontal, *(B)* right lateral and *(C)* left lateral views showing complete resolution of the inflammatory eruption, with multiple discrete hyperpigmented macules at the previously affected sites. *(D)* Anterior and *(E)* posterior trunk showing the same pattern of discrete post-inflammatory hyperpigmentation without residual papules or pustules. The periocular region has been masked to preserve patient anonymity.

The complete chronology of drug exposure, eruption, withdrawal and recovery, together with the trajectory of each individual lesional element, is presented in Figure 5. As shown in Figure 5A, afatinib was started on 3 September 2025, the eruption began on day 3 of therapy, the drug was continued for a further 18 days until the dermatological consultation on day 21, and clinical resolution was achieved 15 days after withdrawal on day 36. Figure 5B tracks the six clinical elements that were documented at each of the four time points; it shows that inflammatory papules, pustules, adherent crusts, erythema and pruritus all peaked at presentation and had disappeared by day 15 after withdrawal, whereas post-inflammatory hyperpigmentation appeared only after the inflammatory phase had begun to subside and persisted as the sole residual finding. Because the reappearance of the eruption on re-exposure would have provided the strongest possible confirmation of causality, it is important to state explicitly that no rechallenge with afatinib was undertaken. The subsequent oncological management of the patient, including whether afatinib was reintroduced at a reduced dose, whether he was switched to another epidermal growth factor receptor inhibitor, or whether targeted therapy was abandoned, was directed by the pulmonology and oncology services, and no dermatological follow-up beyond 9 October 2025 was available to us. We record this as an absence of data rather than as a matter of scope, since the eventual disposition would have added materially to the value of the report.

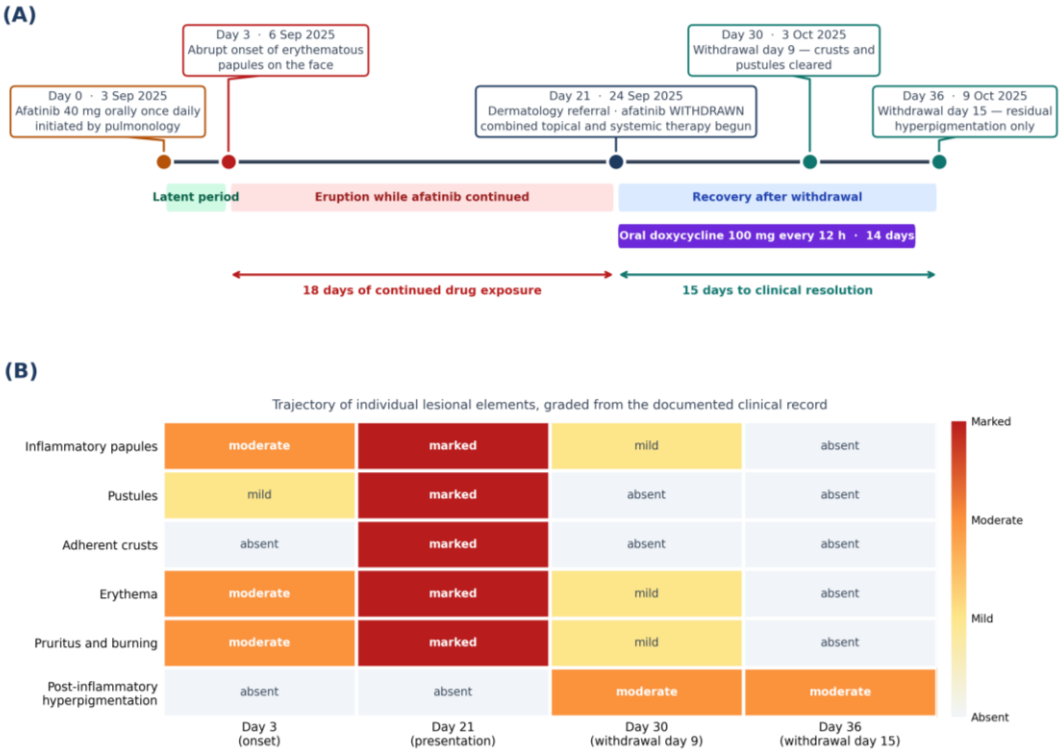

Figure 5. Chronology and lesional trajectory of the eruption. *(A)* Timeline of drug exposure, eruption, withdrawal and recovery, with day 0 defined as the first dose of afatinib. The eruption began on day 3, the drug was continued for a further 18 days, and clinical resolution was reached 15 days after withdrawal. The purple bar indicates the 14-day course of oral doxycycline. *(B)* Semi-quantitative trajectory of the six individual clinical elements documented at each of the four time points, graded retrospectively from the clinical record by two of the authors independently, with disagreements resolved by consensus. Every inflammatory element peaked at presentation and had disappeared by day 15 after withdrawal, whereas post-inflammatory hyperpigmentation emerged only as the inflammatory phase subsided and persisted as the sole residual finding.

2.1. Patient perspective

The only element of the patient's own account that was recorded verbatim in the clinical notes concerns the crusting: at the visit on 9 October 2025 he described the improvement by saying that the red bumps were no longer covered by scabs. It is worth noting what that tells us. The endpoint he selected spontaneously to describe his recovery was neither the pustule count nor the extent of erythema, which are the elements a clinician grades, but the crust, which is the element that had been most visible to other people and most difficult to conceal. Beyond this single documented statement, no structured patient-reported outcome instrument was administered at any visit, and we have deliberately not reconstructed his views retrospectively. The absence of formal patient-reported outcome data is listed among the limitations of this report, and is itself an illustration of the recognised gap between the endpoints clinicians measure and those that patients experience.

3. Discussion

3.1. Diagnostic reasoning: temporal association as the primary evidence

The diagnosis of a drug-induced acneiform eruption is, in the great majority of published cases, a clinical

diagnosis built on three pillars: a compatible morphology, a plausible temporal relationship to a recognised culprit, and the exclusion of the conditions that imitate it. In the present patient, whose full baseline profile is set out in Table 1 and whose chronology is plotted in Figure 5A, the temporal pillar was unusually solid. Afatinib was the only new systemic agent introduced, no new topical product had been applied, and the first lesions appeared on the third day of therapy. A latency of three days is entirely consistent with the published behaviour of EGFR inhibitor-induced papulopustular rash, which characteristically begins within the first week of exposure and peaks between the second and fourth weeks.[8,9] The eruption then behaved exactly as a pharmacological effect should behave: it persisted, and indeed intensified, throughout the eighteen further days during which the drug was continued, and it began to regress within days of withdrawal, with complete clearance of the inflammatory component by day fifteen after cessation. This exposure-response behaviour is displayed element by element in Figure 5B, where every inflammatory component is graded marked at day 21 and absent at day 36.

