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CASE REPORT

Galli-Galli Disease Presenting as Lichenoid Papules in the Flexures

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PALABRAS CLAVE

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Abstract

Galli-Galli disease is a rare genodermatosis currently regarded as an acantholytic variant of Dowling-Degos disease. The 2 diseases have the same clinical features: reticular hyperpigmented macules in the great skin folds, erythematous scaly papules and plaques, comedo-like lesions, and pitted perioral scars, and the only differentiating characteristic is the histological finding of acantholysis, usually without dyskeratosis. We describe the case of a patient with hyperpigmented papules in the skin folds as the only sign of Galli-Galli disease, and we present a review of the literature.

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Presentación de Enfermedad de Galli-Galli Como Pápulas Liquenoides Flexurales

Resumen

La enfermedad de Galli-Galli (EGG) es una genodermatosis rara considerada actualmente como la variante acantolítica de la enfermedad de Dowling-Degos (EDD), con la que comparte sus manifestaciones clínicas: hiperpigmentación reticular en grandes pliegues cutáneos, pápulas y placas eritemato-descamativas, lesiones tipo comedón y cicatrices acneiformes peribucales. El hallazgo histológico de acantólisis, generalmente en ausencia de disqueratosis, constituye el único elemento diferenciador de ambas.

Presentamos el caso de una paciente con pápulas flexurales hiperpigmentadas en pliegues como único hallazgo de EGG y revisamos la literatura.

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Introduction

Although Galli-Galli disease (GGD) was first described by Bardach et al in 1982¹ as an independent dermatological condition, it is currently regarded as a histologic variant of Dowling-Degos disease (DDD), within the spectrum of the reticulate pigmented dermatoses.² Classical DDD and GGD share the same clinical signs and symptoms and the only element that differentiates them is the histologic finding of acantholysis in the case of GGD.

We report the case of this genodermatosis with the rare clinical presentation of hyperpigmented papules in the skin folds as the only sign of GGD, together with suprabasal acantholysis without dyskeratosis, and we present a review of the literature.

Case Description

A 29-year-old Latin-American woman visited our department due to a papular rash in the posterior cervical region, groin, and intergluteal fold; the rash had appeared 2 years earlier and was asymptomatic except in summer, when it was slightly pruritic.

The patient stated that she had no personal or family history of dermatologic disease.

Her gynecologist had diagnosed the lesions as condylomata acuminata a year earlier and had prescribed an undefined topical treatment, with no clinical improvement. The lesions had remained stable since they appeared, except during the summer, until some months previously, when new papules had begun to appear in the cubital fossa, which caused the patient to visit our department.

Physical examination revealed numerous hyperpigmented papules with a flat, shiny surface and a tendency to coalesce into plaques; the papules were located in both inguinal folds and the intergluteal fold (Figure 1). The reticulate



Figure 1 A and B, Hyperpigmented lichenoid papules in the groin and between the buttocks, with absence of reticulate pigmentation. C, Less confluent papules on the neck and D, In the cubital fossa.

flexural pigmentation characteristic of DDD was absent, however, as were other typical findings of the disease, such as scaly erythematous plaques, comedo-like lesions, pitted perioral scars, erythematous or hyperchromic macules, atrophic lesions, and pitting of the palms.

A biopsy of the inguinal papules revealed elongated epidermal ridges with increased melanin in the basal layer, areas of suprabasal acantholysis, and discrete overlying parakeratosis with no dyskeratosis. A mild, predominantly perivascular superficial lymphocytic-histiocytic infiltrate was found in the dermis. No signs of the “dilapidated brick wall” appearance typical of Hailey-Hailey disease were found (Figure 2). The immunofluorescence study was negative (Figure 3).

Discussion

GGD is a rare genodermatosis that is regarded by many authors as an acantholytic variant of DDD. Although the inheritance pattern is thought to be autosomal dominant with variable penetration, many cases, such as ours, lack a family history. The disease typically appears between adolescence and middle-age, though cases have been reported in children with a family history of DDD (Table).

This histologic variant was described by Bardach et al¹ in 1982 in 2 siblings, from whom the name of the disease is taken, as a new polymorphic dermatosis that is clinically and histologically similar to DDD, Darier-White disease, Grover disease, and Hailey-Hailey disease. Although those authors proposed it as a dermatologically independent disease, it is currently regarded by most authors as a variant of DDD. To date, 16 cases of GGD have been reported in the

