Granular parakeratosis, report of a case and review of the literature

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ABSTRACT

Granular parakeratosis is a cutaneous eruption described during the past decade, that is thought to be due to a reactive mechanism. It cinsists of hyperkeratotic erythematous papules that coalesce into reticular plaques. Women in their 5th to 6th decade, are mostly affected, and the eruption shows a preference for axillary folds. This is the first report of a patient a with axillary granular parakeratosis in Argentina, we also review the medical literature on this condition (Dermatol Argent 2010;16(3):190-194).

Keywords:

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Introduction

Granular parakeratosis (GP) is an uncommon entity recently described by Northcutt et al.[1] Although it is usually asymptomatic and without systemic impact, it represents a diagnostic challenge and must be differentiated from other diseases with similar symptoms.

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Case report

68 year old female patient with a history of anal carcinoma, consulted the Department of Dermatology for presenting lesions in both axillas, that had started 20 days earlier. Physical examination showed the presence of hyperpigmented asymptomatic papules with central hyperkeratotic plug, some were isolated and others were confluent forming plaques of 2×3 cm in diameter, in both axillas **(Photo 1)**. The patient reffered the use of talc and antiperspirants.

With a presumptive clinical diagnosis of confluent and reticulated papillomatosis of Gougerot Carteaud versus vegetative pemphigus, we performed a skin biopsy staine with hematoxylin and eosin which revealed an acanthotic epidermis with hyperkeratosis and involvement of the granular layer **(Photo 2)**. A higher magnification showed parakeratosis and retention of keratohyalin granules within the cells of the stratum corneum **(Photo 3)**. There was no evidence of spongiosis or inflammatory infiltrates in the dermis. PAS staining was negative for fungal elements.

With the findings described above we reached the diagnosis for granular parakeratosis.

The patient was treated with tretinoin 0.025% and medium potency topical corticoids for a month, with partial resolution of the lesions **(Photo 4)**.

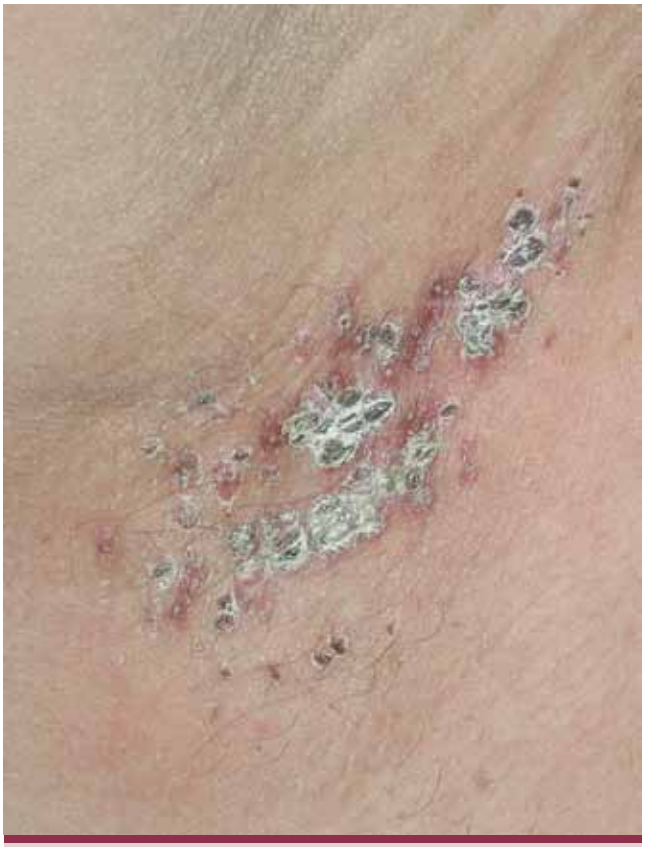

PHOTO 1. Erythematous and hyperkeratotic papules which present as isolated and do also converge forming an irregular plaque in the right axilla. A whitish material is observed that appears to be talc or powder.

