

Familial Graham-Little-Picardi-Lassueur syndrome across 3 generations



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INTRODUCTION

Graham-Little-Picardi-Lassueur syndrome (GLPLS) is a rare variant of lichen planopilaris (LPP) that is characterized by the triad of fibrosing alopecia of the scalp, nonfibrosing alopecia of the axillae and groin, and follicular, spinous papules over the body.^{1,2} Although a genetic predisposition to this disease and other scarring alopecias is suspected, it has not been confirmed yet. Herein, we report the occurrence of GLPLS in a young adolescent boy, his mother, and his grandmother. To our knowledge, they represent the first reported cases of GLPLS affecting several consecutive generations of the same family.

CASE SERIES

Case 1

A 17-year-old adolescent boy was evaluated in our clinic for patches of scalp alopecia. He indicated that he had suffered from episodes of inflammation on the scalp since he was a child. Interestingly, he had a family history of scarring alopecia affecting his mother and maternal grandmother. A physical examination showed small plaques of alopecia in the vertex with some tufted hair and itchy erythematous macules on the periphery. The patient also presented keratotic, follicular papules on the arms (Fig 1, A) and sparse armpit hair. A biopsy performed from the right temple showed a perifollicular, lymphocytic infiltrate involving the basal layer of the isthmic and infundibular follicular epithelium, a minimal superficial perivascular lymphocytic infiltrate, and mild vertical fibrosis (Fig 1, B). A blood test was performed but did not show any abnormalities; antinuclear and anti-Ro/SSA antibodies were

Abbreviations used:

GLPLS:	Graham-Little-Picardi-Lassueur syndrome
HLA:	human leukocyte antigen
LPP:	lichen planopilaris

negative, and endocrinologic tests (including sexual and thyroid hormone levels) were normal. His vitamin B9 and B12 levels were also tested and showed normal levels. All serologic tests (including syphilis, HIV, hepatitis C, and hepatitis B) were negative. There were no alterations in the blood karyotype, and human leukocyte antigen (HLA)-DR1 was not found. Topical clobetasol and hydroxychloroquine (200 mg, once daily) were recommended, but the patient discontinued the treatment after 6 months due to limited therapeutic results. He was lost to follow-up for 2 years and had dramatically worsened when re-evaluated. The initial small patches of scarring alopecia had grown to almost occupy the entire superior surface of the scalp (Fig 1, C). Evident signs of active inflammation, such as perifollicular scale ("collar-like" or tubular casts) and perifollicular erythema, were observed using digital dermoscopy. Milky-red areas, the loss of follicular openings, and abundant tufted hairs were also seen on the borders of the affected area (Fig 1, D).

Case 2

A 40-year-old woman, the mother of the indicator case, was also evaluated. She presented progressive scarring alopecia of the scalp (Fig 2, A and B) and scarce axillary hair since she was 20 (Fig 2, C).

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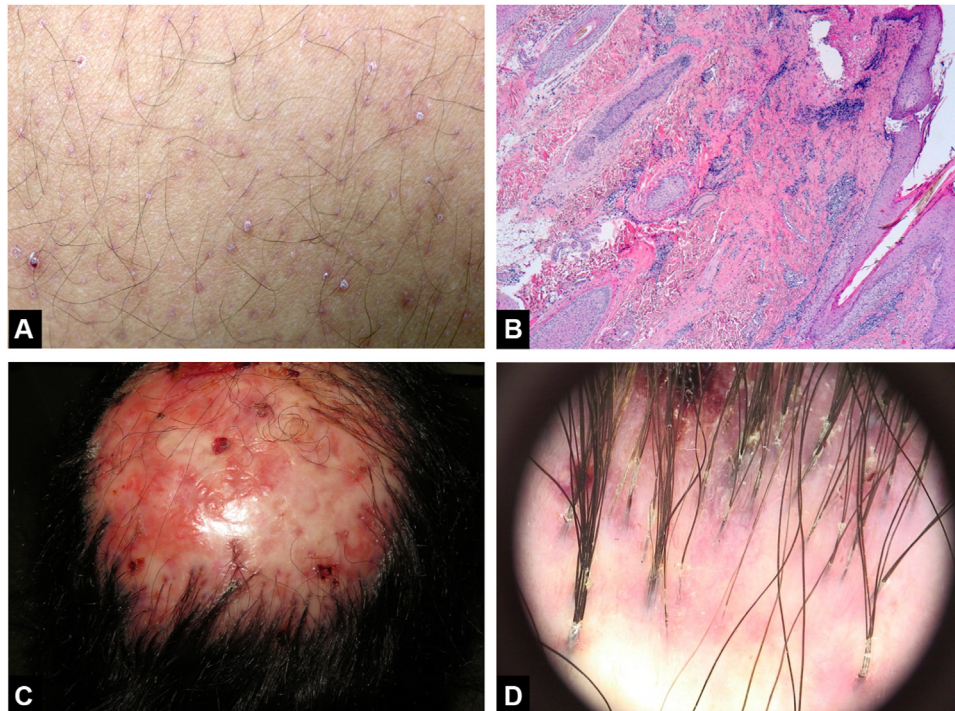