Because temporal association is easy to assert and difficult to falsify, we applied the Naranjo adverse drug reaction probability scale to the case rather than relying on narrative confidence alone.[27] The item-by-item scoring is presented in Table 3. The instrument yielded a total of 7 points, which places the association in the *probable* category. The score is held below the *definite* threshold by three deliberate omissions: no rechallenge was performed, no placebo was administered, and no drug concentrations were measured. None of these would have been ethically or clinically defensible in a man receiving palliative therapy for a stage IVA malignancy. It is also important to concede that the improvement observed after withdrawal was not attributable to dechallenge alone, because doxycycline, a topical antibiotic and a topical corticosteroid were begun on the same day. The design of the case therefore cannot separate the contribution of drug withdrawal from the contribution of the anti-inflammatory regimen, and we do not claim otherwise. A sensitivity analysis is also worth recording. The most contestable allocation in the instrument is item 5, for which +2 was awarded on the grounds that no alternative cause could on its own have produced the reaction. A sceptical reader might argue that this patient's long-standing occupational exposure to wood smoke, industrial air and construction materials, recorded in the environmental-exposure row of Table 1, constitutes such an alternative. If item 5 were scored 0 on that most conservative assumption, the total would fall from 7 to 5, which remains within the *probable* band. The classification is therefore robust to the least favourable plausible reading of the evidence.

Table 3. Naranjo adverse drug reaction probability scale applied to the association between afatinib and the acneiform eruption in thi s patient.

No.	Question	Response	Score	Justification
1	Are there previous conclusive reports on this reaction?	Yes	+1	Papulopustular acneiform rash is the most frequently reported cutaneous adverse event of EGFR inhibitors, affecting 74.3% of patients in a 288-patient cohort
2	Did the adverse event appear after the suspected drug was administered?	Yes	+2	The eruption began on day 3 of afatinib therapy, having been absent before the first dose
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	Yes	+1	Pustules and crusts cleared by day 9 and the eruption resolved by day 15 after withdrawal. The item is scored positive on the conventional reading of the instrument; the scale does not accommodate the simultaneous initiation of active anti-inflammatory therapy, which is an acknowledged confounder here
4	Did the adverse reaction reappear when the drug was readministered?	Not done	0	No rechallenge was attempted; rechallenge would not have been clinically or ethically defensible
5	Are there alternative causes that could on their own have caused the reaction?	No	+2	No other new systemic or topical agent; occupational exposures were long-standing and had never previously produced an eruption; infective and parasitic causes excluded by dermoscopy and potassium hydroxide microscopy. On the most conservative assumption, scoring this item 0, the total falls to 5 and the classification remains probable
6	Did the reaction reappear when a placebo was given?	Not done	0	No placebo was administered
7	Was the drug detected in blood or other fluids in concentrations known to be toxic?	Not done	0	Therapeutic drug monitoring was not available and is not routine for afatinib
8	Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	No dose change	0	Afatinib was given at a fixed 40 mg daily dose throughout and was stopped rather than reduced
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	No	0	No previous exposure to any EGFR inhibitor or other targeted agent
10	Was the adverse event confirmed by any objective evidence?	Yes	+1	Serial standardised clinical photography at three time points, dermoscopic imaging and a documented negative potassium hydroxide preparation
	TOTAL SCORE		**7**	**Probable adverse drug reaction (definite ≥9; probable 5–8; possible 1–4; doubtful ≤0)**

Notes: *EGFR, epidermal growth factor receptor. The scale was applied to the documented record by two of the authors independently, with full agreement on every item.*

3.2. Morphology: monomorphism and the absence of the comedo

The single most useful morphological discriminator between an acneiform eruption and acne vulgaris is the comedo. Acne vulgaris is a polymorphic disease in which open and closed comedones, inflammatory papules, pustules, nodules and scars coexist in the same field, because the disease arises from a chronic process of follicular hyperkeratinisation and sebum retention on which inflammation is superimposed, accompanied by a measurably distinct, though cross-sectionally associated rather than causally demonstrated, facial bacterial microbiota.[1] An acneiform eruption, by contrast, is monomorphic. Every lesion is at the same stage of evolution because every lesion was initiated by the same insult at approximately the same moment. In this patient, careful inspection of all the classical comedonal sites failed to identify a single open or closed comedo, while the inflammatory lesions were uniform in size and configuration across the face and the trunk, as documented in Figure 1A to Figure 1C. Age reinforced the impression. The population in which the microbiota signature of acne vulgaris was characterised had a median age of 13 years;[1] at 59 years, and with no history of adolescent or adult acne, a first episode of a diffuse papulopustular facial eruption in our patient is intrinsically unlikely to represent acne vulgaris. The point-by-point contrast between the two entities is displayed in Figure 6B.

Distribution was a third discriminator. As shown in Figure 1B and Figure 1C, the eruption occupied the face, the neck, the anterior chest and the upper back, that is, the sebaceous-gland-rich territories in which EGFR is most densely expressed, but it extended onto the lateral face, the anterior neck and the lower back, beyond the strictly seborrhoeic zones, an extent confirmed by the truncal views in Figure 1D and Figure 1E. Papulopustular rosacea, which also lacks comedones, is characteristically confined to the central face and sits on a background of persistent erythema and telangiectasia, neither of which was present here.[24]

3.3. Dermoscopy as the bedside arbiter

Dermoscopy converted a morphological impression into an objective observation. The finding in Figure 2A and Figure 2B, of multiple erythematous papules centred on follicular ostia without keratotic follicular plugging, is the expected appearance of a folliculocentric inflammatory process and is incompatible with acne vulgaris, in which comedonal plugs are directly visualised as brown or white follicular structures. The value of dermoscopy in this differential has been demonstrated systematically. In a prospective study of 60 patients with papulopustular rosacea, the most frequent dermoscopic findings were yellow dots, vascular polygons and follicular scales, and patients with concomitant *Demodex* infestation showed significantly more *Demodex* follicular openings than those without.[24] A ten-year clinical and dermoscopic experience with superficial folliculitis of the scalp produced a practical algorithm in which dermoscopic features direct the choice of confirmatory investigation rather than replacing it.[25] Dermoscopy has also been used to characterise acne agminata, another granulomatous facial papular eruption that can be mistaken for acne.[26] In the present case the negative dermoscopic findings, that is, the demonstrable absence of comedonal plugs, of *Demodex* tails and of follicular openings occupied by mites, carried as much diagnostic weight as the positive ones.

