

BRIEF ARTICLE

Galli Galli Disease: A Challenging Diagnosis in a Bahraini Female PatientMcKenzie A. Dirr MD¹, Aysha Almedfa MD², Fatema Khamdan MD¹¹ Medical University of South Carolina, Charleston, SC² Salmayia Medical Complex, Department of Dermatology, Manama, Bahrain**ABSTRACT**

Dowling-Degos Disease (DDD) is an inherited cutaneous disease which presents with classic and atypical cutaneous findings, including macules of hyperpigmentation and hypopigmentation in the flexural creases. A variant, termed Galli-Galli Disease (GGD), presents similarly, with the distinguishing feature of acantholysis on histology. Reports of GGD in the literature are rare, due to the infrequency of the diagnosis. This may contribute to a lack of available information and delayed diagnosis, which can result in a frustrating clinical course for patients. We present a female patient who presented with complaints of a burning sensation and painful rash for the last three years on a background of hypopigmented and hyperpigmented macules on the trunk, upper extremities and flexural creases. Comprehensive dermatopathological evaluation and clinical correlates led to the diagnosis of GGD.

A 50-year-old Bahraini Female patient presented to the dermatology clinic with a 3-year history of painful, pruritic cutaneous lesions concentrated in the flexural creases of the thighs and forearms. Her medical and travel history were negative, aside from dyslipidemia, which was well controlled on Simvastatin. Prior to presentation in clinic, she had been previously evaluated in several private dermatology offices with inconclusive diagnoses. Previous biopsies showed findings consistent with psoriasis, Haily-Haily disease, and urticaria. However, the patient failed multiple therapies, including topical and systemic steroids, cyclosporine, dapsone, and methotrexate.

Physical examination revealed numerous, symmetrically scattered, erythematous hyperkeratotic papules on a background of hypo- and hyper-pigmented macules located in the inguinal area and affecting the medial upper thighs (**Figure 1A**) as well as the forearms (**Figure 1B**). In addition, numerous scattered, hypopigmented macules were found on the trunk and neck (**Figure 2**). Further detailed history revealed that this abnormal pigmentation presented in childhood. Notably, further investigation of family history revealed that the patient's brother and father had similar pigmentary lesions on the trunk, although they did not seek medical attention. Laboratory evaluations of CBC, LFT, and RFTs were grossly normal. Food-specific IgE allergens

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Figure 1. Erythematous, hyperkeratotic papules with background hyperpigmented macules present on the inner thigh (A) bilateral forearms (B).

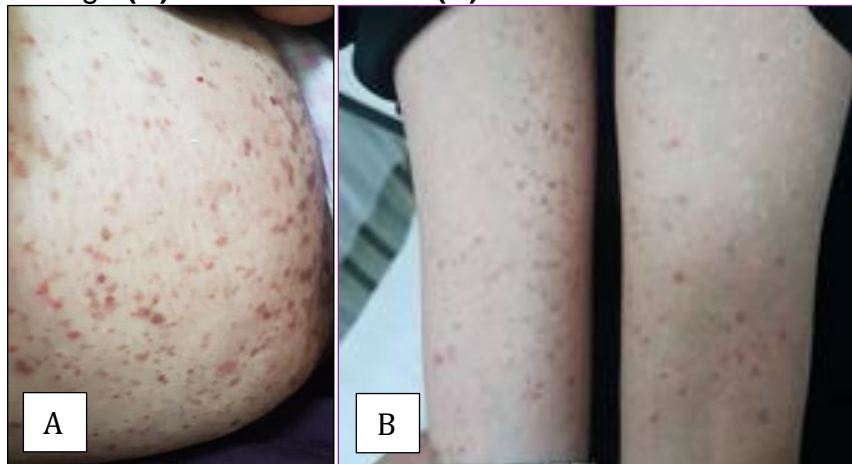


Figure 2. Hyper- and Hypo-pigmented macules on the neck.

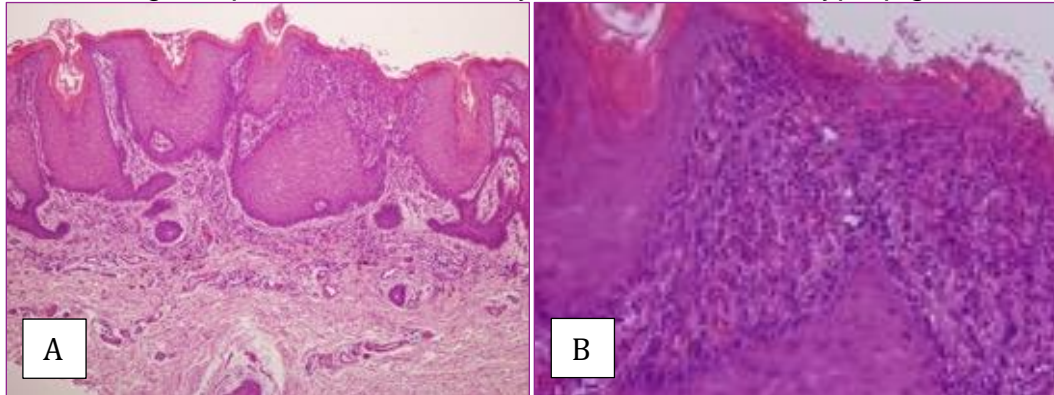


and multiple inhalant-specific allergens were positive, with total IgE elevated to 141 kU/L. Differential diagnosis at that point included Grover's Disease versus Guttate Psoriasis versus Pityriasis Lichenoides Chronica (PLC).