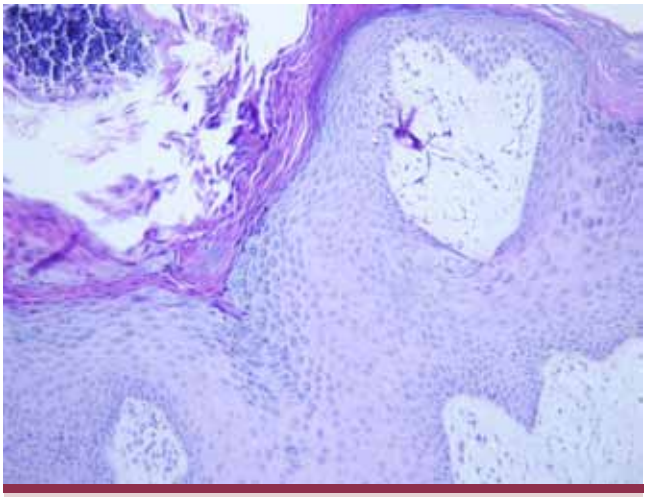

PHOTO 2. Epidermis presenting hyperparakeratosis and acanthosis. Papillary dermis without alterations (H-E).

Discussion

Granular parakeratosis was first described in 1991 by Northcutt et ál.1 with the definition of *axillary granular parakeratosis*, as a benign dermatosis affecting both axillas of women between 50 and 60 years of age. Subsequently, Mehereghan et ál.[2] In a series of cases reported, a case with inguinal location and proposed changing the original name to the currently used: *granular parakeratosis*. Since then, approximately 40 cases have been reported in the literature. **(Table 1)**.

It presents as erythematous papules with a hyperkeratotic center, isolated or coalescing in a reticulate pattern to form plaques. Pruritus is a usual finding although it is not constant.[3,4] It is located in intertriginous areas, most frequently bilaterally in the axillas, although it can affect inguinal fold and perianal and submammary regions. There have been reports of patients with lesions in the abdomen, thighs, cheeks and scalp.[2,5-7] Pediatric cases have also been reported, where the presentation of the lesions was divided into two clinical types: erythematous geometric plaques, in diaper pressure sites, and bilateral linear plaques on inguinal folds.[8]

Almost invariably, the presence of parakeratosis in a biopsy specimen indicates rapid proliferation of keratinocytes to the surface and altered maturation of the epidermis due to various alterations, as seen, for example, in psoriasis.[9] This acceleration of epidermal turnover makes the granular layer vanish. Therefore, these processes are also accompanied by hypogranulosis or agranulosis, a situation not seen in GP. Granular parakeratosis as a histological finding per se does not constitute a disease, but rather a pattern of reaction to various stimuli. It is due to an acquired alteration of keratinization.

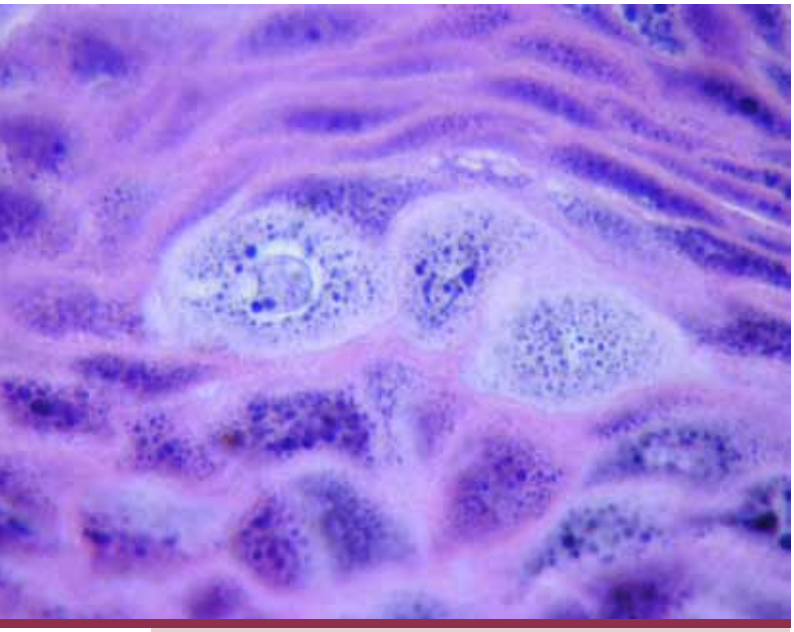

PHOTO 3. Within the corneal layer it is observed retention of nuclei and basophilic keratohyalin granules (H-E).

