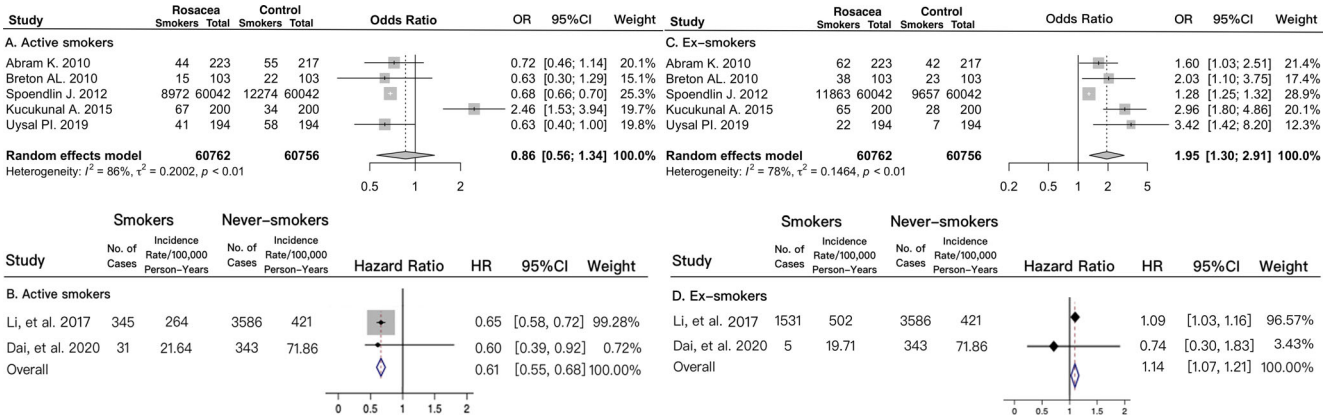

Figure 2 Forest plot for the relationship of smoking status and the occurrence of rosacea. (a) Active smokers and the occurrence of rosacea (based on case-control studies); (b) active smokers and the occurrence of rosacea (based on cohort studies); (c) ex-smokers and the occurrence of rosacea (based on case-control studies); (d) ex-smokers and the occurrence of rosacea (based on cohort studies).

that ETR was a disease of active smokers, while PPR and PhR were related to ex-smokers.[9] Thus, the correlation of ETR and PPR and smoking is still uncertain and requires further research.

This study has several limitations. First, all the included studies in our meta-analysis were retrospective. Second, due to limited data, this study did not evaluate the association between smoking status and the occurrence of ETR, PPR and PhR subtypes. Third, the funnel plot showed high-standard errors between studies with large sample sizes and those with small sample sizes, which suggests selective outcome reporting or publication bias. Finally, the ethnics and baseline comorbidities were varied among the included patients.

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REFERENCES

1. Elewski B, Draelos Z, Dréno B *et al*. Rosacea – global diversity and optimized outcome: proposed international consensus from the Rosacea International Expert Group. *J. Eur. Acad. Dermatol. Venereol.* 2011; **25**: 188–200.
2. Two A, Wu W, Gallo R *et al*. Rosacea: part I. Introduction, categorization, histology, pathogenesis, and risk factors. *J. Am. Acad. Dermatol.* 2015; **72**: 749–58; quiz 59–60.
3. Wilkin J, Dahl M, Detmar M *et al*. Standard classification of rosacea: report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. *J. Am. Acad. Dermatol.* 2002; **46**: 584–7.
4. Del Rosso J. Advances in understanding and managing rosacea: part 2: the central role, evaluation, and medical management of diffuse and persistent facial erythema of rosacea. *J. Clin. Aesthet. Dermatol.* 2012; **5**: 26–36.
5. Higuchi L, Khalili H, Chan A *et al*. A prospective study of cigarette smoking and the risk of inflammatory bowel disease in women. *Am. J. Gastroenterol.* 2012; **107**: 1399–406.
6. Ortiz A, Grando S. Smoking and the skin. *Int. J. Dermatol.* 2012; **51**: 250–62.
7. Sopori M. Effects of cigarette smoke on the immune system. *Nat. Rev. Immunol.* 2002; **2**: 372–7.
8. Abram K, Silm H, Maaroos H *et al*. Risk factors associated with rosacea. *J. Eur. Acad. Dermatol. Venereol.* 2010; **24**: 565–71.
9. Li W, Han J, Choi H *et al*. Smoking and risk of incident psoriasis among women and men in the United States: a combined analysis. *Am. J. Epidemiol.* 2012; **175**: 402–13.

Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Figure S1. Flowchart of the selection process of eligible studies.
Figure S2. Forest plot for the relationship of cigarette smoking and the occurrence of rosacea.
Table S1. Quality assessment of the included studies.
Table S2. Characteristics of the included patients.

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Research Letter

Dear Editor,

Trichoscopy-assisted hair pull test: A helpful adjunct to trichoscopy for diagnosing and managing alopecias

Non-invasive techniques constitute valuable tools in the diagnostic work-up of patients with hair loss. Amongst them, hair pull test and trichoscopy are well-established.[1–3]

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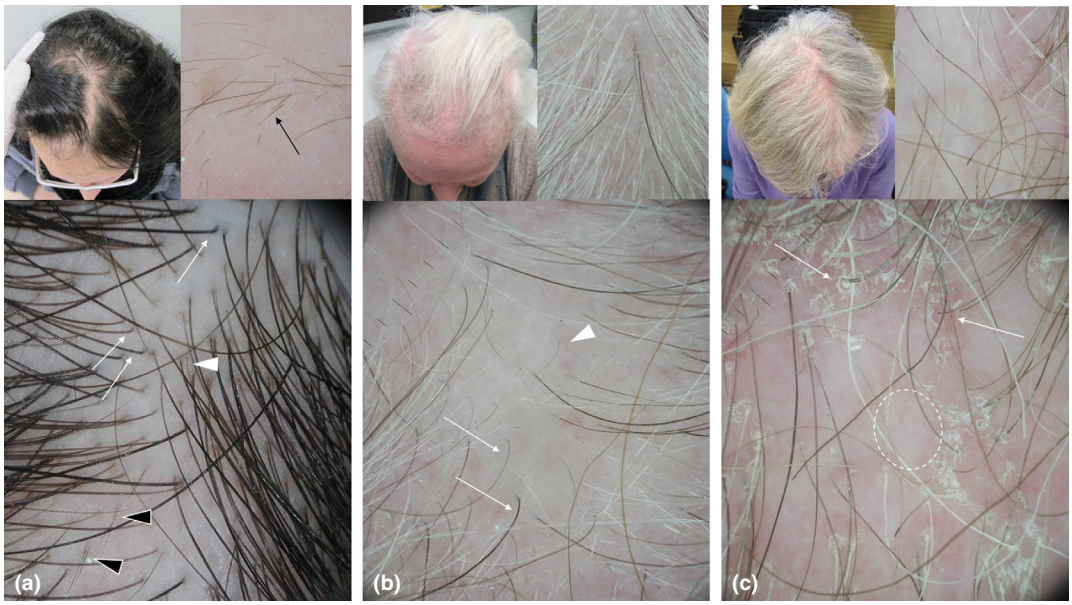

Figure 1 Clinical and trichoscopic images of cases 1–3. (a) Case 1 - diffuse AA. Thinning of the crown area seen on clinical examination (upper left inset). Dermoscopy shows predominance of single hairs emerging from individual follicular ostia (single hair units), subtle bending of several hairs at scalp level (arrows), short bundled regrowing hairs (black arrowheads) and few Pohl-Pinkus constrictions (white arrowhead). The eyebrows display dystrophic hair shafts, such as broken hairs and 'exclamation mark'-hairs (arrow; upper right inset). (b) Case 2 - methotrexate-induced acute TE with AGA. Diffuse thinning of the crown area is seen (upper left inset). Trichoscopy of the frontal scalp shows distinct variability of hair shaft diameter (arrows), predominance of single hairs emerging from individual follicular ostia and presence of multiple short vellus hairs (arrowhead). Trichoscopy of occipital scalp reveals age-appropriate hair and scalp findings (upper right inset). (c) Case 3 – LPP. Diffuse thinning of the crown area with small alopecic patches is seen (upper left inset). Trichoscopy without immersion medium displays reduced hair density, erythema and concentrically arranged layers of scales around remaining hair follicle openings/proximal hair shafts ('peripilar casts'; arrows), and pink-white scalp areas with focal absence of follicular openings (dashed circle). Trichoscopy with immersion medium from the same area accentuates perifollicular erythema below the (consecutively translucent) scales (arrows; upper right inset).

A classic trichogram, as a semi-invasive method, enables visualisation of proximal hair shafts and hair bulbs, which is impossible with trichoscopy.[4] Invasiveness, need of special equipment and time requirements make this method, however, not generally applicable.

To diminish the gap between non-invasive trichoscopy and microscopic assessment of entire hairs under the light microscope, we propose to perform a 'trichoscopy-assisted hair pull test' in patients whose pull test is positive. The addition of dermoscopy enables immediate assessment of proximal hair shafts/hair roots of pulled hairs with magnification.

