Dowling-Degos Disease: A Case Report

Megan Joint, DO,* Michael Garone, DO,** Erica Rushing, MD,***Natalie Depcik-Smith, MD,**** Daniel Hurd, DO, FAOCD*****

*Dermatology Resident, 1st year, LewisGale Hospital Montgomery/VCOM, Blacksburg, VA
**Medical Student, 4th year, West Virginia School of Osteopathic Medicine, Lewisburg, WV
***Dermatopathologist, Greensboro Pathology Associates, Greensboro, NC
****Dermatopathologist, Greensboro Pathology Associates, Greensboro, NC
*****Program Director, LewisGale Hospital Montgomery/VCOM, Blacksburg, VA

Abstract

Dowling-Degos disease is an uncommon genodermatosis characterized by acquired, reticulated flexural hyperpigmentation. We present the case of a patient with pruritic hyperpigmentation of the chest and asymptomatic flexural hyperpigmentation. A literature search revealed multiple case reports, which have been reviewed and presented here. The differential diagnosis includes acanthosis nigricans, neurofibromatosis type 1, and multiple variants of Dowling-Degos such as Galli-Galli disease, Haber syndrome, dyschromatosis symmetrica hereditaria, and reticulate acropigmentation of Kitamura.

Introduction

Dowling-Degos disease is an uncommon genodermatosis for which there is limited up-to-date information in the literature. The small number of case reports makes the disease difficult to recognize, so it can be a challenging diagnosis to make. Classically, DDD is a benign disorder of hyperpigmentation that develops in early adulthood and may be asymptomatic or pruritic. However, there are less-common presentations, including a case described in 2012 by Pickup and Mutasim of a patient with asymptomatic hypopigmented lesions.[33] We present the case of an adult patient with more characteristic exam findings who wasn't even aware she had a skin condition. Although patients may not be concerned, this diagnosis is important to make as the condition imparts an increased risk of certain types of cutaneous squamous cell carcinoma.

Case Report

A 59-year-old Caucasian female presented with a 12-month history of pruritic, scaly patches on the sun-exposed chest and extremities that had been treated with intralesional steroids without improvement. When asked about an incidental exam finding of flexural freckling, the patient stated she'd had it her entire life. She denied exacerbating or alleviating factors. It had never been treated. Past medical history and medications were noncontributory. Family history was positive for similar freckling in two sisters as well as the patient's mother.

Figure 1. Left axilla

Physical exam revealed multiple erythematous, scaly papules and plaques on the central chest and bilateral shins, consistent with disseminated actinic porokeratosis. In addition, symmetric, reticulated dark brown macules were noted on the neck, axillae, inframammary and inguinal folds, popliteal fossae, and chest (Figures 1, 2). Pitting scars were present on both of the oral labial commissures.

Histologic sections of a punch biopsy from the left axilla revealed a normal, basket-weave stratum corneum overlying a slightly thinned epidermis. Finger-like projections of hyperpigmented rete ridges were seen, with more pronounced pigmentation at the tips of the rete. Occasional horn cysts were present. The infundibular portion of the hair follicle was dilated. The thin, branching, pigmented projections involved the infundibula of the follicles, which is characteristic of Dowling-Degos disease. There was also a mild, superficial, dermal perivascular lymphocytic infiltrate with occasional pigment-laden macrophages (Figures 3, 4). A diagnosis of Dowling-Degos disease was made.

Figure 2. Left popliteal fossa

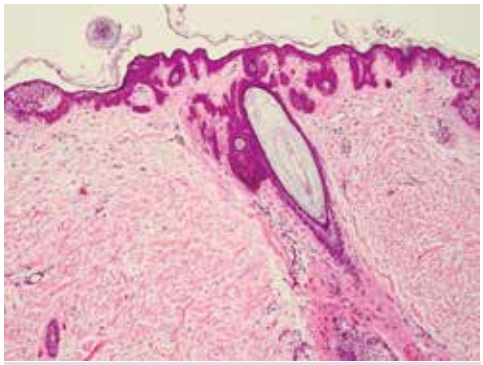

Figure 3. Punch biopsy of left axilla demonstrating involvement of the follicular infundibulum.