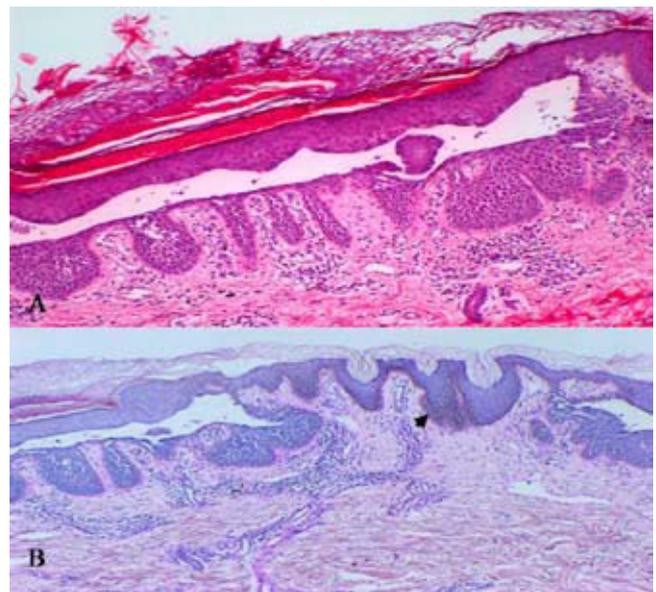


Figure 2 A, Suprabasal acantholysis and areas of parakeratosis in the epidermal clefts (hematoxylin-eosin, $\times 200$). B, Hyperplastic epidermal ridges and increased basal melanin (arrow) (Periodic acid-Schiff, $\times 400$).

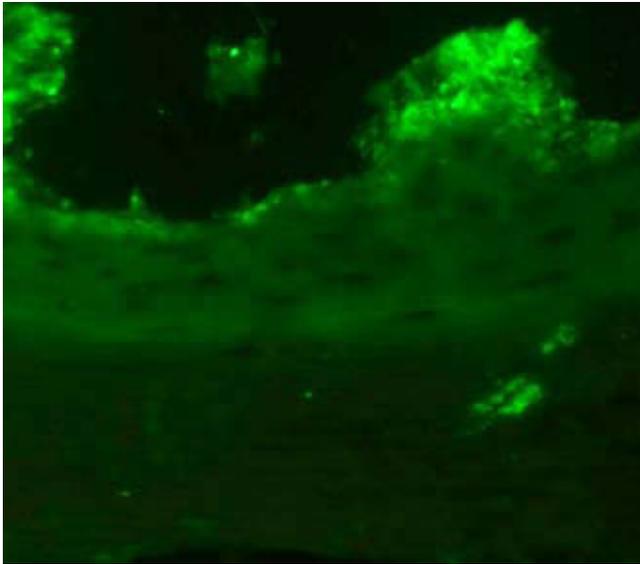


Figure 3 Negative immunofluorescence study: no epidermal deposits of immunoglobulin G are observed.

literature; these cases are listed in Table 1. Some of these cases, however, may, in fact, be Grover disease.¹²

GGD and DDD are clinically indistinguishable and the only differentiating element is the finding of areas of acantholysis, usually without dyskeratosis.

Clinically, the disease usually presents with macular hyperpigmentation of the skin-fold surfaces (DDD was first named “dermatose pigmentaire réticulée des plis” by Degos and Ossipowski in 1954). This pigmentation may sometimes be absent and other findings may include papules, scaly erythematous plaques, comedo-like lesions, and pitted perioral scars.

Only 1 of the 16 patients reported in the literature did not present reticulate pigmentation; in that case, the only finding described was hyperpigmented papules on the torso, extremities, and inguinal and axillary folds.⁸ In our case, the hyperpigmented papules were found only in the skin folds; this is, therefore, the first reported case of GGD located exclusively in this site. Three years after onset, the lesions remained confined to the folds, but the possibility that they may extend to other sites in the future cannot be ruled out.

Table 2 Review of Cases Published in the International Literature With a Diagnosis of Galli-Galli Disease

Authors	Age on Appearance, y	Sex	Clinical Characteristics
Bardach, Gebart, and Luger ¹ (1982)	19	M	Reticulate pigmentation on the face and neck
	15	M	Pigmentation and pruritic erythematous papules on the torso and upper limbs. Patchy involvement of the skin folds
Mittag, Rupec, and Klingmüller ³ (1986)	56	M	Hyperpigmentation in the axillas and groin
	51	M	Axillary hyperpigmentation
	46	F	Hyperpigmentation on the neck, axillas, groin, and abdomen
	15	M	Axillary hyperpigmentation Simple epidermolysis bullosa
Rütten and Strauß ⁴ (1995)	24	M	Hyperpigmentation on the neck, axillas, groin, scrotum, and lower limbs Comedons on the upper lip
De Deene and Schulze ⁵ (1996)	30	F	Hyperpigmentation on the neck, axillas, groin, torso, and forearms Papules on the gums
Braun-Falco et al ⁶ (2001)	49	M	Hyperpigmentation in the skin folds, with a pruritic papular eruption on the neck, axillas, torso, and backs of the hands
Cooper et al ⁷ (2004)	42	F	Hyperpigmentation in the skin folds with pruritic papules on the lower limbs, torso, and forehead
	39	F	Hyperpigmentation in the skin folds with pruritic papules on the lower limbs, torso, and forehead
El Shabrawi-Caelen et al ⁸ (2007)	55	F	Erythematous papules and hyperpigmented macules on the torso and lower extremities Absence of skin-fold hyperpigmentation, comedos, and facial acneiform scars
	54	F	Erythematous papules and lentiginous macules on the submammary fold and on the lower extremities
Wu YH, Lin YC ⁹ (2007)	NS (child)	F	Hyperpigmented, erythematous macules Papules in the skin folds of the limbs and in the perioral region Comedons and perioral scarring
Sprecher et al ¹⁰ (2007)	43	F	Pruritic papules in the axillas, groin, and submammary folds
Gilchrist H et al ¹¹ (2008)	38	F	Hyperpigmented erythematous macules on the neck, torso, and proximal surface of the limbs Hyperpigmentation in the cervical region and skin folds