3.4. Potassium hydroxide microscopy and the exclusion of infective and parasitic mimickers

Malassezia folliculitis, formerly termed *Pityrosporum* folliculitis, is the mimicker that most often derails the diagnosis. It produces monomorphic, pruritic follicular papules and pustules that closely resemble both acne vulgaris and drug-induced acneiform eruption, and misrecognition commonly leads to prolonged and futile antibacterial therapy. The Indonesian multicentre series of 353 cases collected between 2014 and 2018 provides the local reference profile against which our patient can be compared, and the comparison is instructive: that series was dominated by men (66.3%) but concentrated in the 17 to 25 year age group (44.5%), with lesions found predominantly on the trunk and chest, and with pruritus reported by 83.9%.[21] Two caveats apply. The series is hospital-based, so it characterises the patients who reach Indonesian referral centres rather than the population distribution of the disease, and the data are now several years old. Neither caveat weakens the comparison made here, which turns on a difference of age and of anatomical predilection large enough to survive both. Our patient shared only the pruritus and the male sex; he was 59 years old and his eruption was face-predominant, which is the opposite of the characteristic truncal distribution. *Malassezia* folliculitis is additionally favoured by immunosuppression and by antibiotic or corticosteroid exposure, all of which are common in oncology patients, and it has been reported in patients receiving biologic therapy, for example following infliximab treatment for Crohn's disease.[28] The diagnosis rests on demonstrating yeast forms within the follicle by potassium hydroxide preparation, by Wood's lamp examination or by response to antifungal therapy.[21] In this patient the potassium hydroxide preparation shown in Figure 2C contained no yeast cells and no hyphae, and the eruption resolved without any antifungal exposure, which excludes the diagnosis on two independent grounds. The corresponding entry in Table 4 records both.

The same preparation excluded demodicosis. Facial *Demodex* overgrowth can produce a pruritic follicular papulopustular eruption that is clinically indistinguishable from an acneiform drug reaction, and a prospective cohort of 89 patients has shown that a facial mite density above 5 per square centimetre is common enough, and consequential enough, to warrant targeted rather than empirical treatment.[22] Drug-associated follicular eruptions of this kind are also documented outside oncology; ciclosporin prescribed for severe atopic dermatitis has produced a biopsy-confirmed folliculitis and perifolliculitis presenting as

an acne-like eruption.[7] In our patient no mites were identified in any field of the preparation shown in Figure 2C. Bacterial folliculitis, most often due to *Staphylococcus aureus*, remained a theoretical consideration because the crusted areas were a plausible portal for secondary colonisation, but the lesions were neither tender nor asymmetrically distributed, and the eruption was not preceded by any focal pyogenic lesion. The clinical response to a tetracycline given at an anti-inflammatory rather than a bactericidal intent, in a patient in whom the primary process resolved coincident with drug withdrawal, is consistent with a sterile process complicated at most by superficial secondary colonisation of the crusted skin. The investigation that would have settled the question definitively is a swab of the crusted skin for Gram stain and bacterial culture, and it would have had to be taken at the first consultation, before the first dose of doxycycline, to be interpretable. It was not performed, and we regard that as an avoidable omission rather than a defensible one.

3.5. Pathogenesis: why blocking EGFR produces a sterile suppurative folliculitis

The pathogenesis of EGFR inhibitor-induced acneiform eruption is mechanistically distinct from that of acne vulgaris, and understanding the difference explains almost every clinical feature observed in this patient. EGFR is constitutively expressed at high density in the basal keratinocytes of the epidermis, in the outer root sheath of the hair follicle and in sebocytes, where its downstream signalling through the RAS-RAF-MEK-ERK and PI3K-AKT pathways governs keratinocyte proliferation, orderly differentiation, migration during barrier repair and the tonic suppression of pro-inflammatory chemokine transcription. Pharmacological blockade of this receptor removes all of these functions simultaneously. The consequences are aberrant keratinocyte maturation with follicular plugging and a thinned, disorganised stratum corneum, failure of the permeability barrier presenting clinically as xerosis, and a chemokine switch characterised by upregulation of neutrophil chemoattractants with concomitant downregulation of cutaneous antimicrobial peptides. This sequence is not inferred but has been reproduced experimentally: in a model in which human HaCaT keratinocytes were exposed to an EGFR tyrosine kinase inhibitor together with tumour necrosis factor alpha and interleukin 1 beta, chemokine transcription and antimicrobial peptide expression were quantified by real-time polymerase chain reaction and the nuclear factor kappa B pathway was interrogated by western blotting, with parallel in vivo administration of afatinib to mice and analysis of aquaporin 3 expression.[29] The net effect is a massive recruitment of neutrophils into the pilosebaceous unit, producing pustules that are inflammatory but, as the entity is characterised in the published literature, sterile. We use the term in that sense throughout: no culture was taken and no biopsy was performed in this patient, so sterility here is inferred from the mechanism and from the clinical course and was not verified microbiologically. The same phenotype has been described, in a case-based correspondence, with the bispecific EGFR and MET antibody amivantamab, which supports the proposition that the reaction pattern follows the target rather than the molecular format of the drug.[30]

Direct experimental support for a cytotoxic component of this process has recently been provided. In a study combining immunohistochemistry on human lesional skin with in vitro work on HaCaT keratinocytes and SZ95 sebocytes treated with afatinib, EGFR tyrosine kinase inhibitors were shown to induce pyroptosis through caspase-3-mediated cleavage of gasdermin E.[31] The distribution of the cleaved gasdermin E N-terminal fragment mapped precisely onto the clinical phenotype: in acneiform rash it was predominantly expressed in the basal layer of the follicular epithelium and in sebocytes and was absent from the interfollicular epidermis, whereas in xerosis and secondary eczematous rash it was expressed in the basal layer of the interfollicular epidermis and only weakly or partially in the follicular epithelium.[31] This is a mechanistically satisfying finding, because it explains why the same drug produces two different cutaneous phenotypes in the same patient, and why the papulopustular component is folliculocentric while the xerotic component is diffuse. It is also directly relevant here, since afatinib was the agent used in that experimental work.