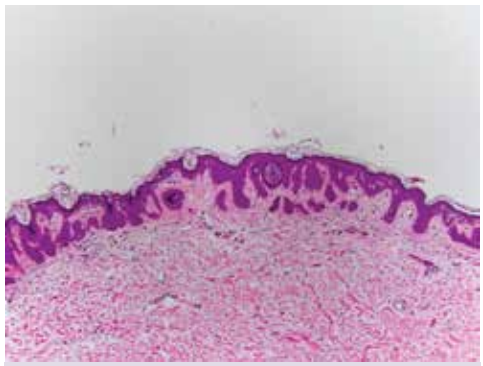

Figure 4. Finger-like projections of hyperpigmented rete ridges and horn cysts.

Treatment included a mixture of CeraVe™ cream and clobetasol solution used twice daily until her three week follow-up, at which time the frequency of use was decreased. Claritin 10 mg three times daily was also recommended, and the patient reported alleviation of her symptoms.

Discussion

Dowling-Degos disease (DDD) is an uncommon genodermatosis characterized by a reticular

pigment pattern that is most pronounced in flexural areas. It was first described in 1938 by Dowling and Freudenthal.[1] In 1954, Degos and Ossipowski termed the disease "dermatose réticulée des plis."[2] DDD can be inherited as an autosomal-dominant mutation, or it can occur sporadically.[3,4] There is no racial predisposition; however, there may be a predilection for females.[5,6] The disease results from a loss-of-function mutation in the keratin 5 gene (KRT5).[5,7] One case report of a family with DDD demonstrated a frameshift mutation in the V1 domain of KRT5.[8] This gene is partly responsible for melanosome trafficking from melanocytes to keratinocytes. There are different variations of DDD, and it is likely that these variations are a result of different mutations within KRT5.

Signs and symptoms manifest around the third to fourth decades of life; however, it has been described in newborns.[9] Brown-to-black macules and papules with variable hyperkeratosis arranged in a reticulated pattern are most prevalent at intertriginous sites.[10,11] Commonly involved areas are the axillae, groin, inframammary folds and neck. The disease progresses over time and can involve less-common locations such as the intergluteal folds, trunk, inner thighs, upper arms, and face.[12,13] The pigment pattern can be localized or generalized. Speckled macules may be found on the external genitalia in males and females.[14-16] The main symptom reported is pruritus localized to the hyperpigmentation.[11] Appearance can worsen during summer months. Additional findings include hypopigmented macules and papules, comedone-like lesions, fingernail dystrophy, and pitted perioral scars.[11] There are several reports of an increased prevalence of epidermal cysts, hidradenitis suppurativa, keratoacanthomas and perianal squamous cell carcinoma among those diagnosed with DDD.[17-21]

Histologically, there is increased pigment along the basal layer with elongated rete ridges and thinning of the suprapapillary epithelium.[22,23] This has been referred to as an "antler-like" pattern. There is also a mild perivascular lymphohistiocytic infiltrate present along with dermal melanophages.[11] Galli-Galli disease, one of the variants, also features acantholysis with parakeratosis.[24,25] The histologic features of Dowling-Degos disease are similar to those seen in an adenoid seborrheic keratosis; however, clinical history and infundibular follicular involvement can help differentiate between the two entities.

The differential diagnosis of DDD includes acanthosis nigricans, which differs both clinically and histologically. Clinically, velvety plaques help to distinguish the two. Histologically, the rete ridges are not as elongated in acanthosis nigricans, and there is no follicular component. Neurofibromatosis type 1 is also in the differential, but the age of onset and clinical picture make the two easily distinguishable.

