Dowling-Degos disease: a therapeutic challenge. Report of a family with no response to laser treatments

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Resumen

La enfermedad de Dowling-Degos (DDD), conocida también como 'anomalía reticulada y pigmentada de las flexuras' es una rara genodermatosis autosómica dominante. Se caracteriza por la aparición de máculas hiperpigmentadas de configuración reticulada; afectando principalmente los grandes pliegues como las axilas e ingles. Pudiendo, además, comprometer otros pliegues como cervicales, antecubitales, submamarios e interglúteos. Otras características asociadas son las lesiones tipo comedones y los pits palmo-plantares.

Presentamos el caso de una familia con enfermedad de Dowling-Degos sin respuesta al tratamiento con laser Nd:YAG y CO2. Se realiza una revisión de la literatura de los tratamientos disponibles.

Palabras claves: Enfermedad de Dowling-Degos disease; láser; Nd:YAG; CO2; tratamiento; familia; genodermatosis

Summary

Dowling-Degos disease (DDD), also known as "reticulate pigmented anomaly of the flexures", is a rare autosomal dominant genodermatosis. DDD is characterized by an acquired reticular skin hyperpigmentation which begins in the axillae and groin. It later involves other body folds, including neck, inner aspects of the arms and thighs, inframammary, and intergluteal folds. Associated features include comedo-like lesions on the neck or back, pitted facial or perioral scars, and epidermoid cysts.

Herein we present a family (proband, mother, grandmother) with DDD that were treated with Q-switched Nd:YAG laser and CO2 laser without response. Treatment options are discussed and the available literature is reviewed.

Key words: Dowling-Degos disease; laser; Nd:YAG; CO2; treatment; family; genodermatosis

Dowling-Degos disease (DDD), also known as "reticulate pigmented anomaly of the flexures", is a rare autosomal dominant genodermatosis. It is associated, in approximately one-half of the cases, with loss-of-function mutation in the gene that encodes keratin 5 (KRT5).[1] Other genes such as POGLUT1 and POFUT1 have also been described. The disease has been reported worldwide and has a slight female preponderance.[2] DDD is characterized by a reticular skin hyperpigmentation that is not present at birth and starts developing during the third to fourth decade of life.[2] It begins in the axillae and groin and later involves neck, inner aspects of the arms and thighs, submammary, and intergluteal folds. Associated features include comedo-like lesions on neck or the back, pitted facial or perioral scars, and epidermoid cysts.[1,2] Diagnosis is made clinically and with the aid of a skin biopsy.[1,2] Histology shows increased pigmentation of the basal layer and finger-like rete ridges with thinning of the suprapapillary epithelium, similar to seborrheic keratosis findings.[2]

Currently, there are no effective treatments for DDD: Topical retinoids, skin lightening agents, and diverse laser therapies have been used in a limited number of patients with varying success.[3-10].

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Herein we report a complete family with DDD that was treated with retinoids and both Nd:YAG and CO2 laser therapies. No response to the treatment was seen in any of the family members.

Case report

A 37-year-old woman (proband) was referred for the evaluation of pigmented lesions in skin folds since adolescence. She reported similar lesions in her mother, grandmother and other relatives in her direct maternal lineage. Physical examination revealed hyperpigmented brownish-gray papules and macules arranged in a reticular fashion, and a few comedo-like lesions on the armpits, mammary folds, and groins (Figure 1aA). The remainder of the skin, its appendages, the mucous membranes, and teeth were unaffected. Examination of her mother and grandmother showed similar lesions (Figure 1bB-d-D). A genogram depicts family involvement (Figure 2). Skin biopsy of the armpit revealed increase pigmentation of basal layer and finger-like rete ridges and thinning of the suprapapillary epithelium (Figure 3). Combined, these clinical and histopathologic findings were compatible with DDD.

The 3 three family members were initially treated with 0.025% retinoic acid cream for 3 months with no response. Treatment was withdrawn because of irritation. They were then treated with Nd:YAG laser (532 nm, 1.5 J/cm^2, 1 Hz, spot size 4 mm and 1064 nm, spot 6 mm, 3.5 J/cm2, 10 Hz) for 2 sessions without response. As a third option, non-fractional CO2 ablative laser (0,05 s, spot size 1 mm, 2.5 W) was used, also without response after 2 sessions. Further treatment options were discussed but patients decided not to continue with additional treatments. Patients were reassured and now continue on regular follow-up.

Discussion

Treatment for DDD is challenging, with no definitive options. Medical therapies such as topical corticosteroids, topical retinoids, hydroquinone and topical azelaic acid, have been used with varying success, but none of them have shown complete or durable remission.[3-9] Systemic retinoids were also used in our cases without successful results.[6] Laser treatments; especially CO2, Er:YAG, Nd:YAG have been reported

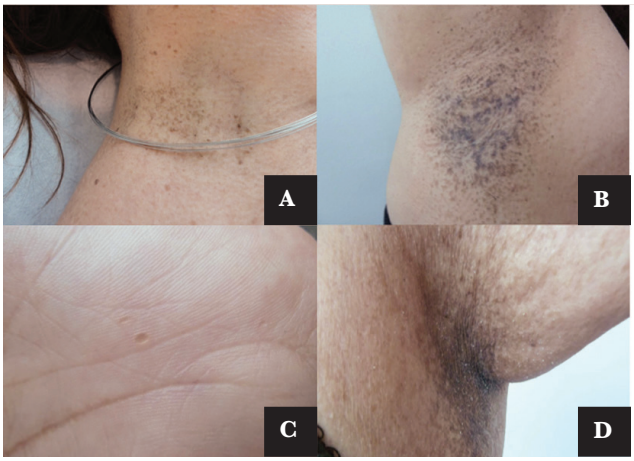

Figura 1
A. Cervical reticulate hyperpigmented macules in the proband.
B. Similar findings in mother with axillay reticulated plaques.
C. Palmar pits in mother.
D. Reticulate hyperpigmented macules on axillae present in the grandmother.

