Follicular Dowling-Degos Disease with Hidradenitis Suppurativa: A Case Report and Review of the Literature

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Abstract
Dowling-Degos disease (DDD) is an autosomal dominant disorder with variable phenotypic expression. Classically, DDD is characterized by progressive reticulate hyperpigmentation on flexures with perioral pitted scars and comedone-like hyperkeratotic papules. Follicular DDD is a rare variant which was introduced by Singh et al. [Indian J Dermatol Venereol Leprol. 2013 Nov–Dec;79(6):802–4]. Follicular DDD differs from other variants because of its notable comedone-like hyperkeratotic hyperpigmented papules and a distinct histopathology which demonstrates pigmented filiform and branching rete pegs originating at the follicular infundibulum with many epidermal horn cysts while the interfollicular epidermis is essentially normal. Hereby, we present a case of follicular DDD with hidradenitis suppurativa (HS). A 37-year-old Thai man presented with slowly progressive hyperpigmented comedone-like papules on the face, neck, axillae, upper trunk, and buttocks with perioral pitted scars. Punch biopsy from a comedonal lesion on his back was consistent with follicular DDD. He also had recurrent painful nodules and abscess on the back, groin, and buttock which matched the clinical criteria for the diagnosis of HS. To date, a paucity of concurrent DDD with HS has been reported. Recent genetic studies speculate a shared pathophysiologic mechanism of DDD and HS.

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Introduction

Dowling-Degos disease (DDD) is a progressive reticulate pigmented disorder first reported by Dowling and Freudenthal [1] and Degos and Ossipowski [2], respectively. It usually is inherited in an autosomal dominant pattern; however, some cases are sporadic [3]. The main genetic mutation associated with DDD is KRT5. Keratin 5 is an element in the cytoskeleton of basal keratinocytes. To date, many genetic mutations have been documented such as POFUT1, POGLUT1, and PSENEN [3]. DDD has multiple variants of DDD including classic DDD, generalized DDD, Galli-Galli disease, Haber's syndrome, pigmentatio reticularis faciei et colli, and follicular DDD [4]. According to literature reviews, DDD has been found to be associated with severe nodulocystic acne, hidradenitis suppurativa (HS), chloracne-like lesions, seborrheic keratoses, dystrophic fingernails, and an accessory tragus [3, 5]. DDD is known to be resistant to treatment, and no standard treatment has been established [3].

Case Report

A 37-year-old Thai man with an underlying disease of hepatitis C cirrhosis presented with slowly progressive hyperpigmented comedone-like papules on the face, neck, axillae, upper trunk, groin, and buttocks with perioral pitted scars and numerous atrophic scars. The skin lesions first appeared 22 years ago. They were mostly asymptomatic, so he did not seek any treatment. There were a few times when he experienced some painful nodules and abscess on his back, groin, and buttock which healed with atrophic scars. On one occasion, he had a tender nodule with pus around his anus which later on was diagnosed as perianal abscess. He received oral antibiotics and did not require surgery. He denied anyone in his family having similar symptoms.

Upon examination, he had numerous hyperpigmented macules and papules with numerous open comedones and atrophic scars on the face, neck, chest, axillae, upper back, groin, and buttocks with few painful nodules on his back, groin, and buttock (shown in Fig. 1). No pus, discharge, or sinus tracts were found. Other mucosa, palms, soles, hair, and nails were normal.

Histopathology from a comedonal lesion at the back revealed dilated follicular infundibulum filled with keratin with filiform-like rete ridges and increased basal melanin pigmentation involving follicular area while interfollicular epithelium remains normal (shown in Fig. 2). Considering the history, clinical presentation, and histopathology, this patient was diagnosed with follicular DDD with HS. In terms of treatment, he received anti-acne lotion which is a mixture of 1% resorcinol, 1% salicylic acid, and 6.7% zinc oxide. The patient did not come for follow-up.

Discussion

DDD is an uncommon autosomal dominant genodermatosis affecting individuals during the third to fourth decade of life with progressive hyperpigmented macules and papules with hyperkeratosis [6]. Lesions initially appear on axillae and groins followed by intergluteal, inframammary folds, neck, trunk, and upper extremities. Most patients are asymptomatic, but few have pruritus on the affected area. At the present, several variations of clinical, histopathology, and genetic mutations have been described such as classic DDD, generalized DDD, follicular DDD, and Galli-Galli disease [3, 4].