The following three cases of female patients with predominant hair thinning of the crown area – a clinical pattern suggestive of androgenetic alopecia (AGA) – will demonstrate diagnostic benefit and therapeutic impact of this method in daily routine.

CASE 1

A 22-year-old female patient reported rapid-onset hair shedding. Patient history and laboratory results were otherwise unremarkable. On clinical examination, there were distinct thinning of the crown area (Fig. 1a) and a positive hair pull test all over the scalp. Trichoscopy showed multiple regrowing hairs beside single hair units, reflecting concomitant hair loss and hair regrowth, as observed in telogen effluvium (TE). Surprisingly, dermoscopy of pulled hairs revealed a pencil point-like appearance of proximal hair portions (Fig. 2a), a characteristic light microscopy finding in alopecia areata (AA).[5] A subsequent dermoscopic examination of eyebrows actually revealed dystrophic hair shafts in-vivo (Fig. 1a). A thorough re-evaluation of scalp hairs showed subtle bending of several hairs at scalp level due to incipient thinning of proximal hair shafts ('coudability hairs'; Fig. 1a), an early trichoscopic finding in AA. In the following, the patient developed alopecia areata universalis with satisfactory response to steroid pulse therapy.

CASE 2

A 78-year-old female patient presented with a two-month history of increased hair shedding. The medical history included arterial hypertension and rheumatoid arthritis, for which methotrexate was initiated three months before her visit. Her blood tests were inconspicuous. Clinical examination revealed reduced hair density, predominantly of the crown area (Fig. 1b), and a positive hair pull test in all scalp areas. Trichoscopy showed features of AGA in the crown area (i.e. hair diameter diversity, single hair units and increased proportion of short vellus hairs) and increase of single hair units in less androgen-dependent

