

A Case of Graham–Little–Piccardi–Lasseur Syndrome Successfully Treated with Minocycline

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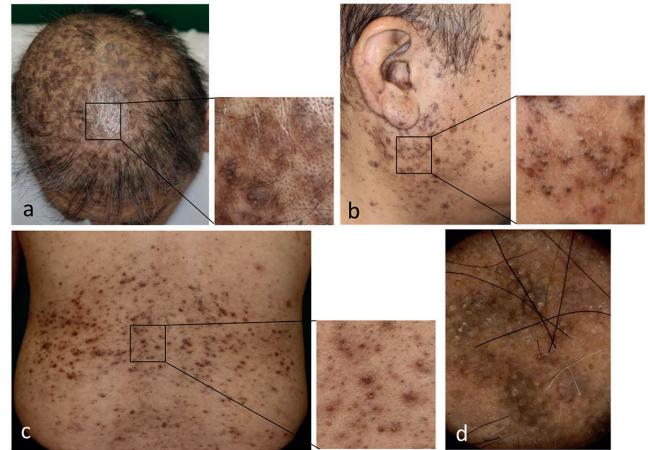
Lichen planopilaris, a chronic lymphocytic inflammatory disease, causes selective destruction of the hair follicles, resulting in scarring alopecia. The Graham–Little–Piccardi–Lasseur syndrome (GLPLS), a rare subtype of lichen planopilaris, is characterized by a triad of scarring alopecia of the scalp, non-scarring alopecia of the axillary and pubic skin, and widespread follicular hyperkeratosis (1). The management of GLPLS remains uncertain, with no currently established therapeutic regimens available. Herein, we report a case of GLPLS that was effectively treated with minocycline.

CASE REPORT

A 56-year-old Japanese man presented with a 3-month history of asymptomatic brown follicular hyperkeratotic plaque/papules disseminated across the body, with subtotal alopecia affecting the scalp (Fig. 1a–c). Some papules showed a comedo-like appearance, and/or were infected. Concurrently, the pubic and axillary hair growth had decreased slightly. Trichoscopy of the scalp revealed keratotic open follicular pores lacking hair shafts as well as hyperkeratosis and hyperpigmentation of the interfollicular epidermis (Fig. 1d). Histological examination of a scalp specimen revealed an enlarged follicular infundibulum, filled with keratin plugs, and follicular lichenoid tissue reactions in the infundibulum and isthmus (Fig. 2a, b). The interfollicular epidermis showed hyperkeratosis and partial vacuolar alteration along with numerous melanophages in the upper dermis (Fig. 2a, c). In the transverse section between the infundibulum and isthmus, a perifollicular lymphocytic infiltrate was seen with lichenoid tissue reactions and mild perifollicular fibrosis (Fig. 2d). A specimen from the trunk also revealed an enlarged follicular infundibulum with keratin plugs as well as dense lymphocytic infiltration with vacuolar alteration and dyskeratotic cells in the isthmus (Fig. 2e). The patient had undergone dialysis for 3 years owing to chronic renal failure. He had no family history of the condition and did not use medications related to the development of the symptoms (Table S1); furthermore, he was not exposed to dioxins. Finally, he did not have coronavirus disease 2019 (COVID-19) and had not received any COVID-19 vaccines. Blood and imaging tests revealed no elevation in the blood dioxin and sex hormone levels, and no evidence of malignancies or collagen diseases (Table S1). The patient was finally diagnosed with GLPLS.

After 6 weeks of minocycline treatment (200 mg/day [body weight: 90 kg]), hair growth resumed, and the hyperkeratotic plaques in the scalp were ameliorated; after 16 weeks, the follicular hyperkeratotic papules gradually decreased and eventually disappeared. After 19 months, minocycline was discontinued, and no relapse occurred during the 4-month follow-up (Fig. 1e–h). No concomitant topical treatment was administered. Trichoscopy revealed slightly sparse but firm hair growth on the scalp, along with some fine hair (Fig. 1g). During the clinical course, before

Before treatment with minocycline (panel a–d)



After treatment with minocycline (panel e–h)



Fig. 1. Clinical findings before and after treatment with minocycline.