Histopathological series across the tyrosine kinase inhibitor class support the concept of a drug-specific inflammatory signature. In a retrospective cohort of 28 patients with 32 biopsy-confirmed dermatological adverse events attributed to BCR-ABL tyrosine kinase inhibitors, the histopathological patterns differed significantly according to the generation and the specific agent implicated, indicating that the cutaneous reaction pattern is a readout of the particular kinases inhibited rather than a generic drug effect.[32] Although that cohort concerned a different kinase target, the principle transfers: the acneiform phenotype of the EGFR inhibitors reflects the specific dependence of the follicular epithelium on EGFR signalling.

The reasoning of the preceding three paragraphs is summarised in Figure 6. Figure 6A traces the cascade from irreversible pan-ErbB inhibition through the three parallel cellular consequences to the sterile suppurative folliculitis and its sequelae, and Figure 6B sets the four pathogenic pillars of acne vulgaris side by side with the corresponding features of the eruption observed in this patient, showing that not one of them was satisfied.

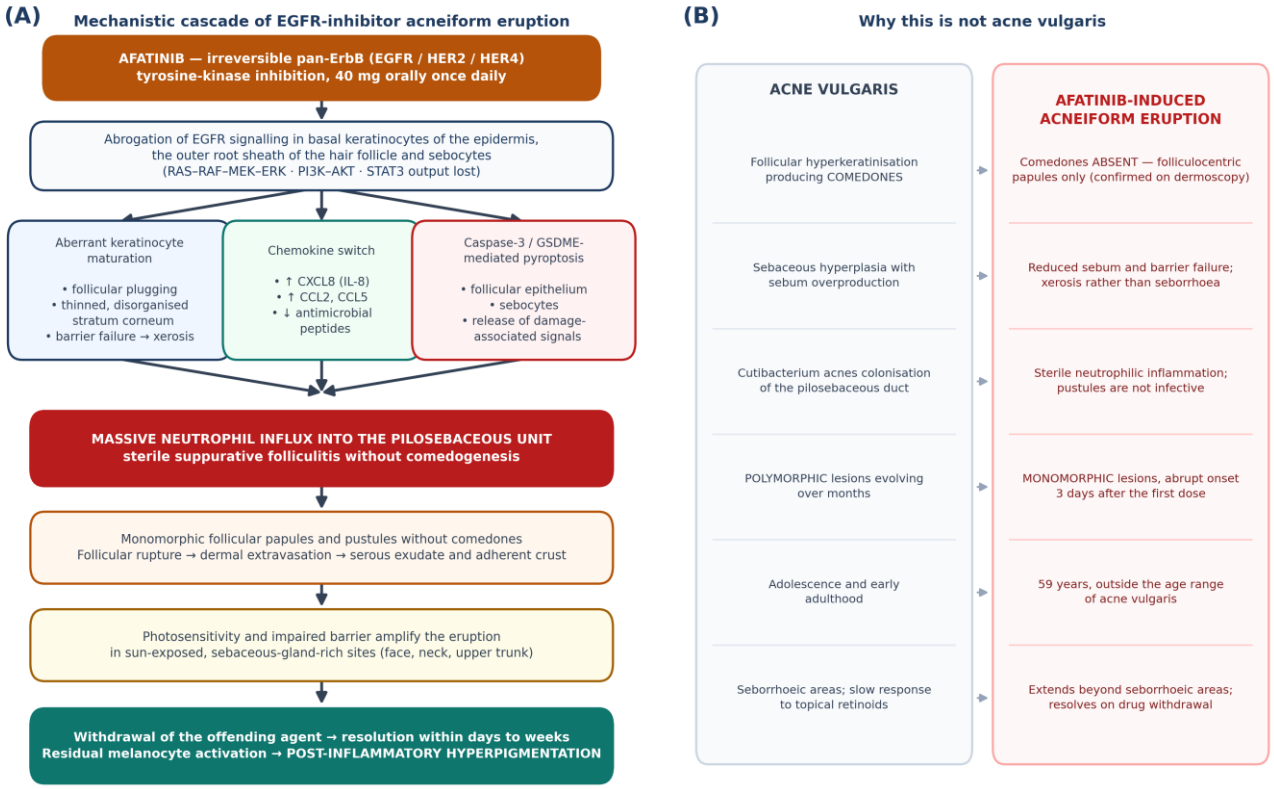

Figure 6. Pathogenesis of afatinib-induced acneiform eruption and its distinction from acne vulgaris. *(A)* Mechanistic cascade. Irreversible pan-ErbB inhibition abrogates epidermal growth factor receptor signalling in basal keratinocytes, in the outer root sheath of the hair follicle and in sebocytes, producing three parallel consequences that converge on a massive neutrophil influx into the pilosebaceous unit and hence a sterile suppurative folliculitis; barrier failure and photosensitivity amplify the eruption at sun-exposed, sebaceous-gland-rich sites, and residual melanocyte activation produces post-inflammatory hyperpigmentation. *(B)* The four pathogenic pillars of acne vulgaris set against the corresponding features observed in this patient; none of the four was satisfied.

3.6. Synthesis of the differential diagnosis

Table 4 draws the clinical, dermoscopic, mycological and mechanistic strands together into a single audit trail. For each alternative diagnosis it records the features that would have supported it, the findings actually observed in this patient, and the resulting verdict. Two entries are deliberately left short of outright exclusion. Superficial secondary bacterial colonisation of the crusted facial skin was never formally excluded, because no swab was taken and because the patient received a systemic tetracycline from the day of presentation; the clinical picture, however, was that of a sterile primary process on which colonisation could at most have been superimposed. Occupational acneiform eruption is likewise recorded as unlikely rather than excluded, since the relevant exposures were real and long-standing; what makes them implausible as the cause is that they had been present for years without producing any eruption, that no comedones or straw-coloured cysts were found, and that the onset coincided precisely with a new systemic drug.

