Unveiling the Uncommon: Graham-Little-Piccardi-Lassueur Syndrome with granuloma annulare

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Abstract

Graham-Little-Piccardi-Lassueur Syndrome (GLPLS) is a rare variant of lichen planopilaris characterized by a triad of patchy scarring alopecia of the scalp, non-scarring alopecia of the axillae and groin, and follicular keratotic papules. Granuloma annulare (GA) is a benign inflammatory dermatosis presenting as annular erythematous papules or plaques. We report an unusual case of a 60-year-old female with GLPLS associated with GA. The patient presented with progressive scarring alopecia of the scalp, non-scarring alopecia of the axillae, and asymptomatic annular papules on the upper back. Histopathology confirmed GLPLS and GA. The patient was initially treated with hydroxychloroquine but was switched to tofacitinib due to a lack of response. The coexistence of GLPLS and GA is extremely rare, and this report highlights the importance of recognizing atypical presentations. Early diagnosis and treatment are crucial to preventing disease progression and managing scarring alopecia effectively.

Keywords: Graham-Little-Piccardi-Lassueur Syndrome, granuloma annulare, lichenplano pilaris, scarring alopecia, non-scarring alopecia, lichen planus, hydroxychloroquine.

Introduction

Graham-Little-Piccardi-Lassueur Syndrome(GLPLS) manifests as a rare subclinical variant of lichen planopilaris, featuring the triad of patchy scarring alopecia of the scalp, non-scarring alopecia of axillae, groins regions and follicular keratotic papules over the body.[1] Granuloma annulare (GA) manifests as a benign inflammatory condition of the dermis/subcutis, characterized by asymptomatic, erythematous, annular papules or plaques that typically affect the extremities and trunk. It encompasses various variants such as localized, generalized, subcutaneous and perforating forms.[2] Herein; we report a case of GLPLS associated with granuloma annulare, an unusual presentation.

Case Report

A 60-year-old female came to our outpatient department with dark pigmentation and progressive loss of hair over the scalp, along with loss of hair over the axillae for the last 2 years. She reported a history of occasional itching over the lesions. She also complained of asymptomatic raised skin-coloured lesions over the right scapular region for the past one year. The patient had no known comorbidities and had been on irregular treatment with oral and topical corticosteroids for six months. Cutaneous examination revealed diffuse hyper-pigmented areas of scarring alopecia over bilateral parietal scalp areas and nonscarring alopecia of the axilla (Figure 1A-C). Well-defined skin-coloured papules arranged in an annular pattern were observed on the right side of the upper back (Figure 2A&B), and well-defined hyperpigmented follicular papules were present over the anterior trunk. A trichoscopic examination of the scalp showed peripilar casts, blue-grey dots, and homogenous white areas, consistent with scarring alopecia. No prominent vascular structures were noted. Trichoscopic examination of the axilla showed non-scarring alopecia (Figure 3A-D). The differential diagnoses considered for the scalp lesions included discoid lupus erythematosus, frontal fibrosing alopecia, and lichen planopilaris. For the annular lesions over the upper back, the differentials considered were granuloma annulare, papular mucinosis, and papular sarcoidosis. Scalp

biopsy revealed orthokeratosis, hypergranulosis with focal loss of rete ridges and dermis containing superficial perivascular lymphohistiocytic infiltrate (Figure 4A). Biopsy from the trunk showed epidermal atrophy exhibiting basal keratinocyte pigmentation and dermis showing perivascular, periadnexal interstitial inflammatory infiltrates composed of lymphocytes, histiocytes, eosinophils and neutrophils degenerated collagen and occasional foci of mucin favouring granuloma annulare (Figure 4B). Based on the clinical presentation, dermoscopic findings, and histopathological examination, a final diagnosis of Graham-Little-Piccardi-Lassueur syndrome—a variant of lichen planopilaris characterized by scarring alopecia of the scalp, non-scarring alopecia of the axillae, and keratotic follicular papules—coexisting with granuloma annulare involving the upper back was made. The patient was treated with hydroxychloroquine 200mg BD for 3 months but showed no response, prompting a transition to tofacitinib 5 mg BD for the treatment of lichen planopilaris, which showed mild improvement after 3 months and under regular follow-up.