Before treatment with minocycline, the patient exhibited subtotal alopecia and disseminated brown hyperkeratotic plaques in the scalp (a). Brown follicular hyperkeratotic plaques/papules also appear disseminated in the mandibular (b) and lumbar (c) regions; some of these show a comedo-like appearance and/or are infected. A trichoscopic image of the scalp lesion shows keratotic and open follicular pores in the absence of hair shafts as well as hyperkeratosis and hyperpigmentation in the interfollicular epidermis (d). After treatment with minocycline, the hair growth has resumed, and brown hyperkeratotic plaques/papules have disappeared without scarring (e–g). Trichoscopy reveals that the hair growth is slightly sparse (with a reduced number of hairs emerging from each follicle) but firm in the presence of some fine hair (h).

minocycline treatment, the patient developed generalized anhidrosis with a reduced sweating response to an intradermal injection of acetylcholine. The association of anhidrosis with GLPLS was unclear, and anhidrosis persisted even after the symptoms of GLPLS improved with minocycline treatment.

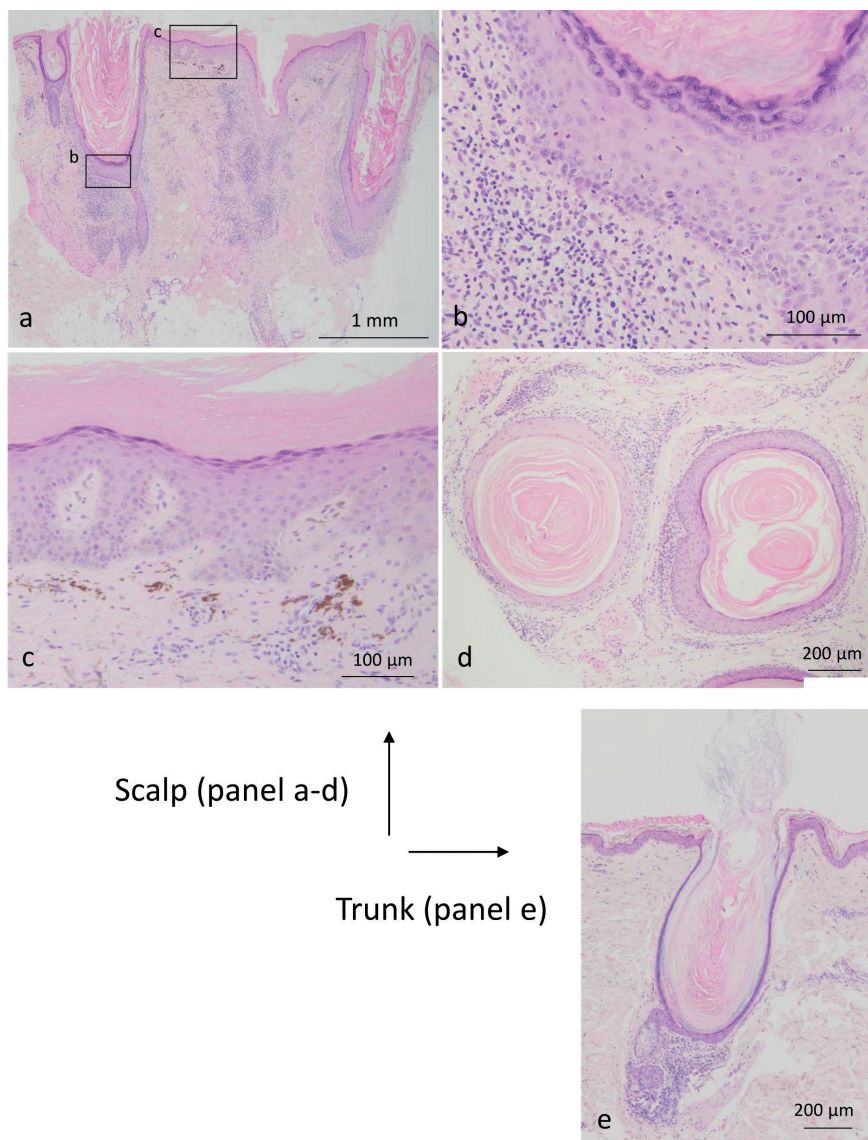


Fig. 2. Histological findings of the specimens obtained from the scalp (a–d) and trunk (e) lesions. (a) A low-power field of haematoxylin and eosin (HE) staining of the vertical sections. The follicular infundibulum is enlarged and filled with keratin plugs in the absence of hair shafts and sebaceous gland lobules. A dense perifollicular inflammatory infiltrate is observed around the upper part of the hair follicles. The interfollicular epidermis exhibits hyperkeratosis. (b) A high-power field (box b, panel a) reveals a dense lymphocytic infiltrate that damages the basal layer and keratinocytes, leading to vacuolar alteration and dyskeratotic cells. (c) A high-power field (box c, panel a) reveals hyperkeratosis and partial vacuolar alteration of the basal layer in the interfollicular epidermis, along with numerous melanophages within the superficial dermis. (d) A transverse section between the infundibulum and isthmus. A perifollicular lymphocytic infiltrate is apparent with vacuolar alteration and dyskeratotic cells as well as mild perifollicular fibrosis. (e) HE staining of the follicular hyperkeratotic papules in the trunk. The follicular infundibulum is enlarged with keratin plugs along with the dense perifollicular lymphocytic infiltrate around the isthmus. The lymphocytic infiltrate is associated with vacuolar alteration in the outer layer of the follicular epithelium.

DISCUSSION

The clinical condition in the present case should be distinguished from conditions exhibiting disseminated comedo-like eruptions, and those associated with chronic renal failure and haemodialysis. Conditions with disseminated comedo-like eruptions include chloracne and folliculotropic mycosis fungoides. Chloracne is a dioxin-induced skin disorder characterized by acneiform comedones, cysts, and pustules, with hyperpigmentation of the face, neck, and forearms (2). Chloracne affects the hair follicles, except those on the scalp (2), resulting in scarring. Our case clinically and histologically mimicked chloracne; however, the patient's condition was distinguished by the absence of dioxin exposure, scalp involvement, and healing without scarring. Folliculotropic mycosis fungoides (3) was excluded due to the absence of atypical lymphocytic infiltrates and follicular mucinosis.