Our patient presented with slowly progressive hyperpigmented macules and papules with numerous open comedones and atrophic scars on the face, neck, chest, axillae, upper back,
Fig. 1. The patient had numerous hyperpigmented macules and papules with numerous open comedones and atrophic scars on the chest (a) and few tender erythematous nodules on the back (b) and both buttocks (c). d He also had hyperpigmented macules on both axillae.

Fig. 2. a Histopathology from a comedonal lesion on the back at scanning power revealed dilated follicular infundibulum filled with keratin and filiform-like rete ridges involving follicular area while interfollicular epithelium remains normal. b, c, d Medium- and high-power examination showed filiform-like rete ridges with basal hyperpigmentation.
and buttock since he was 15 years old. Differential diagnosis at first included HS and familial dyskeratotic comedones. Familial dyskeratotic comedones present at puberty with numerous, discrete, disseminate, open comedones that can heal with scar on the trunk, arms, leg, and shaft of the penis, sparing the palms and soles [7]. These features seem similar to our patient. However, in familial dyskeratotic comedones, the histopathology only shows dyskeratosis and invaginations into the dermis with occasional acantholysis which is not seen in our patient. Therefore, this patient was diagnosed with follicular DDD. Moreover, this patient also had recurrent painful nodules and abscess with multiple atrophic scars on the back, buttock, and perianal area which is not found in DDD alone. These clinical features were consistent with all 3 criteria of HS including one or more typical lesion, typical distribution, and recurrence of symptoms [8]. Typical lesions of HS are painful nodules, abscess, sinus tracts, double-open comedones, and bridges scars. Therefore, we concluded that our patient had concurrent DDD and HS.

To our knowledge, 12 cases (including our case) have been reported so far (shown in Table 1) [4, 5, 9–12]. All cases had clinical and histopathology characteristic of follicular DDD. Dermoscopic examination demonstrated brown pigmented Chinese letter pattern or irregular star shape, central brown hyperkeratotic follicular plugs, and comedones [9]. However, half of the reported cases did not have hyperpigmented macules and papules on flexural areas. Interestingly, most cases of follicular DDD present around childhood and puberty while classic DDD commonly presents after puberty. Additional features include ichthyosis vulgaris, lichen planus, HS, and blepharophimosis-ptosis-epicanthus inversus syndrome [5, 10–12].

HS is a chronic inflammatory disorder of the hair and follicles typically involving axillae, buttocks, groin, perineal, and inframammary regions [8]. According to case reports and clinical studies, concurrent DDD with HS has been reported in 53 cases (including our case) as shown in Table 2 [10, 13–33]: 2 cases of which are follicular DDD variant and 1 case is associated with Galli-Galli disease, a variant of DDD [10, 33]. Most cases reported were of female predominance and more than half presented with at least Hurley stage 2. Almost all had a family history of HS. Recent genetic studies have found that patients with concurrent DDD with HS mostly have mutation in PSENEN, followed by POFUT1 and a case of NCSTN [13, 14, 25, 27, 28, 31].

### Table 1. Case reports of follicular Dowling-Degos disease

| Case no. [Refs.] | Sex | Age of onset, years | Age, years | Family history | Associated disease |
|------------------|-----|---------------------|------------|----------------|--------------------|
| 1 [5]            | Male | 10                  | 25         | Yes            | Ichthyosis vulgaris |
| 2 [5]            | Female | 5                   | 19         | Yes            | n/a                |
| 3 [4]            | Female | Puberty             | 32         | Yes            | n/a                |
| 4 [4]            | Female | Puberty             | 12         | Yes            | n/a                |
| 5 [9]            | Female | 23                  | 35         | Yes            | n/a                |
| 6 [9]            | Female | 27                  | 43         | Yes            | n/a                |
| 7 [9]            | Male   | 36                  | 54         | Yes            | n/a                |
| 8 [10]           | Female | 15                  | 30         | Yes            | Hidradenitis suppurativa |
| 9 [11]           | Female | Childhood           | 29         | No             | Blepharophimosis-ptosis-epicanthus inversus syndrome |
| 10 [12]          | Male   | Childhood           | 28         | Yes            | Lichen planus      |
| 11 [12]          | Male   | Childhood           | 23         | Yes            | Lichen planus      |
| 12 (our case)    | Male   | 15                  | 37         | No             | Hidradenitis suppurativa |

n/a, not available.
Few cases reported association with squamous cell carcinoma, keratoacanthoma, and arthritis [17, 19, 22, 23, 30].

