Granular parakeratosis: a report of six cases in children*
*Paraqueratose granular: relato de seis casos em crianças**

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Abstract: Granular parakeratosis is an alteration of keratinization that was first described in adults. It is characterized by hiperkeratotic plaques and papules in intertriginous areas. The authors describe six cases of granular parakeratosis in children. One patient had lesions on the buttocks; two children presented papules in both axillae and cervical region (presentations never described before in the literature). The remaining three patients presented with lesions in the inguinal folds. Review of the literature and discussion on the pathogenesis of this rare dermatosis are presented.
Keywords: Child; Epidermis; Keratinocytes; Patology

Resumo: *A paraqueratose granular é alteração da queratinização, primeiramente descrita em adultos, caracterizada por pápulas e placas hiperqueratósicas nas áreas intertriginosas. Os autores descrevem seis casos de paraqueratose granular em crianças. Um paciente apresentava lesões nas regiões glúteas, dois em ambas as axilas e região cervical (apresentações inéditas na literatura). Três pacientes apresentavam lesões em pregas inguinais. Realizam também revisão da literatura e discutem a possível etiologia dessa rara dermatose.*
Palavras-chave: Ceratinócitos; Criança; Epiderme; Patologia

INTRODUCTION

Granular parakeratosis (GP) consists of the presence of brown-redish hyperkeratotic papullae and plaques, with a size ranging from three to four milimeters, located in intertriginous areas.[1,2] It has been first described in the axillary folds of adults,[3-6] being later observed in other cutaneous folds, such as sub and intermammary,[1,7] abdominal,[1] inguinal[1,2,4] and perianal[1] ones. Later on, GP was also observed in children with lesions in the perianal area and folds.[2,8-11]

GP is considered to be an alteration of keratinization, and likely causes are still only hypothetical.[1,4,12] Lesions, which might have a six-month evolution, are generally assymptomatic or little pruritic, with spontaneous involution or regression following application of several types of topic medications.[4]

The authors here describe six cases of GP in children, the first one presenting with lesions in the gluteus region, the second in the axillary folds bilaterally, the third in the cervical region, and the others in the inguinal folds. Bilateral axillary and cervical presentations are unprecedented in literature for the pediatric age range.

CASE REPORTS

Case 1

Male patient, dark skin, 10-months old. He had been presenting with brownish plaques in the

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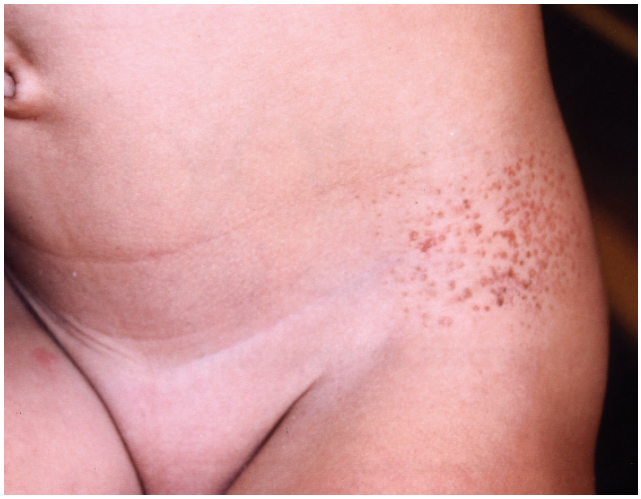

FIGURE 1: Brown keratotic papules in the gluteus region

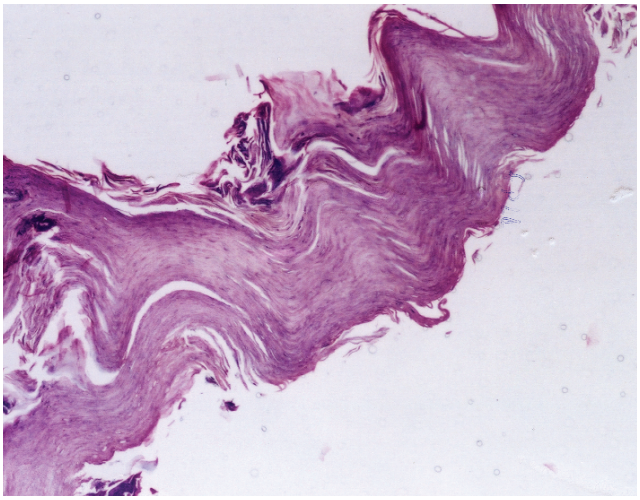

FIGURE 3: Scales curetted from axillary regions displaying hyperkeratosis, intense parakeratosis and numerous dark keratohyalin granules (HE magnification 40X)

gluteus and diaper-covered regions for two months (Figure 1). For the prevention of dermatitis in the diaper region, he had been using daily aplications of zinc oxide ointment with vitamins A and D and boric acid. On examination, presented scales forming brownish and hyperkeratotic plaques from 1 to 3 mm wide, grouped in the gluteus region, leaving a slight depression when removed with a curet. Histopathology of the scales removed by curettage revealed a hyperkeratosis with intense parakeratosis and the presence of inumerous dark granules (keratohyalin granules). PAS and Giemsa stains were negative.