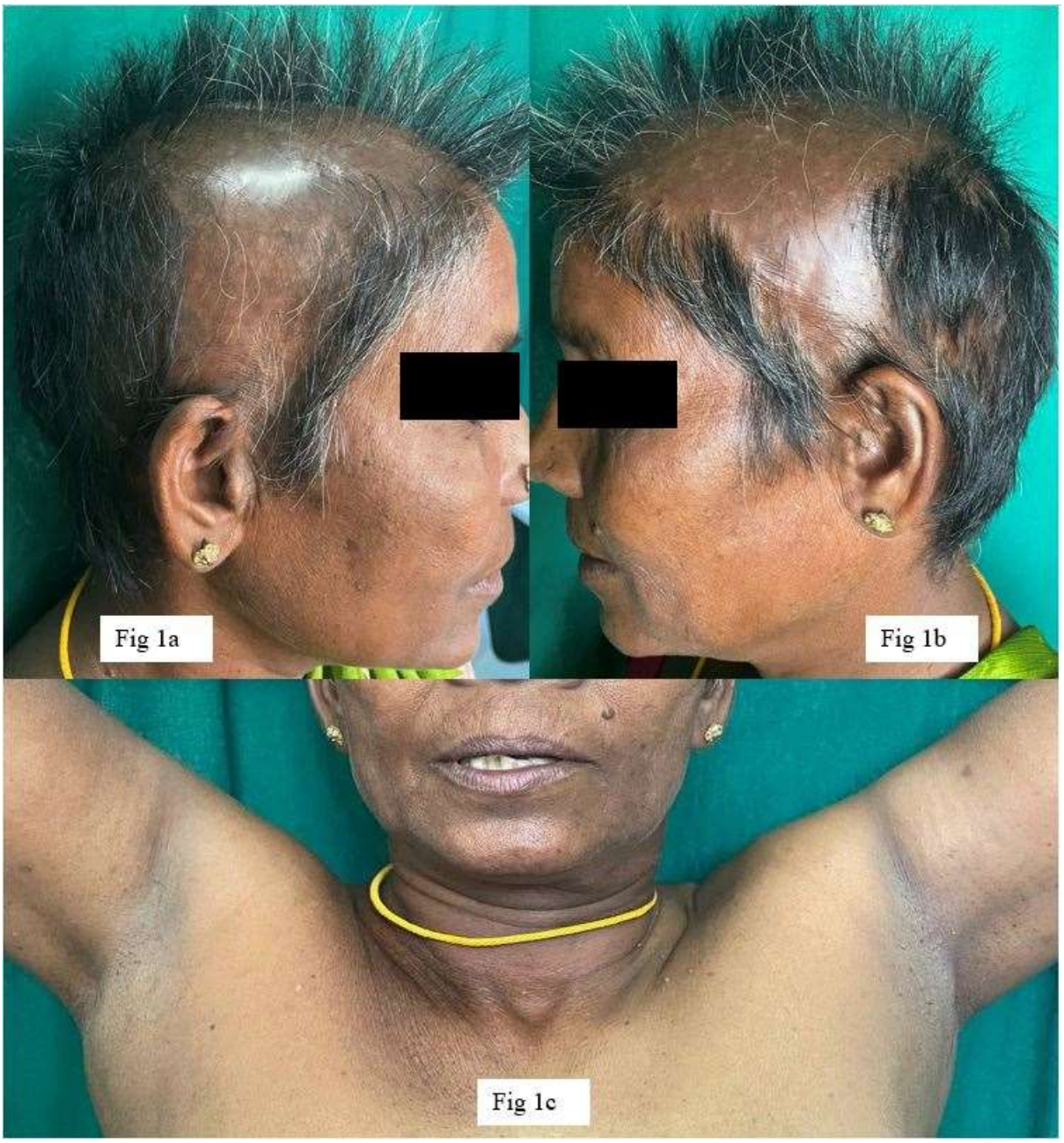

Figure 1: Diffuse areas of (a and b) scarring alopecia noted all over the scalp with sparing of frontal hairline, temporal and occipital areas with multiple discrete violaceous peri-follicular papules of varying sizes and