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Grover's disease: dermoscopy, reflectance confocal microscopy and histopathological correlation

Francesco Lacarrubba[1], Simona Boscaglia[1], Maria Rita Nasca[1], Rosario Caltabiano[2], Giuseppe Micali[1]

1 Dermatology Clinic, University of Catania, Italy
2 Department "G.F. Ingrassia", Section of Anatomic Pathology, University of Catania, Italy

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Corresponding author: Giuseppe Micali, MD, Dermatology Clinic, University of Catania, Via S. Sofia 78, 95123 Catania, Italy. Tel. + 39 095 321705; Fax. + 39 095 3782425. Email: cldermct@gmail.com

ABSTRACT Grover's disease is a benign condition of unknown origin characterized clinically by an erythematous papulovesicular eruption and histopathologically by intraepidermal clefting and four different patterns of acantholysis: Darier-like, pemphigus-like, spongiotic, and Hailey-Hailey-like. A case of a 54-year-old female affected by Grover's disease and showing a Darier-like histopathological pattern is described. Polarized light dermoscopy (PLD) revealed the presence of polygonal, star-like shaped yellowish/brownish areas of various sizes surrounded by a thin whitish halo. Handheld reflectance confocal microscopy (RCM) showed the presence of intraepidermal dark spaces histopathologically corresponding to intraepidermal clefts, roundish, bright cells correlating to acantholytic keratinocytes, target-like cells with a dark center and a highly reflectant halo corresponding to dyskeratotic cells, and epidermal, polygonal, structureless areas reflecting hyperparakeratosis. In conclusion, the use of PLD and RCM combined with clinical presentation, personal/family history, and genetic evaluation may be useful for the non-invasive diagnosis of Darier-like Grover's disease.

Case Presentation

Grover's disease, also called transient acantholytic dermatosis, is a benign condition of unknown origin characterized by an erythematous papulovesicular eruption mainly affecting the trunk of middle-aged or elderly men. UV radiation, heat and sweating may trigger or exacerbate the disease. Although in some patients the disease is self-limited, it may be very persistent [1,2]. Histopathologically, it is characterized by acantholysis and intraepidermal clefting. Four different histopathological patterns of acantholysis have been described: Darier-like, pemphigus-like, spongiotic, and Hailey-Hailey-like [1]. These patterns may occur alone or simultaneously in the same patient.

A case of Grover's disease showing a Darier-like histopathological pattern and evaluated by polarized light dermoscopy (PLD) and reflectance confocal microscopy (RCM) is described.

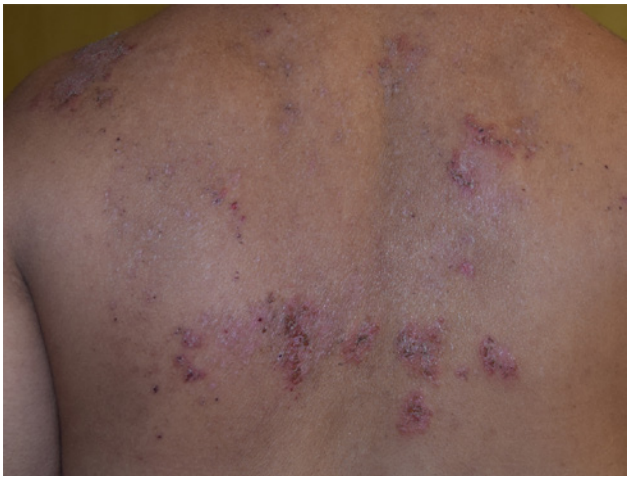

Figure 1. Multiple papules, vesicles, excoriations and crusts of the trunk in a patient with Grover's disease. [Copyright: ©2017 Lacarrubba et al.]

A 54-year-old female presented with a three-year history of itchy papules on her trunk. As reported by the patient, lesions worsened during summer and improved in wintertime. The use of topical antibiotics and corticosteroids in the past determined transient improvements. Familiar history was negative for a similar skin disorder.

Clinical evaluation revealed the presence of multiple papules, vesicles, excoriations and crusts localized on the back and in the infra-mammary regions (Figure 1).

PLD (Dermlite hybrid®, X10; 3 Gen, San Juan Capistrano, CA, USA) revealed the presence of the same features in all lesions, consisting of numerous polygonal, star-like shaped yellowish/brownish areas of various sizes surrounded by a thin whitish halo (Figure 2A).