3.7. Why afatinib, and why this severity

Afatinib, prescribed here at the standard 40 mg once-daily dose recorded in Table 1, is an irreversible inhibitor of EGFR, HER2 and HER4. Its covalent binding produces sustained target suppression, which is advantageous against the tumour and disadvantageous for the follicular epithelium, since recovery of receptor function requires the synthesis of new receptor protein rather than simple dissociation of the drug. This pharmacology is reflected in the toxicity data. Dose reduction for adverse events, predominantly cutaneous and gastrointestinal, was required in 28% to 53% of patients receiving the standard 40 mg daily dose in randomised trials, which is the explicit rationale for the phase II evaluation of a reduced 30 mg starting dose.[14] Retrospective real-world analyses from Malaysia have addressed the same question from the opposite direction, asking whether patients started below 40 mg suffer any efficacy penalty.[15] The German GIDEON study, which enrolled a high proportion of patients aged 70 years or older, examined afatinib tolerability and effectiveness in routine practice in an older population that resembles the patient described here.[16]

Host factors also modulate severity, and one of them is directly observable at the bedside. An ancillary analysis of the FAEISS phase III trial evaluated pretreatment facial photographs of patients with RAS wild-type metastatic colorectal cancer receiving EGFR inhibitors and found that conspicuously enlarged facial pores were closely related to the worst grade of facial acneiform rash subsequently developed, and also to the

therapeutic effect of the EGFR inhibitor.[33] That observation is worth incorporating into routine oncodermatological practice, because it means that a photograph taken before the first dose carries predictive information that can be used to target prophylaxis at the patients most likely to need it.

Table 4. Differential diagnosis of a monomorphic papulopustular facial eruption, the findings that would support each alternative, and the findings actually observed in this patient.

Differential diagnosis	Features that would support it	Findings in this patient	Verdict
Acneiform drug eruption due to afatinib	**Monomorphic follicular papules and pustules; no comedones; acute onset within days to weeks of a new drug; distribution extending beyond seborrhoeic areas; resolution on dechallenge**	**All present: 3-day latency, uniform lesions, no comedones, face plus neck and trunk, complete clearance 15 days after withdrawal; Naranjo score 7**	**Established**
Acne vulgaris	Polymorphic lesions with open and closed comedones; adolescence or early adulthood; strictly seborrhoeic distribution; chronic evolution over months	No comedones on inspection or dermoscopy; age 59 years with no previous acne; acute onset over days	Excluded
Malassezia (*Pityrosporum*) folliculitis	Monomorphic pruritic follicular papulopustules, predominantly truncal; yeast forms on potassium hydroxide preparation; response to antifungal therapy	Potassium hydroxide preparation negative for yeasts and hyphae; face more severely involved than trunk; resolved without any antifungal exposure	Excluded
Demodicosis / *Demodex* folliculitis	Facial follicular papulopustules with scaling; *Demodex* tails and mite-occupied follicular openings on dermoscopy; mites on potassium hydroxide preparation	No *Demodex* tails or mite-occupied follicular openings on dermoscopy; no mites on potassium hydroxide preparation	Excluded
Bacterial folliculitis (*Staphylococcus aureus*)	Tender, asymmetric pustules; often a preceding focal pyogenic lesion; positive Gram stain and culture	Lesions non-tender and symmetrically distributed; no antecedent focal pyogenic lesion; no fever	Unlikely; superficial secondary colonisation of crusted areas not formally excluded
Papulopustular rosacea	Absence of comedones but with persistent centrofacial background erythema and telangiectasia; strictly centrofacial distribution; vascular polygons and yellow dots on dermoscopy	Eruption extended to the neck, chest and back; no persistent background erythema or telangiectasia; no vascular polygons on dermoscopy	Excluded
Perioral dermatitis	Grouped micropapules and micropustules confined to perioral, perinasal or periocular skin with a spared vermilion border; frequent antecedent topical corticosteroid use	Widespread involvement of the face and trunk; no antecedent topical corticosteroid use	Excluded
Occupational (chloracne-type) acneiform eruption	Exposure to halogenated aromatic hydrocarbons, tars or mineral oils; comedones and straw-coloured cysts, especially in the malar and retroauricular skin	Long-standing occupational exposure without any previous eruption; no comedones or cysts; onset coincided precisely with a new systemic drug	Unlikely; exposure predates the eruption by years
Corticosteroid-induced acneiform eruption	Monomorphic papulopustules after systemic or potent topical corticosteroid exposure	No corticosteroid exposure of any route before the eruption	Excluded

Notes: *Dermoscopy and 10% potassium hydroxide microscopy were performed on untreated lesional skin at the first consultation. No skin biopsy and no bacterial or fungal culture were obtained.*

3.8. The therapeutic decision: withdrawal versus continuation

The decision to withdraw afatinib requires careful scrutiny, because it is the point at which dermatological and oncological interests diverge most sharply. Cutaneous toxicity is a recognised driver of dose modification and discontinuation in routine practice, and in the Korean series of 288 patients the severity of the papulopustular rash directly determined the treatment adjustments that were made.[8] Yet discontinuation is not a neutral act in a patient with an EGFR-mutant stage IVA adenosquamous carcinoma. Pooled data in lung adenosquamous carcinoma with EGFR mutation report an objective response rate of 63.4%, a disease control rate of 85.9%, a median progression-free survival of 10.0 months and a median overall survival of 21.4 months with EGFR tyrosine kinase inhibitor therapy.[20] Against a background in which palliatively managed adenosquamous carcinoma carried a median overall survival of only 15.3 months,[19] every month of effective targeted therapy is meaningful.

There is a further consideration that argues for preserving drug exposure wherever the rash can be controlled. Retrospective evidence suggests that patients who receive supportive dermatological therapy during EGFR-directed treatment may fare better oncologically. In a single-centre cohort of patients treated with first-line EGFR tyrosine kinase inhibitors, median progression-free survival was significantly longer in those who received minocycline, at 714 days (95% confidence interval 411 to 1,247), than in those who did not, at 420 days (95% confidence interval 343

to 626).[34] That finding is retrospective and vulnerable to confounding by indication, and it should not be read as evidence that tetracyclines are antineoplastic. Read conservatively, it supports the proposition that effective management of the rash allows the tyrosine kinase inhibitor to be continued at full dose for longer.