plaques over the scalp with peri-follicular scaling and (c) non-scaring alopecia over both axilla.

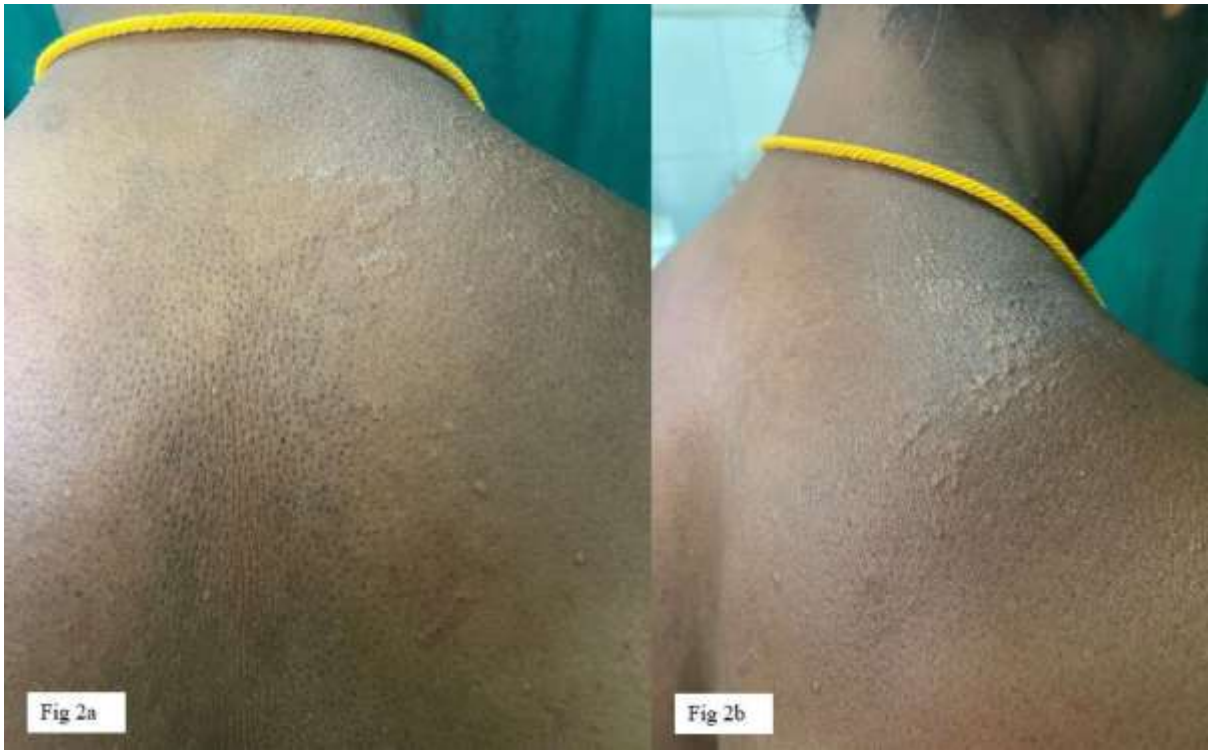

Figure 2: Multiple skin-coloured shiny papules, a few of which are arranged in an annular pattern over the right upper back.