Handheld RCM (Vivascope 3000®, Caliber I.D., Rochester, NY, USA, distributed in Europe by Mavig GmbH, Munich, Germany) performed in different lesions showed the presence of intraepidermal dark spaces; several roundish, bright cells were observed at their periphery and floating within them (Figure 3A). Some of these cells presented a peculiar target-like appearance, with a dark center and a highly reflectant peripheral halo (Figure 3B). The polygonal areas observed at dermoscopy appeared as intraepidermal low-reflectant areas containing structureless, high-reflectant material (Figure 2B).

Histopathological examination from a skin biopsy showed the presence of acantholysis, intraepidermal cleft formation, dyskeratosis with corp ronds and grains, and hyperparakeratosis (Figure 4). Direct immunofluorescence and ELISA testing of anti-desmoglein 1 and 3 antibodies were negative.

Based on anamnestic, clinical, instrumental and laboratory data, the diagnosis of Darier-like Grover's disease was made.

Discussion

The clinical differential diagnosis of Grover's disease includes a variety of skin disorders such as pemphigus foliaceus, pemphigus vulgaris, impetigo, dermatitis herpetiformis, Hailey-Hailey disease and Darier's disease. Histopathology examination represents the gold standard for the diagnosis. In the Darier-like variety, which represents the most frequent pattern seen in Grover's disease, the histopathological aspect is similar to Darier's disease, consisting of acantholysis mainly involving suprabasal layers, dyskeratosis (with presence of grains and corps ronds), hyperkeratosis, acanthosis, and parakeratosis [1,2].

Dermoscopy of Grover's disease has been described [3-5] showing similarities with Darier's disease [6,7], papu-

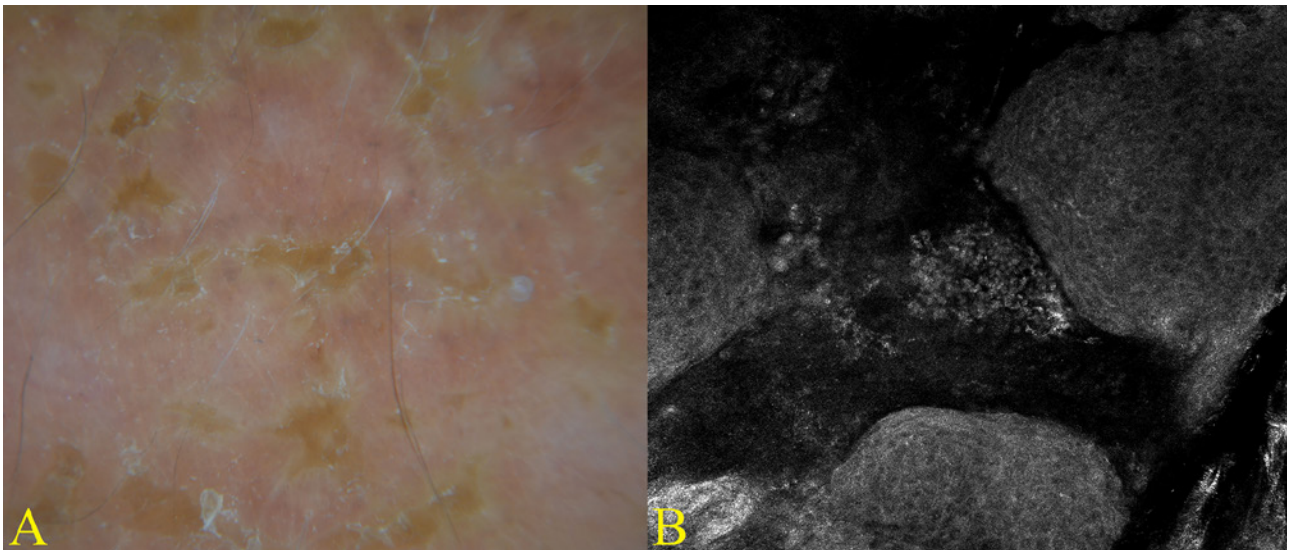

Figure 2. Polarized light dermoscopy showing polygonal, star-like shaped yellowish/brownish areas surrounded by a thin whitish halo (**A**). Reflectance confocal microscopy of the same field showing a polygonal, intraepidermal low-reflectant area containing structureless, high-reflectant material (**B**). [Copyright: ©2017 Lacarrubba et al.]