Case 2

Female patient, dark skin, aged nine months. Fifteen days before, she had the onset of dark brown circular scales with a diameter varying from 1 to 4 mm in diameter, forming plaques in the axillary regions, bilaterally (Figure 2). When curetted, the scales left a small depression on the site. Patient had used an ointment containing zinc oxide, bismuth, aubgalate, magnesium and diiodothymol. When treated with topical salicylic acid cream at 5%, had a complete remission of the lesions in two weeks. Histological examination of a sample collected by curettage revealed keratin with extense parakeratosis and the presence of various dark granules (Figure 3), PAS-CD and Giemsa negative.

Case 3

Eight month-old white female patient had been presenting yellow-brownish papules bilaterally in the cervical region for seven months (Figure 4). Past his-

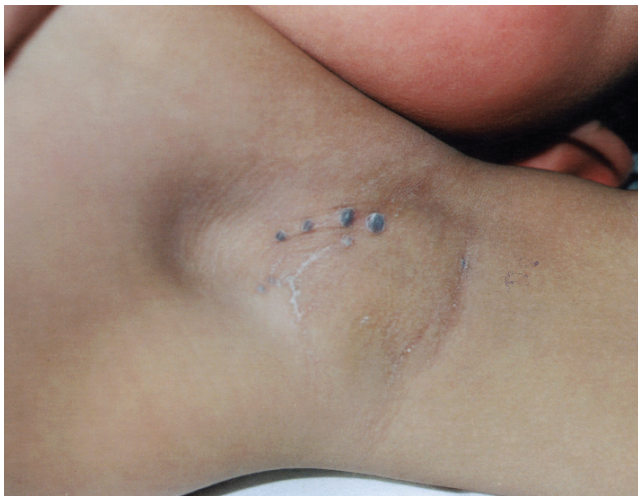

FIGURE 2: Brown keratotic papules in the axillae (detail left axilla)

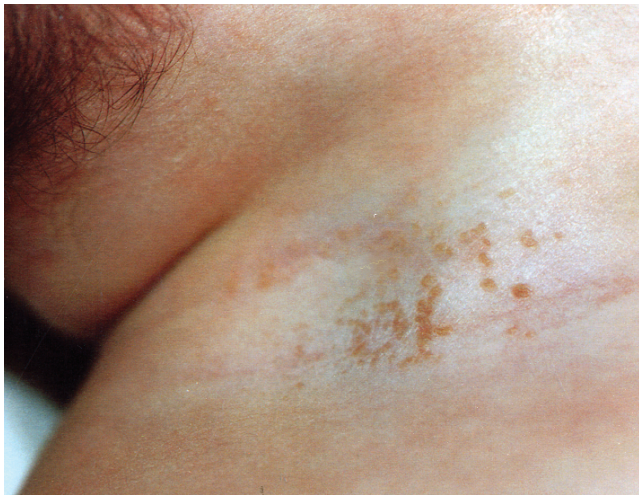

FIGURE 4: Light brown papules and scales in cervical region

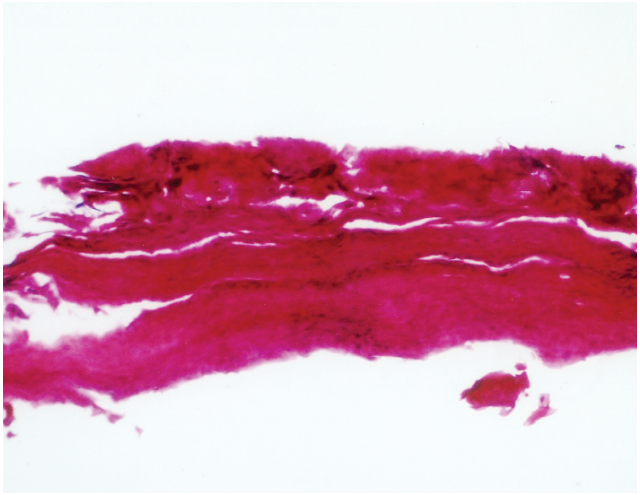

FIGURE 5: Scales curetted from inguinal regions exhibiting dark keratohyalin granules in horny layer (HE magnification 100X)

tory of sudamina in the cervical region with the use of talc powder. As in the previous treatment, topic low-potency steroids were prescribed, with no improvements. Moreover, she presented a café-au-lait spot in the scapulary region, a salmon spot in the glabella, back of the nose and nucha, and some teleangiectasias and flebectasias in the left lower limb, with no signs of atrophy or cutaneous depressions, making these lesions clinically compatible with congenital teleangiectatic cutis marmorata. Treatment with thermal water was instituted for sudamina, along with salicylic acid cream at 4% for two weeks for the scales. There was a complete disappearance of the lesions.

