Dermoscopy of Follicular Dowling–Degos Disease
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Abstract
Dowling–Degos disease (DDD) is a late-onset genodermatosis characterized by hyperpigmented macules on the flexures along with scattered comedo-like lesions and pitted acneiform scars. Follicular Dowling–Degos is a rare type of DDD, with only two reports so far. It presents with follicular papules and comedo-like lesions predominantly on the face and trunk. Dermoscopy of follicular DDD shows irregular star-shaped/Chinese letter pattern pigmentation along with comedo-like lesions. Herein, we describe diagnostic clues including dermoscopy in three patients of follicular DDD which can help in differentiating it from other disorders presenting with comedo-like lesions.

Key Words: Comedones, dermoscopy, Dowling–Degos disease, follicular, genodermatosis

Introduction
Dowling–Degos disease (DDD; MIM 179850) is a late-onset genodermatosis characterized by numerous, symmetrical, hyperpigmented macules over the axillae, groins, face, neck, arms, and trunk along with scattered comedo-like lesions (dark-dot follicles) and pitted acneiform scars.[1] It occurs due to a dysfunctional mutation in the keratin-5 gene on chromosome 12q, leading to abnormal pilosebaceous epithelial proliferation.[1] Other reported mutations include POFUT1 (encoding protein O-fucosyltransferase 1) and POGLUT1 (encoding protein O-glucosyltransferase 1).[2] Several atypical presentations of DDD have been reported in literature, such as those in association with other dyschromatoses, mimicking chloracne,[3] acantholytic variant, or Galli–Galli disease. Herein, we report three cases of the follicular variant of DDD. There have been only two previous reports of follicular DDD,[4,5] and dermoscopy of this variant has not been described previously. We seek to highlight this rare variant with the help of dermoscopy and differentiate it from other conditions that manifest with follicular keratotic macules, papules, and pitted scars.

Case Report
A 35-year-old female presented with asymptomatic, hyperpigmented lesions on the face, upper trunk, and flexures for 12 years. Her mother, younger sister, and elder brother had similar lesions. On examination, multiple hyperpigmented macules, 1–3 mm keratotic follicular papules, open comedones, and pitted scars were present on her face, neck, chest, back, and abdomen [Figure 1a-c]. Dermoscopy in polarized mode using ×10 magnification revealed a brown pigmentation in Chinese letter pattern/irregular star shape, central brown follicular plugs, and comedones [Figure 1d and e]. Histopathology of skin biopsy showed follicular plugging with elongated, branching epithelia and the downward proliferation of infundibular wall with increased melanization at their tips and sides. The interfollicular epithelium was not involved, suggestive of follicular DDD [Figure 1f]. She was prescribed oral isotretinoin, which led to reduction in the follicular lesions and comedones. However, the improvement was partial and reversible on treatment interruption.

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Patient 2 was a 43-year-old female who presented with hyperpigmented lesions over her face, neck, upper chest, and flexures for the past 16 years. A history of similar lesions was present in her grandfather, father, three daughters, and a son. On examination, she had multiple scattered comedo-like lesions over the face, chest, and upper back and pitted perioral scars. Axilla and groin were not involved [Figure 2a-c]. On dermoscopy, brown pigmentation in Chinese letter pattern/irregular star shape surrounding the follicular plugs and comedones was observed [Figure 2d and e]. Histopathology showed similar appearance as in the patient 1 [Figure 2f]. She was also prescribed oral isotretinoin 30 mg/day, which led to mild improvement. However, isotretinoin had to be discontinued because of transaminitis.

Our third patient was a 54-year-old male who presented with an 18-year history of multiple comedones and pitted scars over his face, upper chest, and back. His father, brother, and daughter had a similar illness. On examination, multiple comedones and pitted scars were seen over the face, neck, axilla, upper chest, and back. He also had associated acne, unlike other two patients [Figure 3a-c]. Dermoscopy and histopathological findings were similar to that of patient 2 [Figure 3d, e]. The patient refused treatment with retinoids and was lost to follow-up.

**Discussion**

DDD is an autosomal dominant genodermatosis with variable penetrance, as seen in our series where many members of each family were affected. It presents as an acquired hyperpigmentation of the flexures, beginning in adult life. Most of the patients in our series also had onset in the second decade with a female predominance. Genodermatosis can present with a myriad of clinical presentation owing to different genetic defects and variable penetrance. A few reports including the present case series have highlighted the possible role of follicular pathology in the genesis of DDD, and the indicators include multiple comedo-like lesions, predominantly follicular hyperkeratotic papules, association with acne, hidradenitis suppurativa, and prominent infundibular changes on histology. Recently, Zhou C et al. identified mutation in \( \gamma \)-secretase subunit of PSENEN encoding presenilin enhancer protein in DDD patients and reported that this subset of patients had an increased susceptibility to acne inversa.

The unique features in our series are (1) early onset of disseminated comedones in adolescence in all three families; (2) the presence of very few hyperkeratotic follicular papules which became more apparent with dermoscopy and predominantly comedonal lesions; (3) a predilection for the face, neck, and upper trunk, rather than the extremities; (4) relative sparing of axilla and groin with only few scattered comedones over these sites; (5) the absence of classical reticulate pigmentation; and (6) classical histopathological changes confined to follicular infundibulum. The atypical presentation in our series led us to consider a number of other differentials listed in Table 1. Kershenovich et al. reported a case of DDD mimicking chloracne. Diffuse familial comedones, familial comedones, idiopathic disseminated comedones, and familial disseminated comedones without dyskeratosis all belong to the same spectrum of disease with similar clinical manifestations. Our series highlights the heterogeneity of the disease and need for genetic studies to find out more about this association.