In this patient, withdrawal was nevertheless the correct decision at the moment it was taken, for three reasons. First, the eruption had reached the upper boundary of grade 2 with adherent crusting after 21 days of continuous exposure, as recorded in the severity row of Table 1 and visible in Figure 1A, and was still worsening, so continuation without interruption risked progression to grade 3 with the attendant risk of secondary infection. Second, no prophylaxis had been instituted at the initiation of afatinib, so the patient had no reserve of supportive therapy on which to fall back. Third, and decisively, withdrawal is diagnostically informative: in a patient in whom the culprit had been identified only by history, the response to dechallenge provided the confirmation that no other available investigation could offer. The optimal strategy, however, would have been not to reach this point at all. Both the reduced-dose approach and structured primary prophylaxis are designed precisely to avoid the situation in which a dermatologist must choose between the skin and the tumour.[14,35]

It should be stated explicitly that a third option existed and was considered, namely dose reduction rather than complete withdrawal. This is not a hypothetical alternative: it is precisely the strategy examined by the Malaysian real-world analysis of patients started below 40 mg[15] and by the phase II evaluation of a 30 mg starting dose.[14] It was not adopted here for two reasons. First, dose reduction acts slowly; the pharmacodynamic effect of an irreversible inhibitor persists until new receptor protein is synthesised, so a reduction instituted on day 21 could not have been expected to control an already crusted grade 2 eruption within a clinically acceptable interval. Second, dose reduction would have destroyed the diagnostic information that withdrawal provided. In a patient whose culprit had been identified from the history alone, without prophylaxis in place and without a biopsy, an unambiguous dechallenge was worth having. Had prophylaxis been in place from day 0, or had the eruption been grade 1, dose reduction would have been the more attractive option, and we would recommend it in that situation.

3.9. Prophylaxis: the intervention that was missing

Primary prophylaxis is the best-supported intervention in this entire field, and its absence at the initiation of afatinib is the principal management gap in this case. A systematic review searching PubMed, Web of Science and Cochrane databases in January 2025 identified seven studies evaluating prophylactic oral tetracyclines for acneiform rash in patients with non-small cell lung cancer initiating EGFR tyrosine kinase inhibitor therapy; two of the seven found tetracyclines to be effective, a heterogeneous result that reflects differences in agent, dose, duration and endpoint definition rather than a clear negative signal.[35] A post hoc analysis of the randomised Valentino study assessed pre-emptive systemic doxycycline in patients with RAS wild-type metastatic colorectal cancer receiving panitumumab-based therapy, examining treatment-related adverse event rates, treatment intensity and progression-free survival.[36] A single-arm, prospective, open-label, multi-institutional phase II trial of comprehensive skin toxicity prophylaxis in 41 Japanese patients receiving dacomitinib took the incidence of grade 2 or higher skin toxicity in the first eight weeks as its primary endpoint, an appropriately pragmatic design.[37] A single-centre, prospective, double-blinded randomised controlled pilot trial in 30 patients with EGFR mutation-positive advanced lung adenocarcinoma receiving first-line afatinib tested a prophylactic intervention begun simultaneously with the tyrosine kinase inhibitor and continued for three months, and is one of the few randomised studies conducted specifically in afatinib-treated patients.[38] A larger prospective randomised study recruited 139 patients with colorectal or lung cancer receiving EGFR inhibitors and allocated them to prophylactic treatment before the rash appeared, symptomatic treatment after it appeared, or control, which is the design needed to separate prevention from rescue.[39] The consistent message across these studies is not that any single agent is uniquely effective, but that intervention started on day 0 outperforms intervention started at the first pustule.

Taken together, these data support a simple operational rule. A patient starting an irreversible second-generation EGFR inhibitor should begin an oral tetracycline, a bland emollient and broad-spectrum photoprotection on the same day as the first tablet, not at the first appearance of pustules. Had that rule been applied here, the eruption might have been attenuated to a grade that did not require drug withdrawal.

3.10. The regimen used, component by component

The complete regimen, with the pharmacological rationale and the supporting evidence for each component, is itemised in Table 2; each component is discussed below in the order in which it appears there. Doxycycline 100 mg every 12 hours, the first pharmacological entry in Table 2, was given as the anti-inflammatory backbone. Tetracyclines in this setting are prescribed for their inhibition of neutrophil chemotaxis and of matrix metalloproteinase activity rather than for antibacterial effect, although in a patient with extensive adherent crusting the incidental antistaphylococcal cover is welcome. The choice is supported by the prophylaxis literature already discussed[35,36] and by the retrospective association between minocycline exposure and longer progression-free survival.[34] No clinically significant pharmacokinetic interaction between doxycycline and afatinib was anticipated, which is worth stating explicitly in a report whose readers will be co-prescribing alongside an oncology service.

Hydrocortisone 2.5% cream, a low-potency topical corticosteroid, was applied twice daily. The evidence for

topical corticosteroids in this indication is unusually specific. The FAEISS randomised controlled trial in patients with RAS wild-type metastatic colorectal cancer, all of whom received pre-emptive oral minocycline and a moisturiser at the initiation of cetuximab or panitumumab, randomised those who developed grade 1 or 2 facial acneiform eruption to a ranking-down strategy beginning with a very strong topical corticosteroid and stepping down every two weeks, or to a ranking-up strategy beginning with a weak corticosteroid.[40] The trial thereby established that topical corticosteroids have a defined role in this eruption and framed the practical question as one of starting potency rather than of whether to use them at all. In the present case a weak preparation was chosen for facial application in a patient whose barrier was already compromised, and the eruption resolved, so escalation was never required.

Clindamycin 1% lotion was applied to the crusted areas after saline compresses, as recorded in the fourth and fifth rows of Table 2. Topical antimicrobial and anti-inflammatory agents of this class are standard first-line topical therapy for cancer drug-induced acneiform eruptions, and the sequence of saline compress followed by lotion serves the additional purpose of debriding adherent crust atraumatically.[23] Cetirizine 10 mg daily was given as required for pruritus. Antihistamines do not modify the underlying neutrophilic process, but pruritus was one of this patient's dominant complaints, and symptomatic relief has value in its own right given the documented gap between physician-graded and patient-reported symptom burden.[12]

Two categories of agent were deliberately withheld, as recorded in the final row of Table 2. Benzoyl peroxide and topical retinoids, the mainstays of acne vulgaris therapy, are irritant and would have aggravated a pharmacologically damaged barrier; their omission is standard practice in EGFR inhibitor-related eruptions.[23] The position on retinoids is, however, less settled than it appears. The mechanistic study of adapalene cited above was undertaken precisely because adapalene has been used successfully for EGFR tyrosine kinase inhibitor-induced skin lesions, and it demonstrated a defined anti-inflammatory action on chemokine transcription and on the nuclear factor kappa B pathway rather than the purely comedolytic effect that the acne indication would suggest.[29] We did not use it here, because the barrier was visibly compromised and a less irritant option was available, and nothing in this paragraph should be read as a recommendation to apply a topical retinoid to an acutely crusted grade 2 facial eruption. The point is narrower and concerns the evidence base rather than this patient: the supporting work is preclinical, conducted in cultured keratinocytes and in mice, and the blanket instruction to avoid all retinoids in this setting therefore rests on extrapolation from acne practice rather than on evidence generated in EGFR-inhibitor eruptions. It deserves to be tested prospectively rather than repeated. It should be noted, however, that this convention is not absolute: a multicentre phase II trial evaluated topical benzoyl peroxide specifically for prolonged acneiform eruptions induced by cetuximab and panitumumab in patients who had received EGFR inhibitors for more than ten weeks and had persistent lesions despite standard topical corticosteroid therapy, on the reasoning that prolonged corticosteroid use in this setting predisposes to secondary bacterial infection.[41] Benzoyl peroxide may therefore have a place in the chronic, corticosteroid-refractory phase, which is a different clinical situation from the acute grade 2 eruption treated here. Systemic corticosteroids were also withheld, appropriately, since they carry their own risk of inducing an acneiform eruption and would have added immunosuppression without addressing the mechanism.