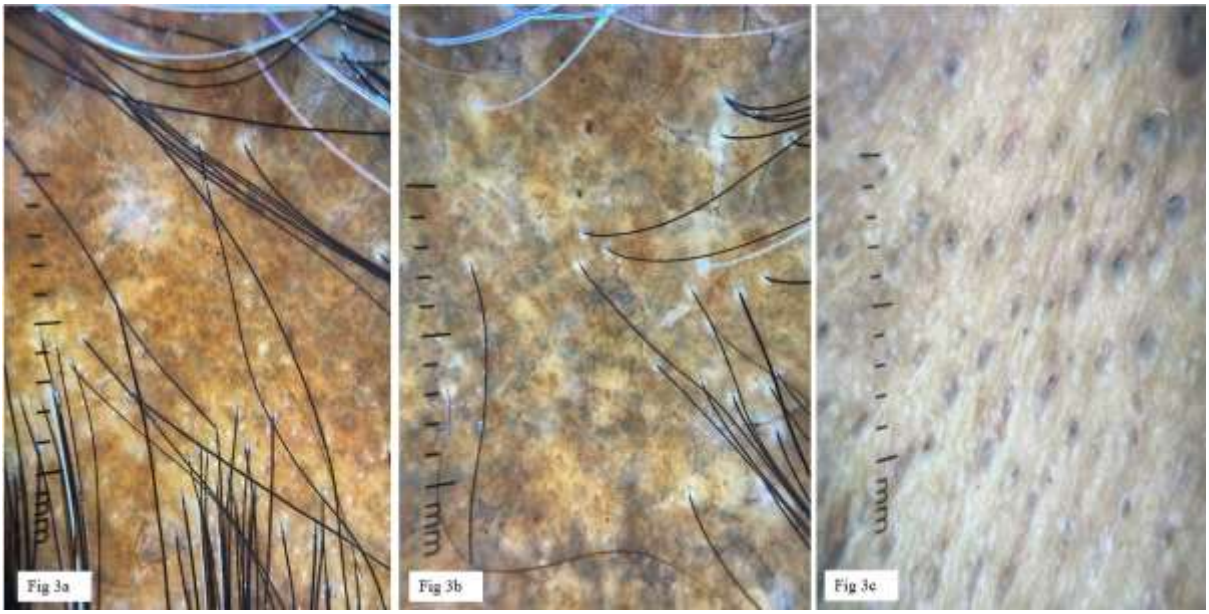

Figure 3: (a and b) Polarised dermoscopy of the scalp shows yellow dots with keratotic plugging, peri-follicular and interfollicular violaceous pigmentation and peri-pilar casting with white scaling and (c) dilated follicular opening with keratotic plugging over the axilla. (Dermlite DL4 dermoscope, 10x, polarised).