Dermoscopy in these patients helped in differentiating it from other diseases presenting with only comedones.
Table 1: Differential diagnosis of dermatoses with follicular keratotic macules, papules, and comedones as in our series

|                        | Age of onset | Sites involved | Inheritance | Symptoms | Associated features | Dermoscopy | Histology | Treatment                          |
|------------------------|--------------|----------------|-------------|----------|---------------------|------------|-----------|------------------------------------|
| Follicular DDD          | Second to fourth decade | Face, chest, upper back, flexures | AD          | Numerous, discrete, symmetrical hyperkeratotic folliculocentric papules, and open comedones | Acne, hidradenitis suppurativa | Irregular brown star shaped and Chinese letter pattern structures, brown folliculocentric papules and open comedones | Follicular plugging with filiform projections and branching of the rete ridges arising from the follicular epithelium | Retinoids, Er:YAG laser, fractional carbon dioxide laser |
| Familial dyskeratotic comedones | Puberty | Predilection for the trunk, arms, leg and shaft of the penis, sparing the palms and soles | AD | Numerous, discrete, disseminate, open comedones | Acne cysts | No reports | Dyskeratosis and invaginations into the dermis, occasionally acantholysis may be seen | Lack of response to retinoid treatment, frequent sun exposure and carbon dioxide laser |
| Familial comedonal Darier Disease[8] | Second to sixth decade | Face, scalp, trunk | AD | Follicular and extrafollicular greasy, hyperkeratotic papules and plaques in seborrheic areas | Nail involvement, palmar pits, pruritus, leonine face, syringo cystadenoma papilliferum | Polygonal, star-like or roundish-oval-shaped yellowish/brownish areas surrounded by a thin whitish halo[8] | Dyskeratosis with corps ronds and grains, suprabasal acantholysis | Systemic retinoids, minocycline |
| Familial comedones without dyskeratosis[9] | Childhood | Face, back, buttocks | AD | Closely arranged, dilated follicular openings with keratinous plugs | Acne | No reports | Dilated crateriform hyperkeratotic infundibulum filled with laminated debris | Retinoids |
| Chloracne              | Adolescence | Periocular, periauricular, genital and axillary regions, trunk, arms, chest while the nose is spared | Sporadic after exposure to halogenated hydrocarbons | Numerous comedo-like lesions and yellowish cysts on the face, and other body regions not usually affected by acne with diffuse Grayish skin pigmentation | Hypertrichosis, folliculitis | No reports | Absence of sebaceous Glands and hyperpigmented stratum corneum, follicular Hyperkeratosis, and infundibular cysts and dilatation | Avoidance of further exposure |

Contd...
Table 1: Contd...

| Nevus comedonicus[^12] | At birth or before the age of 10 years | Face and neck; mostly unilateral | Sporadic | Closely arranged, dilated follicular openings with keratinous plugs | Acne, cyst, nevus comedonicus syndrome with skeletal, ocular, and central nervous system abnormalities | Circular and barrel-shaped, homogeneous areas in light and dark-brown shades, with remarkable keratin plugs | Large grouped, dilated follicular ostia devoid of hair shafts and filled with keratin layers | Retinoid, laser therapy (diode laser, ultrapulse CO\textsubscript{2} or Er:YAG) surgical excision |

DDD: Dowling-Degos disease, AD: Autosomal dominant, Er:YAG: Erbium:yttrium-aluminum-garnet

Figure 3: Clinical and dermoscopic findings in Patient 3-Multiple comedones and pitted scars with acne on (a) face, chest, (b) neck, back, and (c) axilla. (d) On dermoscopy in polarized mode using ×10 magnification, brown pigmentation surrounding follicular plugs and pigmentation in Chinese-letter pattern (arrows) with telangiectasias is seen. Histopathology of skin biopsy in patient 2 showed (e) keratin plugs with elongated, branching hyperpigmented infundibular epithelium with normal epidermis (H and E, ×100)

such as familial dyskeratotic comedones and chloracne. Classical histopathology helped in clinching the diagnosis of follicular DDD as the branching, elongated, hyperpigmented rete ridges were restricted to the follicular epidermis. Dermoscopy of the DDD has been described only once previously and it shows an irregular star-shaped brown outline on a red-brown background along with follicular plugging and inclusion cysts.[^11] In our series, this irregular star-shaped or linear thready pigmentation in Chinese letter pattern was seen on normal skin as well as hyperpigmented background. In patient 3, these irregular star-shaped structures were present over follicular papules, suggestive of follicular DDD. Thus, dermoscopy can be used as a tool to diagnose follicular DDD.

The management of DDD is difficult. Although the lesions in DDD are asymptomatic, involvement of face is very distressing, increasing the psychological disability of the patients. Retinoids have proved ineffective in DDD, and Er:YAG and fractional CO\textsubscript{2} are being considered to decrease pigmentation in DDD.[^12] Our patients presented with predominantly comedones; therefore, oral isotretinoin was initiated, and the patients are being followed up to assess long-term safety. To conclude, presence of follicular papules, comedones, and pitted scars along with classical irregular star-shaped/Chinese letter pattern on dermoscopy are diagnostic clues for follicular DDD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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