Fig 1. All images correspond to case 1. **A**, Follicular, keratotic papules located on the arm. **B**, Dermal fibrosis with perifollicular, lymphocytic infiltrate, without interface dermatitis. Hematoxylin-eosin; original magnification: 40×; scalp biopsy. **C**, Scarring alopecia with erythematous and inflammatory areas with follicular accentuation. Tufted hairs are also seen macroscopically. **D**, Dermoscopy (original magnification: 10×; performed in the periphery of the alopecic plaque). Hair tufts with several hairs and perifollicular scales surrounded by milky-red areas.

The scalp biopsy showed orthokeratotic hyperkeratosis; a perifollicular, lymphocytic infiltrate at the level of the infundibulum; and fibrosis around the follicles (Fig 2, D). Serum antinuclear and anti-Ro/SSA antibodies were negative. A treponema pallidum hemagglutination assay test and a rapid plasma reagin test were both negative. Nutritional laboratory investigations showed normal serum concentrations of ascorbic acid, vitamin B9, and vitamin B12. There were no alterations in the blood karyotype, and HLA-DR1 was not found. The patient was being treated with haloperidol, oxcarbazepine, and risperidone for bipolar disorder, but she indicated that the scalp and axillary alopecia had started years before she began taking any medication. These characteristics were concordant with the GLPLS diagnosis.

Case 3

The third case was a 77-year-old woman, the maternal grandmother of the indicator case, who presented with an almost—complete-scalp cicatricial alopecia and perifollicular scales in the lonely hairs of the periphery of the alopecic plaque (Fig 3, A and B). These clinical findings were confirmed with a

scalp biopsy that showed concentric perifollicular fibrosis with minimal inflammation (Fig 3, C). She indicated that her hair loss had started when she was 20 and had had a progressive course since it appeared. Nonscarring alopecia of the axillae (Fig 3, D) and keratotic, follicular papules in the arms and trunk were also present.

DISCUSSION

GLPLS was first described by Piccardi in 1913.¹ A second case was described by Graham-Little in 1915, in a patient referred by Lassueur, resulting in the name it bears today.³ Approximately 50 similar, sporadic cases have been reported since then.¹ It is believed to be 4 times more common in women in the age group of 30 to 70 years than in all other demographics. Only a few cases have been reported in literature wherein the disease has affected men, as in our case.^{4,5}

The syndrome is characterized by the classical triad of scarring alopecia of the scalp with or without follicular plugging, nonscarring alopecia of the axillae and groin, and the presence of keratotic,