In 2017, Pavolsky et al. [14] discovered that patients who presented with features of both DDD and HS have heterozygous mutation in \textit{PSENEN}. A year later, González-Villanueva et al. [13] found that \textit{POFUT1} mutation is associated with combined DDD and HS as well. Lately, \textit{NCSTN} mutation was found in a concurrent DDD with HS patient [27]. All \textit{PSENEN} and \textit{POFUT1} are critical genes that regulate the Notch signaling pathway and have been speculated to be the pathophysiologic mechanisms of patients with combined DDD and HS [3]. However, \textit{NCSTN} may not have a direct effect on the NOTCH pathway but is believed to stimulate inflammatory response via type I interferon gene expression [27].

As other variants of DDD, follicular DDD is also resistant to treatment. Oral isotretinoin has been prescribed in many cases and had shown to reduce follicular lesions and comedones. However, when discontinued, follicular DDD relapses [9]. Other treatments include topical hydroquinone, retinoids, and corticosteroids [6].

| Case no. [Refs.] | Sex | Age, years | Family history of DDD | Family history of HS | Genetic mutation | Associated disease |
|------------------|-----|------------|-----------------------|---------------------|-----------------|--------------------|
| 1–15 [24]        | 8 female/7 male | 43.2±12.36 | 9 yes/6 no | Yes | n/a | n/a |
| 16–20 [25]       | 3 female/2 male | n/a | n/a | n/a | \textit{PSENEN} | n/a |
| 21 [26]          | Male | 47 | No | Yes | n/a | n/a |
| 22 [27]          | Male | 54 | No | Yes | \textit{NCSTN} | n/a |
| 23–26 [14]       | 3 female/1 male | n/a | Yes | Yes | \textit{PSENEN} | n/a |
| 27 [13]          | Female | 33 | n/a | n/a | \textit{POFUT1} | n/a |
| 28 [28]          | Male | 31 | Yes | Yes | \textit{PSENEN} | n/a |
| 29–30 [29]       | 2 female | 39/45 | Yes | Yes | n/a | n/a |
| 31 [30]          | Female | 40 | Yes | Yes | n/a | Arthritis |
| 32 [31]          | Female | 34 | Yes | Yes | \textit{POFUT1} | n/a |
| 33 [32]          | Female | 38 | Yes | Yes | n/a | n/a |
| 34* [10]         | Female | 30 | Yes | No | n/a | n/a |
| 35 [15]          | Female | 43 | Yes | Yes | n/a | n/a |
| 36 [16]          | Female | 44 | Yes | Yes | n/a | n/a |
| 37–38 [17]       | 2 female | 23/48 | Yes | Yes | n/a | Arthritis |
| 39 [18]          | Female | 49 | Yes | Yes | n/a | n/a |
| 40 [19]          | Male | 68 | No | Yes | n/a | SCC |
| 41* [33]         | Female | 33 | No | No | n/a | n/a |
| 42 [23]          | n/a | n/a | n/a | n/a | n/a | SCC |
| 43 [20]          | Female | 39 | n/a | n/a | n/a | n/a |
| 44 [22]          | Female | 38 | n/a | n/a | n/a | KA |
| 45–52 [21]       | n/a | n/a | n/a | n/a | n/a | n/a |
| 53* (Our case)   | Male | 37 | No | No | n/a | n/a |

\(n/a\), not available; SCC, squamous cell carcinoma; KA, keratoacanthoma.

*Follicular DDD.

\*Galli-Galli disease.
In conclusion, follicular DDD, a new variant of DDD, is diagnosed based on clinical characteristics and distinct histopathology. Concurrent DDD with HS was reported increasingly. Further studies are needed to clearly explain the pathophysiology and genetic mutation involved.

**Statement of Ethics**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The study has been done according to the Declaration of Helsinki. Ethical approval was not required for this study in accordance with national guidelines.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

All authors participated in writing and are fully responsible for the manuscript.

**Data Availability Statement**

All data supporting this study are available from Dr. Charussri Leeyaphan upon request.

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