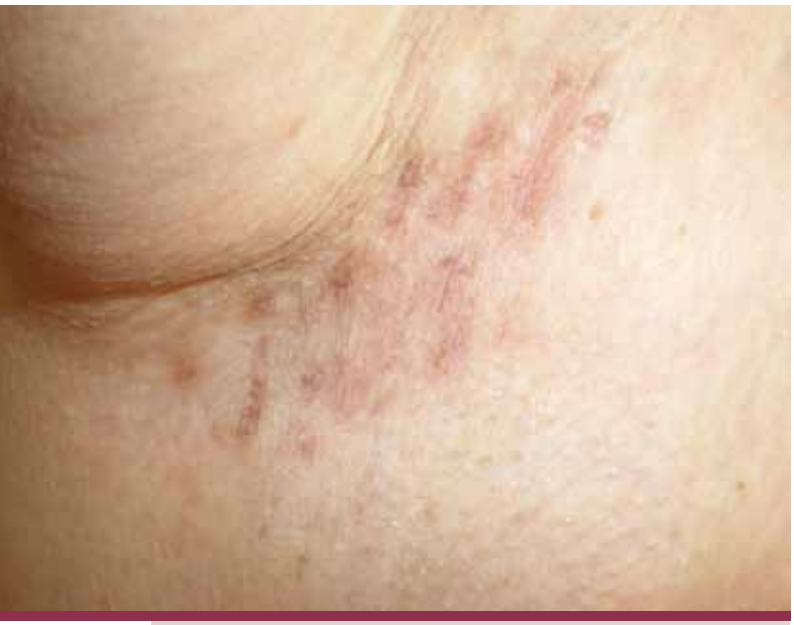

PHOTO 4. Partial improvement of lesions after one month of treatment.

Therefore granular parakeratosis as a dermatosis, with characteristic clinical and histological features as described in this case, should be distinguished from granular parakeratosis found in the context of the histological findings seen in other dermatoses such as molluscum, dermatophytes, dermatomyositis solitary acanthoma.[5,10]

The etiology of GP is still unknown. Different theories have been proposed to explain its pathogenesis.

The excessive use of deodorants, talcs or powders and the continuous friction of the affected area, causing a secondary epidermal proliferation as a defense mechanism is one of them,[3] but the absence of these factors and the unilateral compromise in many patients the absence of a marked inflammatory infiltrate and spongiosis in the histology, do not support this theory.[6] The predominant involvement of folds or sites under occlusion indicate that friction, moisture and local heat represent key factors for the disease.[8]

Immunohistochemichal techniques have demonstrated the absence of filaggrin in the cytoplasm of the corneocytes and positive response in the basophilic granules of keratohyalin for profilaggrin and filaggrin. Thus, the pathogenesis in PG would be caused by a defect in the processing of the precursor protein, profilaggrin, towards the effector, filaggrin.[11,12]

The histology shows a acanthotic epidermis with some isolated vacuolated keratinocytes and compact hyperkeratosis. Parakeratosis with retention of nuclei and keratohyalin granules of the granular layer which gives a particular basophilic staining of the stratum corneum can be seen.The granulosar layer is not affected. In the dermis there are slight signs of papillomatosis and vascular proliferation[2]. To date, there are two cases with a folliculotropic subtype.[6.13] Clinical differentiation from Hailey-Hailey disease must be made, as well as for acanthosis nigricans, pemphigus vegetans, seborrheic keratosis, Darier's disease, contact dermatitis, inverse psoriasis, reticulated and confluent Gougerot-Carteaud papillomatosis, among others.[2] In pediatric cases the differential diagnosis include candidal intertrigo, diaper contact dermatitis, seborrheic dermatitis, acrodermatitis enteropathica, Hailey Hailey disease and abuse.[8]

Numerous treatment strategies have been described, with varying results. Among these, the use of corticosteroids and topical retinoids, isotretinoin, tacalcitol and even botulinum toxin and cryosurgery.[3,14-16]

Patients should be advised to minimize the use of deodorant and avoid excessive washing of the affected, actions that can sometimes be sufficient for lesions to resolved without further treatment.[17] There are no controlled studies supporting the use of a certain medication over others. With regards to evolution, spontaneous involution has been reported in some cases, others with good response to treatment and even a case with persistence over 20 years.[18]

A study conducted by Scheinfield and Mones,[6] over 363,343 biopsies evaluated in the Ackerman Institute of Dermatopathology, found that 18 of them had a diagnosis of the entity (representing 0.005% of cases) but, of these, only one was remitted with a presumptive clinical diagnosis of GP. In turn, all lesions were localized in the axillas and a large majority among women (15 of 18 cases) was observed. The authors suggest that the absence of references to this condition in dermatology textbooks would be the cause for

TABLE 1. Granular Parakeratosis cases published in the literature.