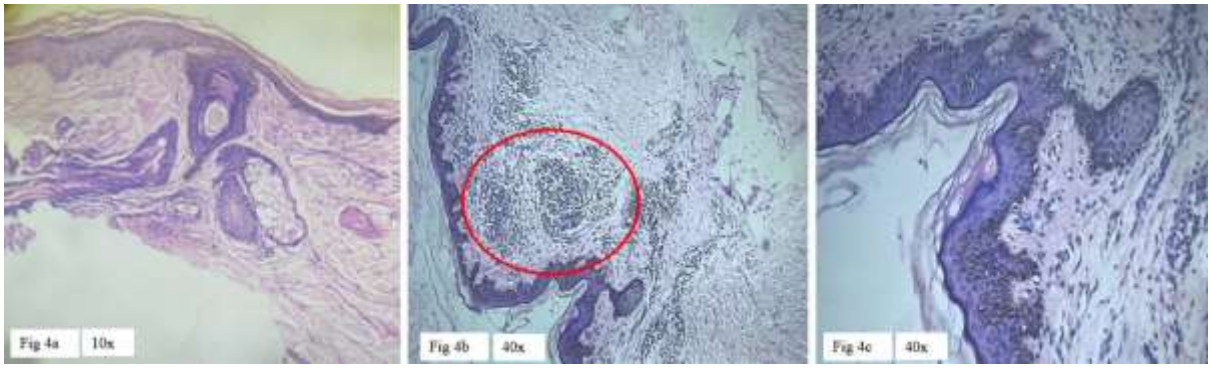

Figure 4: (a) H&E section from scalp biopsy shows epidermis with basketweave orthokeratosis and underlying dermis showing follicular plugging and fibrosis and hair tufting with infundibular involvement with inflammatory infiltrates around the hair follicle suggestive of lichenplanopilaris. (b and c) H&E section from upper back shiny papules shows epidermal atropy with underlying dermis showing perivascular, periadnexal and interstitial infiltrates of lymphocytes, degenerated collagen, and foci of mucin.

Discussion

Graham-Little-Piccardi-Lassueur syndrome was initially described by Piccardi in 1913; a second case was referred by Lasseuer in 1915, leading to the naming of the syndrome.[3] Since then, approximately 50 cases have been reported. GLPLS primarily affects middle-aged white women and is characterized by the triad. Although its exact mechanism remains unknown, it is more likely to be a T-cell-mediated autoimmune condition as it is a variant of lichen planopilaris.[4] Recently, the presence of autoantibodies to centromere passenger INCENP has been documented. This protein is a major component of the centromere during several phases of the mitotic cell cycle, where it plays an essential role in chromosomal segregation and participates in the mechanisms regulating these mitoses.[5] Few other studies showed a decrease in the expression of peroxisome proliferator-activated receptor (PPAR), resulting in the disease.[6] The diagnosis of GLPLS is clinical, supported by trichoscopy showing perifollicular scale, blue-grey dots, and loss of follicular ostia, and histopathology consistent with lichenoid interface dermatitis. GA diagnosis relies on clinical morphology and is confirmed histopathologically by the presence of palisading granulomas, collagen degeneration, and mucin, which can be highlighted by Alcian blue or colloidal iron staining. Few reports show the association of GLPLS with lichen planus, lichen planus pigmentosus, androgen sensitivity syndrome.[7-9] From topical to systemic or intralesional steroids, retinoids, hydroxychloroquine, cyclosporine, tacrolimus, tetracycline, phototherapy, thalidomide, griseofulvin, dapsone and mycophenolate mofetil are among the treatments that may be used.[8]

Granuloma annulare is a relatively common skin disorder of uncertain etiology, described as "ringed eruption" in 1895 by Thomas Colcott Fox. Over the years, Radcliffe Crocker 1902 used the term granuloma annulare to characterize it.[10] Little is known about its etiopathogenesis. Recent studies have implicated dysregulation in the T-helper 1(Th1) cells and Janus Kinase signal transducer and activator of transcription (JAK-STAT) pathway.[11] Tofacitinib, a JAK inhibitor, has shown promise in recent studies for both lichen planopilaris and granuloma annulare, targeting the immune dysregulation common to both conditions. However, its use remains off-label, and long-term efficacy data are limited. GA was significantly associated with solid organ malignancy, HIV, Cardiovascular Disease, Unspecified Osteoarthritis, Depressive Disorder, Anxiety Disorder, Systemic Lupus Erythematosus, Type II Diabetes Mellitus, Liver Disease, Dyslipidemia, Hypothyroidism, Essential Hypertension, Migraine and Non-Migraine Headache.[12] Actinic granuloma annulare is associated with diabetes, leukaemia, polymyalgia rheumatica, relapsing polychondritis and pseudoxanthoma elasticum, although the relevance of these associations remains unproven[13]

Conclusion

GLPLS is a chronic and challenging case to treat, so the main goal of the treatment is to prevent the progression of scarring alopecia. This case of GLPLS is reported because of the extreme rarity of presentation with concomitant granuloma annulare. To our knowledge, this is the first documented case of co-existing GLPLS and granuloma annulare, suggesting a potential common autoimmune or immune-dysregulated pathway.

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