There are several variants of DDD that result in many experts considering the disease as a spectrum. Localized and generalized Dowling-Degos and Galli-Galli disease were discussed above. Haber syndrome presents with rosacea-like facial redness beginning in childhood along with keratotic papules, comedones, scars, and reticulated hyperpigmentation on the trunk, proximal extremities, and axilla.[26] Dyschromatosis symmetrica hereditaria (DSH) is another variant that appears during infancy as hyper- or hypopigmented macules on the dorsal hands.[27] Dyschromatosis universalis hereditaria is similar but has more generalized pigmentation than DSH.[28] Reticulate acropigmentation of Kitamura (RAPK) consists of pigmented freckles on the dorsum of the hands and feet, palmar pits, epidermoid cysts, hypopigmented macules and papules, and discontinuity of dematoglyphics.[29] Signs and symptoms typically start to develop around adolescence. There is some controversy as to whether or not RAPK is a distinct entity from DDD. A recent study identified a mutation in the ADAM10 gene as the cause of RAPK and proposed to classify it as a distinct disease.[30]

The diagnosis of DDD is made based on clinical features and histopathologic findings. There have been no successful treatments for DDD.[11] Topical steroids, azelaic acid, topical and systemic retinoids, and hydroquinone have been used with varying success. One case report demonstrated success in treating the pruritus and pigmentation with adapalene; however, once treatment was stopped the lesions and symptoms reappeared. Improvement of lesions with the erbium:YAG laser has been reported.[31,32]

Conclusion

Dowling-Degos disease is an uncommon entity with multiple variants that are often considered to lie on a disease spectrum. Although limited to the skin and relatively harmless, it is important to diagnose the condition as these patients can have increased risk of other, concerning cutaneous diseases.

References

1. Dowling GB, Freudenthal W. Acanthosis nigricans. Br J Derm. 1938;50:467-471.

2. Degos R, Ossipowski B. Dermatose pigmentaire réticulée des plis. Ann Derm. 1954;81:147-151.

3. Crovato F, Nazzari G, Rebora A. Dowling-Degos disease (reticulate pigmented anomaly of the flexures) is an autosomal dominant condition. Br J Derm. 1983;108:473-476.

4. Biltz H, Kiessling M. Dowling-Degos disease--an autosomally dominant genodermatosis. Zeitsch Hautk. 1988;63:642-644.

5. Liao H, Zhao Y, Baty DU, et al. A heterozygous frameshift mutation in the V1 domain of keratin 5 in a family with Dowling–Degos disease. J Invest Dermatol. 2007;127:298–300.

6. Azulay-Abulafia L, Porto JA, Souza MAJ, et al. Doença de Dowling-Degos. An Bras Dermatol. 1992;67:275-8.

7. Betz RC, Planko L, Eigelshoven S, et al. Loss-of-function mutations in the keratin 5 gene lead to Dowling-Degos disease. Am J Hum Genet. 2006;78:510-519.

8. Liao H, Zhao Y, Baty DU, et al. A heterozygous frameshift mutation in the V1 domain of keratin 5 in a family with Dowling–Degos disease. J Invest Dermatol. 2007;127(2):298–300.

9. Zuo YG, Ho MG, Jin HZ, Wang BX. Case report: a case of newborn onset reticulate pigmented anomaly of the flexures in a Chinese female. J Eur Acad Dermatol Venereol. 2008;22(7):901–903.

10. Muller CSL, Tremezaygues L, Pfohler C, Vogt T. The spectrum of reticulate pigment disorders of the skin revisited. Eur J Derm. 2012;22:596-604.

11. Kim YC, Davis MD, Schanbacher CF, Su WP. Dowling-Degos disease (reticulate pigmented anomaly of the flexures): a clinical and histopathologic study of 6 cases. J Am Acad Dermatol. 1999;40:462-467.