Author	Sex	Age	Location	Symptoms	Presumptive diagnosis	Treatment	Evolution
Northcut 1991	F		Bilateral Axilla	Pruritus	NS	NS	Improvement
	F		Bilateral Axilla	No	NS	NS	Persistence
	M		Unilateral Axilla	No	NS	Corticosteroid	Improvement
Meheregan 1995	F	73	Bilateral Axilla	No	HaileyHailey	Corticosteroids+antimycotics	Years
	F	43	Left Axilla	Pruritus	NS	Corticosteroids+antimycotics	3 days
Webster 1997	F	40	Bilateral Axilla	NS		Isotretinoin	Good response
Meheregan 1998	F	43	Left Axilla	Pruritus	NS	NS	NS
	F	52	Bilateral Axilla	Pruritus	Acanthosis nigricans	Corticosteroids	NS
	F	60	Left Axilla	NS	Wart	NS	NS
	F	51	Right groin	Pruritus		NS	Spontaneous resolution
Brown 2002	F	50	Bilateral Axilla	No	Mycosis	Topical tretinoin	2 month
Resnik 2003	F	83	Trunk	No	NS	Topical	10 years without response
Srivastava 2004	M	71	Bilateral Axilla	Pruritus	NS	Topical corticosteroid	Without response
Chang 2004	M	22m	Diaper	Pruritus	NS	Topical steroids without response	Spontaneous resolution
	M	18m	Bilateral groin	No	NS	Tacrolimus without response	Spontaneous resolution
	F	12m	Diaper	No	Mycosis	Pimecrolimus	Improvement
Scheinfeld 2005	F	67	Axilla	NS	Seborreic keratoses	NS	NS
	F	56	Axilla	NS	Darier	NS	NS
	F	19	Axilla	NS	Acanthosis nigricans, Darier, Gougerot-Carteaud	NS	NS
	F	53	Axilla	NS	Idiopatic papule	NS	NS
	F	20	Axilla	NS	Acanthosis nigricans	NS	NS
	F	53	Axilla	NS	Inverse Psoriasis, Hailey-Hailey	NS	NS
	F	30	Axilla	NS	Vulvar wart, Tinea	NS	NS
	F	66	Axilla	NS	Rash	NS	NS
	F	40	Axilla	NS	Discoid Lupus, Post-inflammatory hyperpigmentation	NS	NS
	F	44	Axilla	NS	HaileyHailey	NS	NS
	M	50	Axilla	NS	Acanthosis nigricans	NS	NS
	F	45	Axilla	NS	Flat wart	NS	NS
	F	44	Axilla	NS	Macula, melanoma	NS	NS
	F	50	Axilla	NS	HaileyHailey, HPV	NS	NS
	M	41	Axilla	NS	Granular parakeratosis	NS	NS
	M	46	Axilla	NS	Lineal wart	NS	NS
	F	60	Axilla	NS	Atypical nevi	NS	NS
	F	54	Axilla	NS	Irritant dermatitis	NS	NS
González de Arriba 2007	F	50	Bilateral Axilla	No	NS	Tacalcitol	Improvement
Compton 2007	F	60	Bilateral Axilla	No	NS	Isotetroin 40 mg/day	Improvement
Stierman 2007	NS	NS	Scalp	No	NS	NS	NS
Joshi 2008	F	27	Left cheek	Pruritus	NS	Oral corticoids	Resolution 15 days
Reddy 2008	M	25	Axillas, penis, groin, perianal	No	HaileyHailey, pemphigus vegetans	Oral and Topical corticosteroids, tretinoin, isotretinoin	20 years without response
Ezra 2008	F	52	Unilateral Axilla	No	Mycosis	Topical corticosteroids	Improvement
Gunn 2008	F	48	Left Axilla	Pruritus	NS	Topical corticosteroids	No response
Jaconelli 2008	F	58	Axillas, groins, submammary	No	Mycosis	Topical antimycotics	Spontaneous resolution

NS: not specified. **m:** months.

which there was clinical suspicion in only one case.
This allows the conclusion that GP constitutes a new infrequent entity, and that might not be recognized by the all dermatologists, who should begin to include it in differential clinical diagnosis of verrucous lesions in the folds.

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