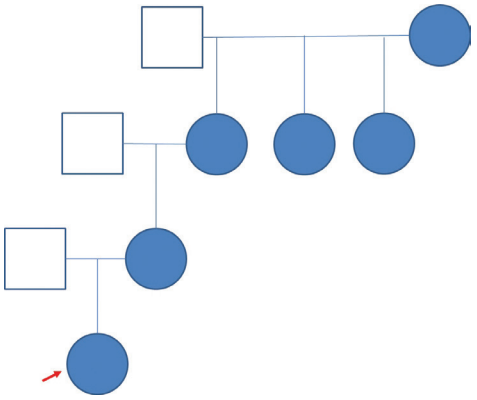

Figura 2
Genogram. Red arrow points index case.

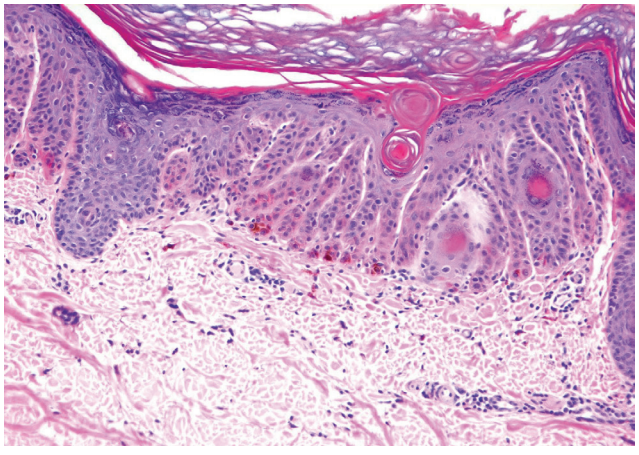

Figura 3
Histopathology. Elongated rete ridges with basal hyperpigmentation (H&E, 200X).

in the literature with variable results.[10-13] Wenzel et al. reported a case of DDD efficaciously treated using an ablative Er:YAG laser; however, their follow-up was only 2.5 years, and it was not clear whether the results were permanent. Adverse effects were not reported.[10] Yun et al. described excellent response and no adverse effects with fractional Er:YAG in an Asian woman with dark skin.[11] Recently, Gupta et al. reported a case suggesting that intense pulsed light (IPL) may be effective and safe for the treatment of DDD, although they acknowledged that more studies are needed.[12] Finally, Tambe et al. reported an effective response with no recurrences in a 19-year-old patient with the combination of Nd:YAG and CO2 laser.[13] A review of the available treatments and its outcomes is available in Table 1. Despite the successful cases described in the literature with the different laser modalities, the clinical response in a complete family with DDD presented herein was disappointing, even after undergoing two different laser modalities. The reason why Tambe *et al.*13 found a good response in their patient with a similar treatment schema needs further evaluation, but probably includes factors as ethnicity, skin type, and different laser settings, among others.

Although many treatments are available for DDD, no modality has been established yet as therapeutic standard. Unfortunately, the family presented herein didn't show any improvement with Nd:YAG or CO2 lasers. Optimizing the treatment of DDD while minimizing the associated risks remains a therapeutic challenge.

Conclusion

DDD is an uncommon genodermatosis presenting as flexural reticulate hyperpigmented macules. Although many treatments have been tested, none have shown good clinical response. This low efficacy rate should be discussed with patients when deciding whether to treat or monitor DDD patients. We encourage clinicians to seek for new effective treatments for this genodermatosis.

Table 1
Review of the published treatment options for Dowling-Degos disease.

Author	Year	Treatment method	Treatment response
Topical treatment			
Jones *et al*[3]	1978	Topical corticosteroids	No response
Jones *et al*[3]	1978	Topical Hydroquinone	No response
Jones *et al*[3]	1978	Topical retinoids	No response
Oppolzer *et al*[6]	1987	Systemic retinoids	No response
Gatti *et al*[4]	1993	Topical Azelaic acid	No response
Altomare *et al*[5]	1999	Adapalene	Temporary effect, then recurrence
Valdés *et al*[9]	2003	Topical retinoids	o response
Vázquez *et al*[7]	2013	Tazarotene 0.1%	Partial response, recurrence 8 weeks after withdrawal
Hinojosa *et al*[8]	2014	Topical and systemic retinoids	No response
Laser treatment			
Wenzel *et al*[7]	2003	blative Er: YAG Laser	Good results reported until 2.5 years after treatment
Yun *et al*[8]	2013	Fractional Er: YAG laser	Low effectiveness
Gupta *et al*[9]	2015	IPL	Effective, no recurrence
Tambe *et al*[10]	2017	Q-switched Nd:YAG and CO2 laser	Effective, no recurrence

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