Abbreviations: M, male; F, female; NS, not specified.

Reference has also been made of the overlap between DDD and other pigmented dermatoses, and all these skin diseases are usually regarded as part of a single, broad spectrum of reticulate pigmented dermatoses. In support of this classification are several cases that included the following findings, as well as the typical manifestations of DDD: acral hyperpigmented atrophic macules and pits or fissures on the palms (characteristic of reticulate acropigmentation of Kitamura), acral hypopigmented macules (acropigmentation of Dohi), roseate facial erythema (Haber syndrome), and hypopigmented or lentiginous macules on the torso and extremities (present in dyschromatosis universalis hereditaria and in dyschromatosis symmetrica hereditaria).^{13,14} As a variant of DDD, one of the published cases of overlap with the above dermatologic conditions was GGD, as the biopsy of the axillary lesions revealed acantholysis. The fact that no acantholysis was found in biopsies of lesions from other sites on the same patient indicates that either the classic and acantholytic variants can coexist in the same patient or that this acantholytic variant is simply an incidental finding in typical DDD lesions. The report by El Shabrawi et al⁸ mentions the fact that biopsies of the macular lesions generally do not show acantholysis and that this finding occurs in the papular lesions.

The principal differential diagnoses of GGD include Hailey-Hailey disease (erosions in the skin folds with acantholysis and dilapidated wall images in histology), Darier disease (keratotic papules on the face and central areas of the torso, with frequent involvement of the mucosa and intense dyskeratosis in the biopsy), pemphigus vulgaris (with cutaneous and mucosal erosions, positive Nikolsky sign, and positive immunofluorescence), and Grover disease, the differentiation of which is more complicated (intensely pruritic keratotic papules on the torso with acantholysis and dyskeratosis).

Elongation of the epidermal ridges and increased melanin in the basal regions, associated with acantholysis, an absence of dilapidated-wall images and of dyskeratosis, negative immunofluorescence, and the location and morphology of the lesions (absence of erosions, vegetative lesions, or keratotic papules) rule out all the above-mentioned dermatoses, leading to a diagnosis of GGD.

The pathogenic mechanisms of DDD remain unknown. Mutation of the keratin 5 gene has been put forward as a possible cause of modifications to the structure of the intermediate filaments that cause the disease. However, these findings have not been found in all patients. Betz et al¹⁵ described a haploinsufficiency of keratin 5 in 2 families suffering from DDD and suggested that the resulting excess of unpaired keratin 14 would alter keratinocyte adhesion and melanosome migration, as appears to be shown by the histologic findings. Sprecher et al¹⁰ found a mutation of keratin 5 in 1 case of GGD. Recently, Liao et al¹⁵ showed a deletion of a pair of bases that, again, resulted in a mutation of keratin 5. Nevertheless, it has not been possible to demonstrate a link between the mutations of keratin 5 and a specific histologic variant, so that even the Ile140fs mutation may be present in both variants.¹⁶ Keratin 5 is also abnormal in simple epidermolysis bullosa, although only 1

of the reported cases associated both diseases, according to the author (1986). Other associations occasionally mentioned with DDD are squamous cell carcinomas and multiple keratoacanthomas.

Treatment of the lesions is generally disappointing. Topical and systemic retinoids and phototherapy have been used with little response.

Our patient presented a slight improvement after topical application of isotretinoin, with acceptable tolerance, but this was finally lost to follow-up as the patient ceased to appear for the scheduled follow-up visits.

We report the first described case of GGD with the sole clinical manifestation, at least initially, of hyperpigmented papules in the skin folds and none of the other characteristic findings of DDD. In our opinion, both our case and the review of the literature contribute to consolidating the theory that GGD is simply a histologic variant of DDD, characterized by a highly polymorphic clinical presentation but with some clearly defined histologic findings.

Conflicts of Interest

The authors declare no conflicts of interest.

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