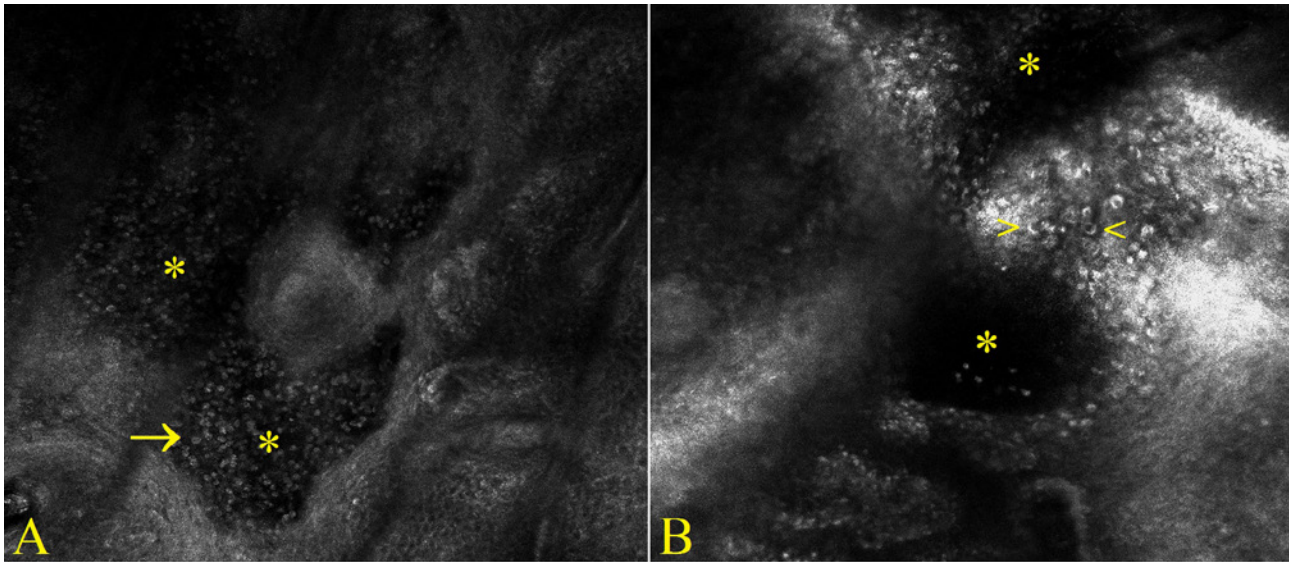

Figure 3. Reflectance confocal microscopy (**A** and **B**) of another field showing the presence of intraepidermal clefts (asterisks), acantholytic cells (arrows) and dyskeratotic cells (arrowheads). [Copyright: ©2017 Lacarrubba et al.]

lar Dowling–Degos disease [8], and solitary acantholytic dyskeratoma [3]. Common dermoscopy findings consist of polygonal, star-like shaped yellowish/brownish areas that histopathologically correspond to marked hyperparakeratosis and acanthosis, and a peripheral whitish halo that correlates with orthokeratosis and hypergranulosis.

The use of RCM has been reported for the diagnosis of some vesicobullous disorders [9-13], not for Grover's disease. In our case, RCM allowed to recognize *in vivo* the histopathological aspects of the Darier-like variety of Grover's disease: intraepidermal dark spaces corresponding to intraepidermal clefts; roundish, bright cells observed at the periphery and within these spaces correlating to acantholytic keratinocytes; epidermal, polygonal, structureless areas reflecting hyperparakeratosis; target-like cells with a dark center and a highly reflectant halo corresponding to dyskeratotic cells. These cells rule out other acantholytic disorders such as pemphigus and Hailey-Hailey disease, in which dyskeratosis is generally absent. Similar RCM features, however, may be seen in Darier's disease [6,14].

In conclusion, the pattern seen with PLD may point towards a diagnosis of Darier-like Grover's disease but cannot exclude other diseases that may show similar features. RCM imaging can further narrow down the differential diagnosis to Darier-like Grover's disease and Darier's disease. Differentiating these two entities by histopathology is difficult to achieve, and the combined use of PLD with RCM may obtain similar results without requiring skin biopsy. Clinical presentation, absence of family history and, in selected cases, genetic evaluation (absence of ATPA2 mutations) may address the definitive diagnosis. Further PLD/RCM studies on other histological variants of Grover's disease are desirable.