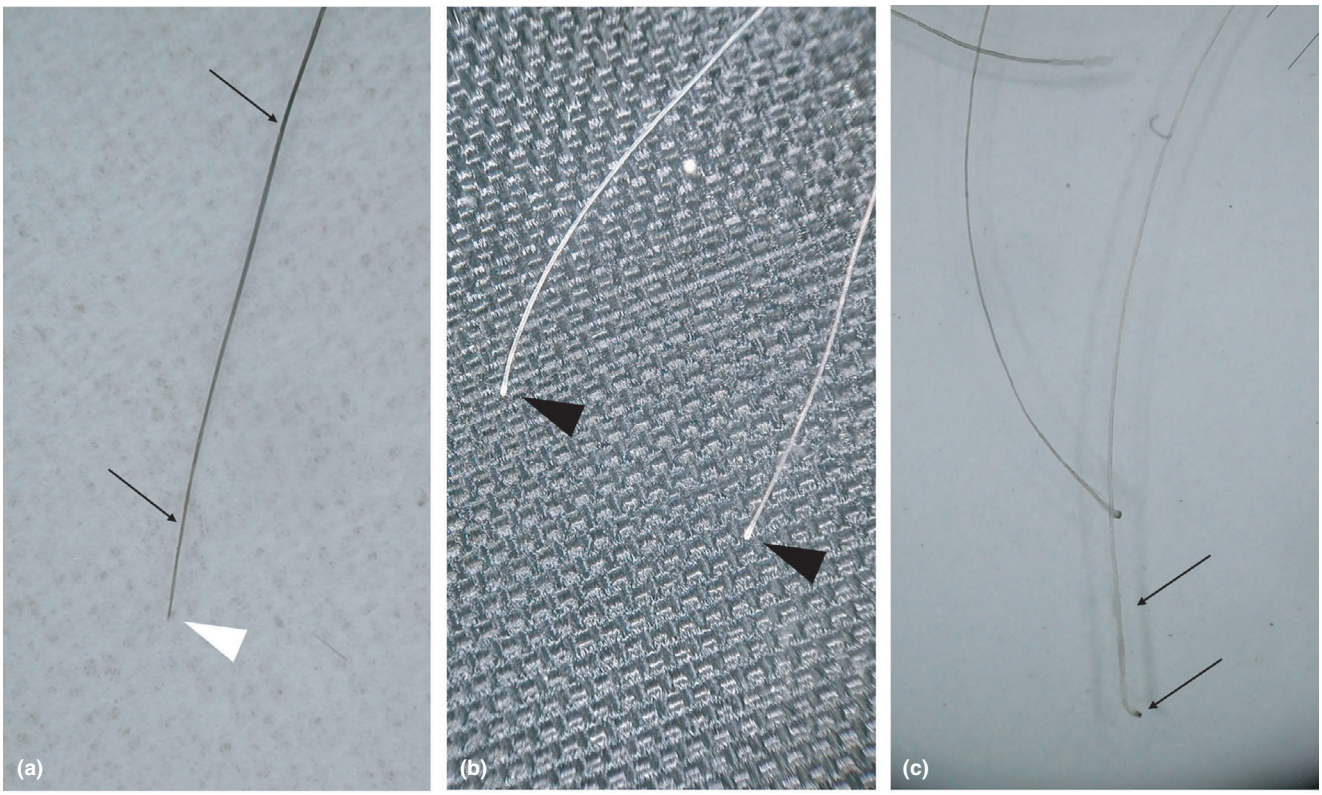

Figure 2 Dermoscopic pictures of hairs pulled out in cases 1–3. (a) Case 1- Hair shaft with thinning towards the proximal end (arrows) and dystrophic hair bulb ('pencil point-like appearance'; arrowhead) in case 1. (b) Case 2 shows telogen hairs with non-pigmented, small, stiff, club-shaped hair bulbs without inner root sheaths (arrowheads). (c) Case 3 - Anagen hairs with translucent hair root sheaths around proximal hair shafts and smooth, darkly pigmented hair bulbs positioned at an acute angle to the shaft are seen (arrows).

scalp areas. Dermoscopy of pulled hairs showed telogen roots (Fig. 2b), and we suspected methotrexate-induced acute TE in pre-existing AGA. Indeed, hair shedding improved significantly within four months after switching her disease-modifying anti-rheumatic drug.

CASE 3

A 65-year-old female patient noticed slowly progressive hair thinning for one year. The patient's medical history was unremarkable. Clinical examination revealed thinning of the crown area with small alopecic patches, widening of the central part line, recession of the frontal hairline and decrease of eyebrows (Fig. 1c). The hair pull test was positive in clinically affected areas. Trichoscopy showed pink-white scalp areas lacking follicular openings, erythema and scaling around remaining hair follicle openings/proximal hair shafts, and hair tufting. Dermoscopy of pulled hairs revealed anagen roots (Fig. 2c), which is indicative for a progressive scarring process.[6] Punch biopsies confirmed the clinically suspected diagnosis of lichen planopilaris (LPP).

The conventional hair pull test is a basic diagnostic method to confirm and quantify hair loss in different scalp regions.[7] Dermoscopic examination of pulled hairs with the same device used for trichoscopy can provide key pathophysiological information. The identification of dystrophic hair roots can help differentiate diffuse AA from other common hair loss diseases, such as shown in Case 1 (Fig. 1). In a study of *Quercetai et al*., the presence of dystrophic hairs was found to be the only clue for early detection of AA incognita in many patients with profuse hair shedding, clinically diagnosed as having TE or AGA.[5] Dermoscopy of hairs extracted from frontal and occipital scalp areas in Case 2 displayed regular telogen roots, substantiating the clinically suspected diagnosis of acute TE related to methotrexate intake in association with long-standing AGA. The hair pull test displaying anagen roots in Case 3 served as confirmatory diagnostic tool, facilitated selection of appropriate biopsy site, and – most important in scarring alopecias – enabled non-invasive monitoring of response to systemic therapy during follow-up.[6,8]

We conclude that a 'trichoscopy-assisted hair pull test' is a helpful non-invasive diagnostic adjunct in the evaluation of patients with hair loss and positive hair pull test.

PATIENT CONSENT FOR PUBLICATION STATEMENT

All patients in this manuscript gave written informed consent to the publication of their clinical and dermoscopic photographs.