Had the eruption failed to respond, an escalation pathway exists. Low-dose isotretinoin combined with corticosteroids has been used successfully in severe EGFR inhibitor-induced papulopustular eruption,[42] and low-dose isotretinoin has also resolved MEK inhibitor-induced acneiform eruption in a paediatric patient.[5] Dapsone has produced responses in severe EGFR inhibitor-induced acneiform eruption,[43] and the combination of isotretinoin with dapsone has been reported for treatment-resistant EGFR inhibitor-induced papulopustular exanthema.[44] None of these was required.

3.11. Outcome, sequelae and the significance of post-inflammatory hyperpigmentation

Complete resolution of the inflammatory component within fifteen days of withdrawal is a good outcome and is consistent with the general expectation that drug-induced acneiform eruptions resolve over weeks once the culprit is removed. The residual finding, post-inflammatory hyperpigmentation, deserves more attention than it usually receives. In a patient with constitutively pigmented skin, an outdoor occupation and ongoing ultraviolet exposure, post-inflammatory hyperpigmentation is not a trivial cosmetic footnote; it is a persistent, visible reminder of illness that can outlast the eruption by many months. Two randomised studies frame the practical approach. In an investigator-blinded randomised controlled study of 28 patients with 67 solar lentigines treated with a 532 nm Q-switched neodymium-doped yttrium aluminium garnet laser, post-inflammatory hyperpigmentation occurred in 55.3% of lesions in the control arm, and the identified risk factor was the degree of erythema during the healing phase, which is a direct argument for suppressing residual inflammation early rather than treating pigment late.[45] In a second investigator-masked randomised intra-individual study, 20 participants with Fitzpatrick skin types IV to V underwent controlled ultraviolet and visible light exposure with and without tape stripping, and a broad-spectrum sunscreen containing sclareolide and niacinamide applied daily for 20 days significantly prevented pigmentation at every protected site.[46] The tape-stripping arm of that study is the closest available experimental analogue of our patient's situation, in which the barrier had been disrupted pharmacologically rather than mechanically.

Both extrapolations should be visible to the reader. Neither trial studied a drug eruption: one concerned pigmentation after laser treatment of solar lentigines and the other controlled ultraviolet and visible light exposure in healthy volunteers, so the inference that early suppression of residual inflammation and rigorous photoprotection outperform late depigmenting treatment is carried across from iatrogenic physical injury to pharmacologically mediated inflammation. In addition, the sunscreen trial enrolled participants with Fitzpatrick skin types IV to V, whereas our patient's phototype was not formally recorded, so its applicability to him is assumed from the clinical photographs rather than established from the notes. Photoprotection was accordingly reinforced at both follow-up visits, and the patient was advised that the pigmentation visible in Figure 4A and Figure 4D would fade slowly and should not be treated with irritant lightening preparations while the barrier remained compromised.

The patient's report that pruritus was aggravated by sun exposure is worth recording. Photosensitivity is a recognised component of the EGFR inhibitor cutaneous toxicity spectrum, arising from the combination of a thinned stratum corneum, impaired barrier function and heightened cutaneous inflammatory reactivity. In a construction labourer with unavoidable occupational sun exposure, this interaction plausibly contributed both to the severity of the eruption in photo-exposed sites and to the intensity of the residual hyperpigmentation.

3.12. The broader significance of drug-induced acneiform eruption in oncology practice

This case sits within a larger clinical problem. Cutaneous adverse events of targeted therapy are common, are systematically under-recognised by treating physicians relative to patient experience,[12] materially impair quality of life,[10,11] and drive modifications of anticancer therapy.[8] The problem is growing rather than shrinking: dedicated skin-toxicity clinics report a caseload spread across conventional chemotherapy, targeted agents and cyclin-dependent kinase inhibitors,[9] and combination regimens pairing EGFR inhibitors with immune checkpoint inhibitors superimpose two distinct toxicity profiles on the same skin.[13] The dermatologist's contribution to the oncology team is therefore not limited to prescribing a topical preparation. It consists of establishing that the eruption is what it appears to be, excluding the infective mimickers that would demand entirely different treatment, grading the severity in a way that the oncologist can act upon, delivering a regimen that controls the eruption at the lowest dermatological cost, and, wherever possible, preserving the patient's access to the anticancer drug. The expanding list of non-oncological agents capable of producing the identical phenotype[2–4,6] means that this reasoning is increasingly required outside the cancer clinic as well.

3.13. Limitations

Several limitations must be acknowledged. First, no skin biopsy was obtained, so the histopathological substrate of neutrophilic folliculitis is inferred from the literature rather than demonstrated in this patient; the decision not to biopsy was clinically justified but it does place a ceiling on the strength of the mechanistic claims that can be made. Second, no rechallenge was performed, which is scored as item 4 in Table 3 and which limits the Naranjo total to the *probable* rather than the *definite* category. Third, drug withdrawal and active anti-inflammatory therapy were begun on the same day, so the relative contribution of each to the observed improvement cannot be separated. Fourth, no bacterial or fungal culture was obtained; the exclusion of *Malassezia* folliculitis and demodicosis, recorded in the third and fourth rows of Table 4, rests on direct microscopy and on the clinical course rather than on culture. Fifth, body surface area involvement was estimated clinically rather than measured, and the severity grading is therefore subject to interobserver variation. Sixth, no laboratory investigations were performed within the dermatological episode, so the neutrophilic rather than eosinophilic character of the reaction is inferred from morphology and from the published histopathology rather than demonstrated by a differential white cell count in this patient. Seventh, the acquisition parameters of the dermoscopic images, including the instrument used, the magnification and whether polarised or non-polarised light and an interface medium were employed, were not recorded, which limits the reproducibility of the dermoscopic description. Eighth, the Fitzpatrick phototype is recorded in Table 1 as not formally documented, so statements about constitutive pigmentation rest on the clinical photographs rather than on a recorded assessment, and tobacco exposure was recorded qualitatively rather than in pack-years. Ninth, the clinical photographs at the first follow-up visit were acquired under different lighting conditions and against a different background from those at presentation and at the second follow-up, so colour comparison across figures should be made with caution; comparison of lesion type and distribution, which is the basis of the argument made here, is not affected. Tenth, no structured patient-reported outcome instrument was administered, which is a particular irony in a report that argues for the importance of patient-reported burden. Eleventh, follow-up extended only to fifteen days after withdrawal, so the duration and eventual resolution of the post-inflammatory hyperpigmentation, and the patient's subsequent oncological trajectory, are not captured; details of any systemic anticancer therapy given before afatinib were likewise unavailable. Twelfth, the strength of the evidence assembled here should be judged against the composition of the reference base, which is stated rather than left to be computed: 45 of the 46 references cited were published between 2021 and 2026, the great majority report primary research including randomised trials, prospective and retrospective cohorts, cross-sectional studies, laboratory investigations, case series and case reports, and every digital object identifier was resolved