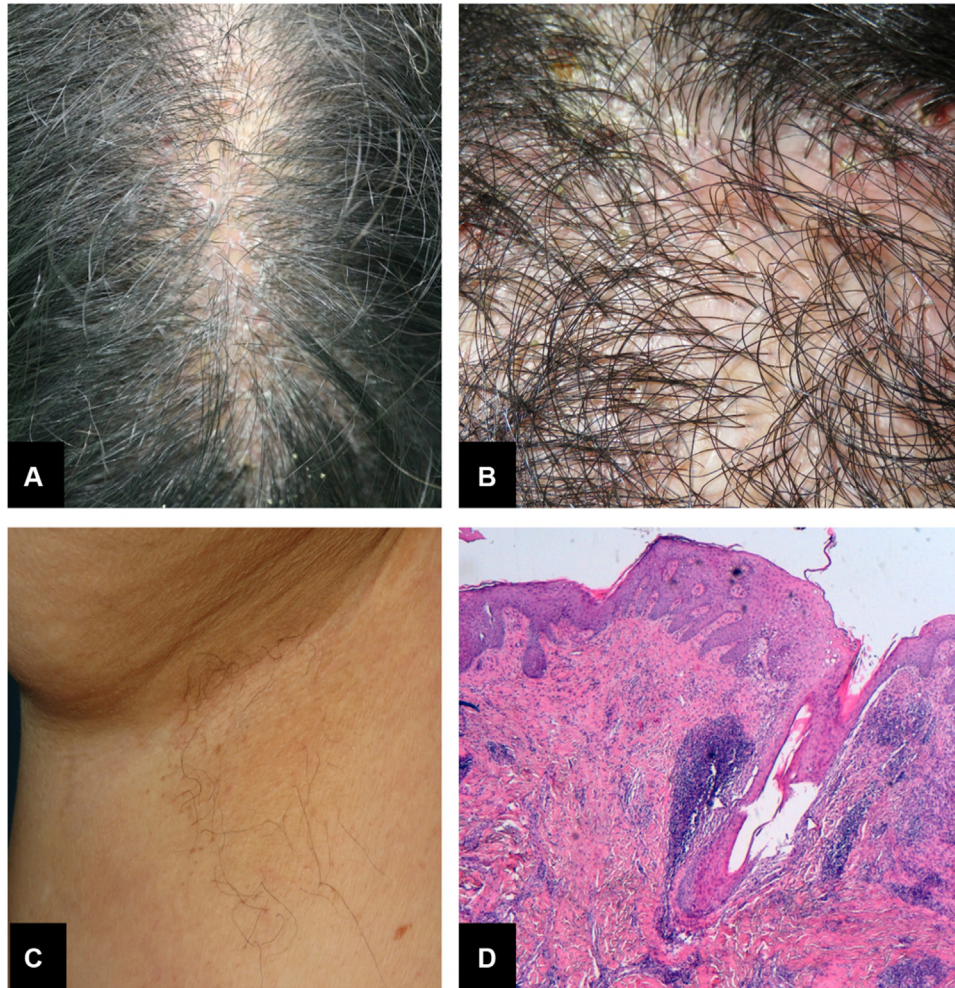


Fig 2. All the images correspond to case 2. **A**, Scarring scalp alopecia with perifollicular scales. **B**, Detailed view of some tufted hairs and perifollicular corneal papules (scalp). **C**, Close appearance of axillary nonscarring alopecia patches. **D**, Diminished number of hair follicles, surrounded by a dense lymphocytic infiltrate at the level of the infundibulum and the isthmus along with perifollicular fibrosis. Scalp biopsy; hematoxylin-eosin (40 \times).

follicular papules.¹ GLPLS and frontal fibrosing alopecia are considered to be variants of LPP.^{1,6}

At the first stages, and especially in the periphery of scalp, alopecic patches, corneal papules, and a perifollicular erythema can often be found.⁷ However, when the condition progresses, only patches of cicatricial alopecia are found. The pubis and axillae, although they present the loss of hair follicles, do not show atrophy or involvement of the epidermis, and no other signs of cicatricial alopecia are noticeable. Hair loss can also be present in the eyebrows or in the forearms, as in our first case.^{1,7} Follicular, keratotic papules are located mainly on the trunk and extremities, although they sometimes involve the eyebrows and the lateral part of the face. All of these symptoms do not need to occur simultaneously, and frequently, alopecia of the scalp

precedes the widespread keratosis pilaris by months or years.⁸ The course of the disease is usually chronic and slowly progressive.⁹

The histopathology of GLPLS is identical to that of LPP.² The histologic appearance of alopecia on the scalp differs depending on the stage of development. Early lesions usually show perifollicular, lymphocytic infiltrates at the level of the infundibulum and the isthmus (as in cases 1 and 2) that may extend down the length of the follicle. Vacuolar changes of the outer root sheath may also be seen. In evolved lesions, only nonspecific signs of cicatricial alopecia are found (case 3)—eg, concentric perifollicular fibrosis and the replacement of the pilosebaceous units by fibrous tracts, called follicular scars.^{1,2} Furthermore, these different characteristics can coexist in the same patient, as the histopathology