12. Bardach HG. Dowling–Degos disease with involvement of the scalp. Hautartz. 1981;32(4):182–186.

13. Rebora A, Crovato F. The spectrum of Dowling–Degos disease. Br J Dermatol. 1984;110:627–630.

14. Schwartz RA, Birnkrant AP, Burgess GH, et al. Reticulate pigmented anomaly. Cutis. 1980;26(4):380–381.

15. O'Goshi K, Terui T, Tagami H. Dowling–Degos disease affecting the vulva. Acta Derm Venereol. 2001;81(2):148.

16. Massone C, Hofmann-Wellenhof R. Dermoscopy of Dowling–Degos disease of the vulva. Arch Dermatol. 2008;144(3):417–418.

17. Dixit R, George R, Jacob M, et al. Dowling–Degos disease, hidradenitis suppurativa and arthritis in mother and daughter. Clin Exp Dermatol. 2006;31(3):454–456.

18. Ujihara M, Kamakura T, Ikeda M, Kodama H. Dowling–Degos disease associated with squamous cell carcinoma on the dappled pigmentation. Br J Dermatology. 2002;147(3):568–571.

19. Loo WJ, Rytina E, Todd PM. Hidradenitis suppurativa, Dowling-Degos and multiple epidermal cysts: a new follicular occlusion triad. Clin Exp Dermatol. 2004;29(6):622-4.

20. Bedlow AJ, Mortimer PS. Dowling-Degos disease associated with hidradenitis suppurativa. Clin Exp Dermatol. 1996;21(4):305-6.

21. Fenske NA, Groover CE, Lober CW, Espinoza CG. Dowling-Degos disease, hidradenitis suppurativa, and multiple keratoacanthomas. A disorder that may be caused by a single underlying defect in pilosebaceous epithelial proliferation. J Am Acad Dermatol. 1991;24(5 Pt 2):888-92.

22. Harper JI, Trembath RC. Rook's textbook of dermatology. 7th ed. Malden, Mass: Blackwell Science; c2004. Chapter 15, Genetics and Genodermatoses; p. 111-113.

23. Howell JB, Freeman RG. Reticular pigmented anomaly of the flexures. Arch Dermatol. 1978;114:400–403.

24. Hanneken S, Rutten A, Pasternack SM, et al. Systematic mutation screening of KRT5 supports the hypothesis that Galli-Galli disease is a variant of Dowling-Degos disease. Brit J Derm. 2010;163:197-200.

25. Sprechere E, Indelman M, Khamaysi Z, et al. Galli–Galli disease is an acantholytic variant of Dowling–Degos disease. Brit J Dermatol. 2007;156:572–574.

26. McCormack CJ, Cowen P. Haber's syndrome. Australas J Dermatol. 1997;38(2):82-4.

27. Hayashi M, Suzuki T. Dyschromatosis symmetrica hereditaria. J Dermatol. 2013;40(5):336-43.

28. Miyamura Y, Suzuki T, Kono M, et al. Mutations of the RNA-specific adenosine deaminase gene (DSRAD) are involved in dyschromatosis symmetrica hereditaria. Am J Hum Genet. 2003;73(3):693–699.

29. Griffiths WA. Reticulate acropigmentation of Kitamura. Br J Dermatol. 1976;95:437-443.

30. Kono M, Sugiura K, Suganuma M, et al. Whole-exome sequencing identifies ADAM10 mutations as a cause of reticulate acropigmentation of Kitamura, a clinical entity distinct from Dowling-Degos disease. Hum Mol Genet. 2013;22(17):3524-33.

31. Altomare G, Capella GL, Fracchiolla C, Frigerio E. Effectiveness of topical adapalene in Dowling–Degos disease. Dermatology. 1999;198(2):176–177.

32. Wenzel G, Petrow W, Tappe K, et al. Treatment of Dowling-Degos disease with Er:YAG-laser: results after 2.5 years. Dermatol Surg. 2003;29:1161-1162.

33. Pickup T, Mutasim D. Dowling-Degos disease presenting as hypopigmented macules. J Am Acad Dermatol. 2011;64;1224-1225.

Correspondence: Megan Joint, DO; 2617 Sheffield Drive, Blacksburg VA 24060; Ph: 540-953-2210; Fax: 540-951-9112; meganjo@pcom.edu