Among chronic renal failure- and haemodialysis-associated conditions, dialysis-related β 2-microglobulin amyloidosis is characterized by osteoarticular symptoms caused by amyloid deposition. Skin lesions are rare but can present with a lichenoid appearance with clusters of small papules (4). This condition was ruled out in our case due to the absence of amyloid deposition and orthopaedic symptoms. Acquired perforating disorders are common skin conditions in patients with chronic renal failure and are characterized by transepidermal elimination of altered keratin, collagen, and/or elastic fibres (5). In our case, no transepidermal elimination of altered dermal structures and parakeratotic plugs with basophilic materials of cellular debris were noted; thus, acquired perforating disorders were ruled out. Therefore, a diagnosis of GLPLS was accordingly considered based on the occurrence of follicular lichenoid changes in the scalp, sparse axillary and pubic hair growth, and generalized follicular hyperkeratosis.

GLPLS management is challenging (1). For classic lichen planopilaris, the European S1 guidelines suggest topical/intralesional corticosteroids, systemic corticosteroids, cyclosporine, hydroxychloroquine, methotrexate, and topical tacrolimus as the first-line treatments (6). The efficacy of tetracyclines, proposed as second-line treatment, has been demonstrated in a single retrospective case-series (7). For GLPLS, however, an isolated case report revealed that a combination of hydroxychloroquine and doxycycline did not improve it but helped stabilize the disease (8). In our case, minocycline treatment restored scalp hair growth and diminished follicular hyperkeratosis over the body. We administered minocycline instead of the immunosuppressive medications because some hyperkeratotic papules/plaques were infected. Moreover, minocycline was chosen instead of doxycycline, because doxycycline was unavailable at our institution.

The present case might represent an early or mild case of GLPLS, i.e., before the development of severe damage to the follicular stem cells involved in lichen planopilaris (9), such that they could assist with hair regrowth following inflammatory regulation by minocycline. Subsequently, remarkable regrowth of scalp hair was achieved without obvious scarring, although the microscopic perifollicular fibrosis affected normal hair growth, reducing the number of hairs emerging from each follicle. In addition to its antimicrobial effects, tetracyclines have multiple non-antimicrobial actions, including suppression of inflammatory cytokine production, inhibition of inflammatory enzymes, down-regulation of major histocompatibility complex class II expression in the macrophages, suppression of T-cell proliferation and activation, and induction of tolerogenic dendritic cells (10).

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Consent: The patient gave consent for his photographs and medical information to be published in print and online and with the understanding that this information may be publicly available.

Conflict of interest: ST has no conflicts of interest to declare. AT has received honoraria from Pfizer as a speaker.

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