A general pathologist conducted a dermatopathologic evaluation of a punch biopsy tissue sample, which revealed ulceration, reduced granular layer, acanthosis, perivascular infiltrate, and

neutrophilic microabscess, raising suspicion for psoriasiform dermatitis or guttate psoriasis. However, given the patient's clinical history and persistent symptoms despite psoriatic-specific treatment, the diagnosis was not convincing. The expertise of a board certified dermatopathologist was sought, who further evaluated the biopsy sample. The second evaluation revealed psoriasiform acanthosis, elongated rete ridges, occasional hyperpigmentation, and focal acantholysis. Based on clinical

Figures 3A and B. Histologic evaluation of skin biopsy in a patient showing acanthosis, elongation of rete ridges, sparse focal acantholysis and occasional hyperpigmentation.



pathological correlation, including the lesion presentation, family history, and age of onset, the diagnosis of GGD (acantholytic variant of DDD) was made (**Figures 3A and 3B**).

The patient was counseled on the disease course and prognosis, including limited available treatment options. She was started on topical mometasone and phototherapy treatment. However, she did not tolerate phototherapy, which caused symptomatic flares. She was subsequently switched to oral acitretin 25mg, which was also discontinued due to the development of severe headaches, jaw pain, toothache, and new skin lesions. Despite treatment drawbacks, the patient was able to remain successfully controlled with mometasone cream, as she was reluctant to use other systemic treatments.

Galli-Galli Disease is a rare variant of DDD, which are inherited reticulate pigmentary skin conditions characterized by erythematous hyperkeratotic papules and hyperpigmented/hypopigmented lesions in a net-like, or reticular, pattern in the flexural creases.¹⁻³ These lesions may be associated with unpleasant symptoms of burning sensation and pruritus that may be severe and affecting the quality of life.² Other rare variants of DDD may occur as generalized,

follicular, vesicular, “comedone-like,” lesions and atypical presentations, including fingernail and localized, focal involvement including depressed, or “pitting,” scars near the mouth.^{2,4}

The etiology of both DDD and GGD is thought to be due to either autosomal dominant or sporadic mutations in genes essential to the integrity, development, or distribution of keratin or melanocytes.⁴ Among implicated genes is KRT5, responsible for the proper formation of keratin 5, which plays an important role in multiple cellular processes including the uptake of melanocytes into the keratinocytes and structural integrity of the cell.^{1,2,6,7} Other genes that have been linked to GGD include POFUT1 and POGLUT1, critical genes to the Notch signaling pathway, and their mutations are linked to loss of keratinocyte structure and dysregulated melanocyte development.^{1,2,8} It is important to emphasize that these rare diseases are typically inherited in an autosomal dominant manner, and family history may also be a pertinent positive which can provide clues to the diagnosis.⁴

While clinical evaluation and history can raise suspicion for DDD, dermatopathologic evaluation is necessary to accurately diagnose this condition.⁴ On histopathology,

DDD presents with downward epidermal growth, described as “rete ridges” with distal hyperpigmentation, “comedo-like” configurations, and “horn cysts.”^{2,3} GGD is identical to DDD but is distinguishable from it by the presence of acantholysis in the pathological examination.^{2,4,5} GGD is described as having “secondary acantholysis,” in which the keratinocytes themselves are altered, as opposed to primary acantholysis, in which the initial pathology lies within the connection system itself.⁵ Unique to GGD, in addition to the characteristic acantholysis, are hyperkeratosis, acanthosis, hyperpigmentation in the stratum basale and filiform or thread-like, pattern downward projection of rete ridges.^{1,3}

Several treatment approaches have been attempted for DDD and GGD, but they are often difficult to treat and the disease still frequently progresses.⁴ Efforts at preventing progression include sun protection among other irritant-avoidance tactics.⁴ Some success has been found in laser therapy, phototherapy, and topical steroid and retinoid formulations.^{1,2,9} In a case report published by Dupuy et. al, low-dose isotretinoin for 6 weeks was found to be effective.¹ Notably, our patient was treated with Acitretin, but therapy was discontinued due to adverse events and dissatisfaction with the result of treatment.

DDD and GGD are rare cutaneous conditions that can present a challenging clinical diagnostic task, but with increased awareness and expanding available literature, they can be easily identified using distinguishing clinical and histologic features. This case demonstrates the challenges that patients with this condition may face in obtaining the final and correct diagnosis. Thus, our case adds to the growing body of literature regarding presentation of GGD, an

important tool to aid swift identification and treatment. Further studies should be done to develop and evaluate the most effective treatment modalities for both diseases.

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