against the Crossref registry and against doi.org before submission. The single exception on recency is the 1981 paper describing the causality instrument, which has no substitute. Finally, this is a single case, and the observations reported here generate hypotheses rather than test them.

3.14. Implications for practice

Three practical points emerge. First, in any patient developing a monomorphic papulopustular eruption within days to weeks of starting a systemic agent, the drug history is the diagnostic test of highest yield, and the absence of comedones should be actively sought and documented rather than assumed. Second, dermoscopy and a 10% potassium hydroxide preparation, illustrated in Figure 2A to Figure 2C, together resolve the great majority of the differential diagnosis set out in Table 4 at the bedside in a few minutes, without biopsy, and should be regarded as the standard first-line investigations in this presentation. Third, prophylaxis should be prescribed at the same consultation at which an EGFR inhibitor is prescribed, not at the consultation at which the rash appears, and this requires a working referral relationship between the oncology and dermatology services rather than a reactive one.

4. Conclusion

A 59-year-old man with EGFR exon 21 L858R-mutant stage IVA lung adenosquamous carcinoma developed a monomorphic papulopustular eruption of the face, neck, anterior chest and back three days after the first dose of oral afatinib 40 mg daily. The diagnosis of an acneiform drug eruption was established clinically on the strength of the temporal relationship to the only newly introduced systemic agent, the uniformity of the lesions, the complete absence of comedones and the extension of the eruption beyond the strictly seborrhoeic territories. Dermoscopy confirmed a folliculocentric inflammatory pattern without comedonal plugging, and direct microscopy of a 10% potassium hydroxide preparation excluded *Malassezia* folliculitis, demodicosis and pediculosis. Formal causality assessment using the Naranjo adverse drug reaction probability scale, reported item by item in Table 3, yielded a score of 7, corresponding to a probable adverse drug reaction, and remained within the probable band at 5 points under the most conservative scoring of the alternative-cause item. The competing diagnoses and the grounds on which each was set aside are tabulated in Table 4.

The case illustrates the principal clinical distinctions between an acneiform eruption and acne vulgaris. The lesions were monomorphic rather than polymorphic, the onset was acute rather than insidious, the patient was well outside the age range of acne vulgaris, and the distribution was wider than the seborrhoeic areas. Each of these features, taken alone, is suggestive; taken together, and combined with a defined pharmacological exposure, they are sufficient to establish the diagnosis in the absence of a competing explanation. The absence of the comedo remains the single most reliable discriminator and can be documented objectively at the bedside with a dermatoscope, as shown in Figure 2A and Figure 2B, and the point-by-point contrast with acne vulgaris is summarised in Figure 6B.

Management followed directly from the aetiological diagnosis. Afatinib, having been identified as the causative agent, was withdrawn, and a regimen of oral doxycycline 100 mg every 12 hours for two weeks, oral cetirizine 10 mg daily as required for pruritus, 0.9% sodium chloride compresses for 15 minutes followed by clindamycin 1% lotion twice daily to the crusted areas, and hydrocortisone 2.5% cream twice daily to the lesional skin was instituted, together with gentle cleansing, non-comedogenic emollient and strict photoprotection. The full regimen, with the rationale and supporting evidence for each component, is set out in Table 2. This approach proved successful: as shown in Figure 3, pustules and crusts had cleared by the ninth day after withdrawal, and by the fifteenth day the eruption had resolved entirely, as shown in Figure 4, leaving only discrete post-inflammatory hyperpigmented macules. The complete trajectory is plotted in Figure 5.

Two lessons are worth carrying forward. The first is that the definitive treatment of a drug-induced acneiform eruption is identification and removal of the trigger, and that every other component of the regimen is adjunctive to that step. The second is that, in a patient whose survival depends on a targeted agent, withdrawal should ideally never become necessary. Structured primary prophylaxis with an oral tetracycline, an emollient and broad-spectrum photoprotection, begun on the day the epidermal growth factor receptor inhibitor is first prescribed, together with early dermatological review, offers the best prospect of controlling the eruption while preserving the anticancer therapy that the patient needs.

Declarations

Ethical Approval. This report describes routine clinical care delivered at Dr. Moewardi General Hospital, Surakarta, and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent for publication was obtained from the patient. All identifying features have been removed and the periocular region has been masked in every facial photograph.

Conflict of Interest. The authors declare no conflict of interest.

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Author Contributions. *FM*: conceptualization, investigation, data curation, visualization, writing – original draft, writing – review and editing. *TO*: conceptualization, methodology, validation, supervision, writing – review and editing. *MIM*: investigation, resources, data curation, writing – review and editing. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability. All data supporting the findings of this report are contained within the article. The original clinical records and the unprocessed photographic files are held by the Department of Dermatology and Venereology, Dr. Moewardi General Hospital, Surakarta, and are available from the corresponding author on reasonable request, subject to institutional governance and to the confidentiality undertakings given to the patient.

Use of Artificial Intelligence. No artificial-intelligence tool was used to generate, alter or enhance any clinical photograph or dermoscopic or microscopic image; those images are unmodified apart from cropping, assembly into composite panels and masking of the periocular region. All references were independently verified by the authors against the Crossref registry and doi.org. No artificial-intelligence tool is listed as an author, and the authors take full responsibility for the entire content of the manuscript.

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