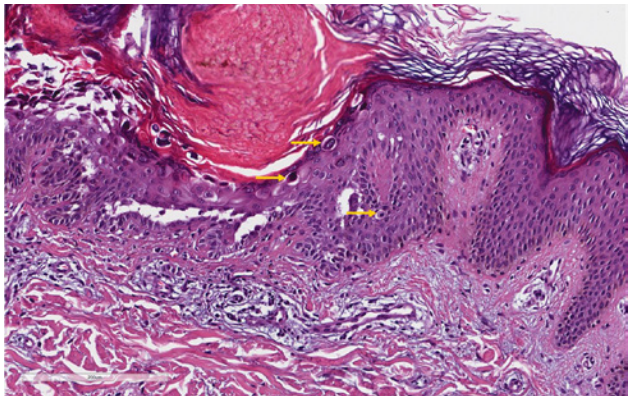

Figure 4. Histopathology showing hyperparakeratosis, intraepidermal clefts, acantholysis and dyskeratotic cells with irregular nucleus surrounded by clear halo enclosed in eosinophilic shell (arrows). [Copyright: ©2017 Lacarrubba et al.]

References

1. Quirk CJ, Heenan PJ. Grover's disease: 34 years on. *Australas J Dermatol.* 2004;45:83-6; quiz 87-8.
2. Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, eds. *Rook's Textbook of Dermatology*. 9th edition. Oxford, UK: Wiley-Blackwell, 2016.
3. Giacomel J, Zalaudek I, Argenziano G. Dermatoscopy of Grover's disease and solitary acantholytic dyskeratoma shows a brown, star-like pattern. *Australas J Dermatol.* 2012;53:315-316.
4. Specchio F, Argenziano G, Tiodorovic-Zivkovic D, et al. Dermoscopic clues to diagnose acantholytic dyskeratosis. *Dermatol Pract Concept.* 2015;5(1):11.
5. Errichetti E, De Francesco V, Pegolo E, Stinco G. Dermoscopy of Grover's disease: variability according to histological subtype. *J Dermatol.* 2016;43(8):937-9.
6. Lacarrubba F, Verzì AE, Errichetti E, Stinco G, Micali G. Darier disease: dermoscopy, confocal microscopy, and histologic correlations. *J Am Acad Dermatol.* 2015;73(3):e97-99.

7. Errichetti E, Stinco G, Lacarrubba F, Micali G. Dermoscopy of Darier's disease. *J Eur Acad Dermatol Venereol*. 2016;30(8):1392-1394.
8. Geissler S, Dyall-Smith D, Coras B, Guther S, Peters B, Stolz W. Unique brown star shape on dermatoscopy of generalized Dowling–Degos disease. *Australas J Dermatol.* 2011;52:151-3.
9. Lacarrubba F, Verzì AE, Pippione M, Micali G. Reflectance confocal microscopy in the diagnosis of vesiculobullous disorders: case series with pathologic and cytologic correlation and literature review. *Skin Res Technol.* 2016;22(4):479-486.
10. Angelova-Fischer I, Pfeuti T, Zillikens D, Rose C. In vivo confocal laser scanning microscopy for noninvasive diagnosis of pemphigus foliaceus. *Skin Res Technol.* 2009;15:40-44.
11. Kurzeja M, Rakowska A, Rudnicka L, Olszewska M. Criteria for diagnosing pemphigus vulgaris and pemphigus foliaceus by reflectance confocal microscopy. *Skin Res Technol.* 2012;18:339-346.
12. Levi A, Ophir I, Lemster N, et al. Noninvasive visualization of intraepidermal and subepidermal blisters in vesiculobullous skin disorders by in vivo reflectance confocal microscopy. *Lasers Med Sci.* 2012;27:261-266.
13. Debarbieux S, Depaepe L, Poulalhon N, Dalle S, Balme B, Thomas L. Reflectance confocal microscopy characteristics of eight cases of pustular eruptions and histopathological correlations. *Skin Res Technol.* 2013;19:e444-452.
14. González S, Rubinstein G, Mordovtseva V, Rajadhyaksha M, Anderson RR. In vivo abnormal keratinazation in Darier-White's disease as viewed by real-time confocal imaging. *J Cutan Pathol.* 1999;26(10):504-508.