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REFERENCES

1. Mubki T, Rudnicka L, Olszewska M *et al*. Evaluation and diagnosis of the hair loss patient: Part I. History and clinical examination. *J. Am. Acad. Dermatol.* 2014; **71**: 415.e1–e15.
2. Mubki T, Rudnicka L, Olszewska M *et al*. Evaluation and diagnosis of the hair loss patient: part II. Trichoscopic and laboratory evaluations. *J. Am. Acad. Dermatol.* 2014; **71**: 431.e1–e11.
3. Jain N, Doshi B, Khopkar U. Trichoscopy in alopecias: diagnosis simplified. *Int. J. Trichol.* 2013; **5**: 170–8.
4. Serrano-Falcón C, Fernández-Pugnaire MA, Serrano-Ortega S. Hair and scalp evaluation: the trichogram. *Actas Dermosifiliogr.* 2013; **104**: 867–76.
5. Quercetani R, Rebora AE, Fedi MC *et al*. Patients with profuse hair shedding may reveal anagen hair dystrophy: a diagnostic clue of alopecia areata incognita. *J. Eur. Acad. Dermatol. Venereol.* 2011; **25**: 808–10.
6. Harries MJ, Trueb RM, Tosti A *et al*. How not to get scar(r)ed: Pointers to the correct diagnosis in patients with suspected primary cicatricial alopecia. *Br. J. Dermatol.* 2009; **160**: 482–501.
7. McDonald KA, Shelley AJ, Colantonio S *et al*. Hair pull test: Evidence-based update and revision of guidelines. *J. Am. Acad. Dermatol.* 2017; **76**: 472–7.
8. Griggs J, Trueb RM, Gavazzoni Dias MFR *et al*. Fibrosing alopecia in a pattern distribution. *J. Am. Acad. Dermatol.* 2020; S0190-9622(20)30030-X. https://doi.org/10.1016/j.jaad.2019.12.056

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Research Letter

Dear Editor,

Primary cutaneous aggressive epidermotropic CD8$^+$ T cell lymphoma mimicking pyoderma gangrenosum

Primary cutaneous aggressive epidermotropic CD8$^+$ T-cell lymphoma [CD8$^+$ PCAETL] is a rare, distinct subtype of cutaneous T-cell lymphoma (CTCL) that is characterized by aggressive nature, a tendency to spread rapidly to extracutaneous areas, poor prognosis.[1–5] Here, we present a case with CD8$^+$ PCAETL due to its rarity, mimicking pyoderma gangrenosum with no systemic involvement.

A 68-year-old man presented to our outpatient clinic with painful lesions on his body. The lesions started on the left leg one year ago and spread to the entire body surface over time. After histopathological confirmation, the patient was diagnosed with pyoderma gangrenosum and administered systemic corticosteroid, cyclosporine, and infliximab. The patient, who did not benefit from treatments and whose lesions progressed rapidly, stopped the infliximab treatment and applied to our clinic. The patient's history revealed diabetes mellitus and hypertension and the family's history was unremarkable. Dermatological examination revealed multiple irregularly bounded plaques with ulceration and necrotic crusting on the face, neck, trunk, bilateral upper and lower extremities. In addition, there was an erythematous-violaceous irregularly bounded 23 × 30 cm-sized ulcer extending behind the leg of the patient, accompanied by necrotic crusts and purulent discharge (Fig. 1).

The high glucose and CRP level, low serum albumin and hemoglobin level, and prolonged erythrocyte sedimentation rate were revealed in laboratory investigations. Other laboratory tests for narrowing the differential diagnosis showed normal findings. A new biopsy from the ulcerated plaque on the left leg was taken. Histopathology revealed ulceration, widespread necrotic keratinocytes in the epidermis, and vacuolar degeneration in the basal layer. Mononuclear inflammation that destroys the hair follicle structure was observed in the dermis. Vasculopathic changes characterized by fibrin deposition and infiltration of neutrophil leukocytes in the wall of some vessels were observed. The patient was diagnosed as pyoderma gangrenosum and intravenous immunoglobulin 0.2 g/kg for 5 days and mycophenolate mofetil 2 g/day treatments were started. Secondary excisional skin biopsy was taken from the erythematous plaque on the trunk due to the lack of response to the treatment applied for a few weeks and the continued appearance of new lesions. Histopathology revealed atypical lymphocytes in the epidermis, which showed linear alignment in the basal layer in the areas of the epidermis adjacent to the ulcer and small-medium-sized atypical lymphocytes with largely folliculotropism and syringotropism in the dermis (Fig. 2). Immunohistochemically, atypical lymphoid cells showed CD3, CD8, TIA-1, granzyme-A, TCR-BF1 positivity, and CD2 and CD5 expression loss. While small lymphocytes were stained with CD4, CD30 resulted as negative (Fig. 3).

With clinical, histopathological, and immunohistochemical findings, the patient was evaluated as CD8$^+$ PCAETL. PET-CT imaging showed no involvement other than widespread 18F-FDG involvement in the skin. Stem cell transplantation was planned after the electron beam treatment with the recommendation of radiation oncology, but the patient died 2 weeks after the diagnosis without treatment.

CD8$^+$ PCAETL is still classified as a provisional entity in the recent lymphoma classification due to its rarity, relatively variable clinical appearance, and continued improvement of clinicopathological features in the literature.[1] Overactivation of JAK2 signaling underlies the pathogenesis of the disease.[4] Clinically, the disease

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