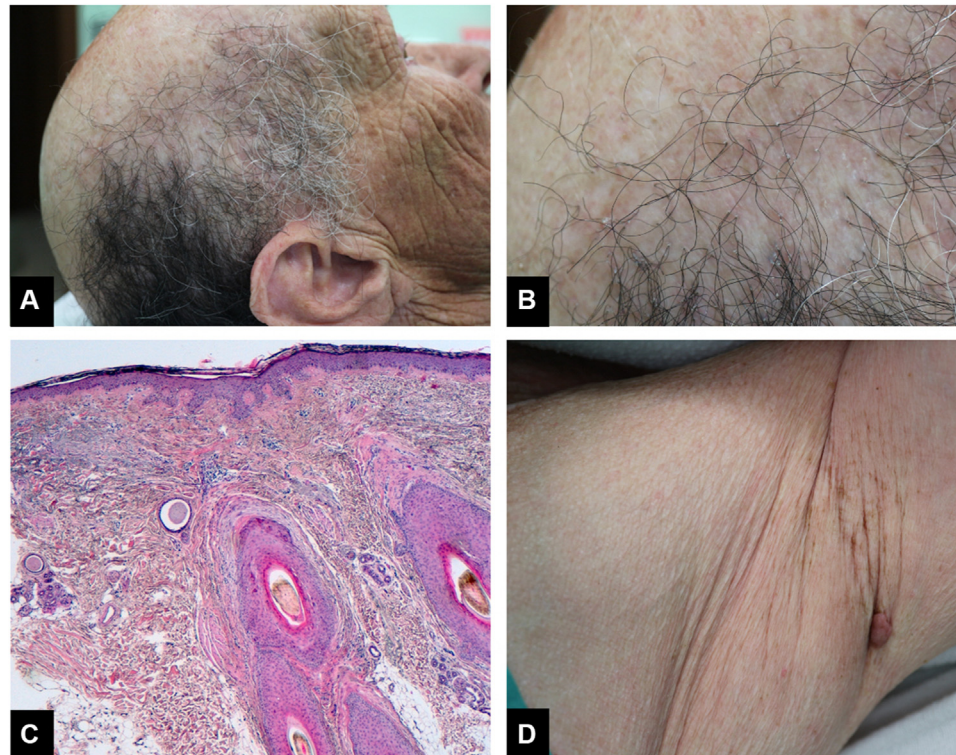


Fig 3. All the images correspond to case 3. **A**, Extensive scalp alopecia with cicatricial characteristics and lonely hairs in the periphery. **B**, Detailed view of the right temple. Keratotic, follicular scales and tufted hairs are seen macroscopically. **C**, Perifollicular and dermal fibrosis without evident inflammation. Scalp biopsy; hematoxylin-eosin (40 \times). **D**, Axillary alopecia.

differs depending on whether the biopsy is performed in the center of an alopecic area or on the periphery.

Our first patient's alopecia showed dermoscopic characteristics superimposable to LPP, such as hair tufts with several hairs and perifollicular scales surrounded by milky-red areas (which is concordant with the GLPLS diagnosis). The main dermoscopic findings of LPP are perifollicular scales, which typically form tubular structures; perifollicular inflammation; irregular, large, white dots (fibrotic white dots); the loss of follicular openings; white areas; milky-red areas; and small hair tufts of 5 to 9 hairs.¹⁰ Recently, white casts along the hair shaft have also been linked to GLPLS.¹¹

Hormonal influences (like menopause or androgen insensitivity syndrome), stress, hepatitis B virus vaccination, and deficits of vitamin A are proposed triggers of GLPLS, but the evidence is yet insufficient.^{1,7,12} Up until now, no genetic alteration has been described as responsible for GLPLS.

The treatment of GLPLS is a hard challenge. The majority of the GLPLS treatments are used due to their effectiveness in LPP, as no gold-standard approach exists for GLPLS. The therapeutic aims in

LPP and in GLPLS mainly consist of reducing possible associated symptoms and halting disease activity, thereby preventing the development of further alopecic areas.^{2,6,13} Most treatment methods lead to the reduction of perifollicular erythema and inflammation without effects on the scalp cicatricial alopecia or perineal and axillary noncicatricial alopecia. The therapeutic options include topical or systemic steroids, hydroxychloroquine, methotrexate, retinoids, psoralen plus ultraviolet A therapy, cyclosporine, and thalidomide, with variable clinical responses reported.^{1,2,4,5} The limited number of GLPLS cases precludes any meaningful interpretation of data about which is the best option.

There have been only 2 previous reports of familial GLPLS, 1 including a mother and her daughter and the other including 2 siblings.^{6,8} In the first one, the HLA types were determined; both patients shared HLA-DR1, the same found in familial cases of lichen planus.^{8,14} In the second one, they did not perform this test. In our case 1 and case 2, HLA-DR1 was not found. To the best of our knowledge, we report the first cases affecting several consecutive generations.

In conclusion, the appearance of GLPLS across at least 3 generations suggests a genetic factor with dominant inheritance in this family. We recommend a full-body examination in any case of suspected LPP in order to avoid missing GLPLS.⁶ Further literature reports should be encouraged as they could support a genetic predisposition for this rare condition that could help to provide a better understanding of scarring alopecias.

Conflicts of interest

None disclosed.

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