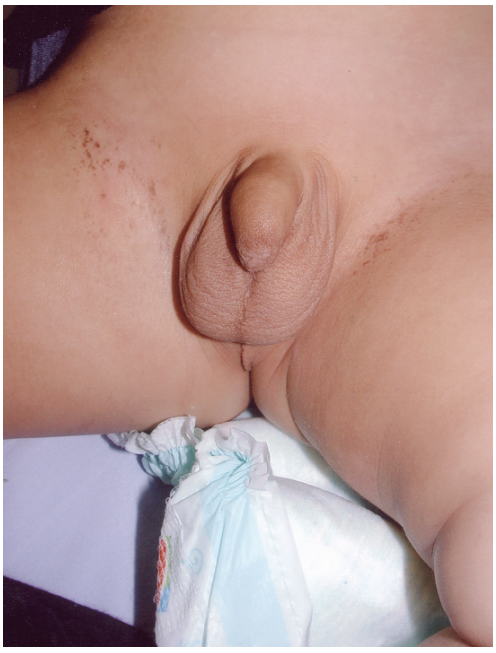

FIGURE 6: Brownish scales in inguinal regions

Case 4

Two year-old asian male patient with the onset of brownish desquamating crusts bilaterally in the inguinal folds two weeks before (Figure 5). Under examination, presented with small brownish scales measuring from 2 to 3 mm in diameter, forming plaques in the inguinal region. Lesions left a small depression on their base when excised with a curet. As past medical history, had achondroplasia and various episodes of diaper dermatitis and of perianal candidiasis. Made regular use of zinc oxide, boric acid and vitamins A and D ointment, as well as nistatin ointment and disposable diapers. Following curettage of the lesions, anatomopathological examination revealed the presence of granular parakeratosis (Figure 6). He was treated with salicylic acid at 3% in a lanette base, in a single application after bathing. Weobserved complete disappearance of the lesions after 14 days of treatment.

Case 5

White six month-old male patient, who had had dark brown scales in the inguinal folds for two months. He had been a premature child, with an otherwise uneventful medical history. His mother had been treated with progesterone during the secoond trimester of her pregnancy. Positive family history for atopy. Regular use of an ointment containing zinc oxide, boric acid, vitamins A and D, benzalconium chloride and cetrimonium bromide in the perineum. Under examination, presented with brownish scales forming small plaques of 2 or 3 cm in the inguinal folds and suprapenian region. Scales dettached easily on curettage, leaving a slight depression on the site. He was treated with 3% salicylic acid in vaseline, applied daily on the lesions. The patient did not return for reevaluation.

Case 6

White five month-old female patient, with the onset of brown scales in the inguinal folds two months before. Examination revealed the presence of brownish scales going from 2 to 3 mm in diameter, which left a slight depression when removed with a curet. As in previous cases, she made regular use of an ointment containing zinc oxide, boric acid and vitamins A and D. When treated with a salicylic acid cream at 3% (in lanette) in a single application after bathing, lesions remitted completely. She returned at the age of eight years and four months still with absence of either lesions or scars in the inguinal folds bilaterally, presenting only ephelids in the face and xerosis.

CHART 1: Review of pediatric cases of granular parakeratosis described in world literature from 1991 to 2005

Author/year	N. of cases	Age	Gender	Color	Location	Medications used	Treatment	Evolution
Trowers et al. [2]	1	9m	M	W	inguinal folds	Zinc oxide, vitamins A and D, ointment, lanoline, talc powder	Suspension of medications in use	–
Patrizi et al.[9]	4	13m/17m /10m/24m	F/F/M/F	W/W/W/W	inguinal folds, lumbar region, abdomen, buttocks and flanks/perineum, lower abdomen/Lumbar sacral region,flanks, perineal folds/ perineal folds, pubis	Liquid soaps, zinc oxide, ointment and talc powder	Suspension of medications in use and of diaper use	–
Neri et al.[10]	1	6y	F	W	Left axilla	roll-on deodorant	–	Spontaneous resolution
Pimentel et al.[11]	2	3m/5m	–	–	perineum/perineum	ointments	–	–
Chang et al.[8]	2	22m/ 18m/18m	M/M/F	W/W/W	inguinal folds/inguinal folds, mid perineal raphe and perianal/ inguinal folds and suprapubic region	Topic steroids, hydrophilic petrolate/ tracolimus 0,03%, desonid, zinc oxide ointment/nistatine cream, cetoconazol associated to hydrocortisone	zinc oxide / zinc oxide /pime crolimus cream at 1%	–
Giraldi et al.	6	10m/9m/8m/ 2 a/6m/5m	M/F/F/ M/M/F	B/B/W /Y/W/W	glúteos/axilas/ região cervical/pregas inguinais/pregas inguinais/pregas inguinais	zinc oxide ointment vitamins A and D ointment, boric acid, bezalconium chloride, cetrimonium bromide	Salicylic acid 3%, 4%, 5%	Total disappearing of lesions

M: male F: female W: white Y: yellow B: brown y: years m: months

DISCUSSION

In 1999, Northcutt and his collaborators described four cases of a new entity, naming it axillary granular parakeratosis. The lesions, located in the axillae, were characterized by hyperpigmented or erythematous plaques, either uni or bilateral, and pruritic. Histology demonstrated the presence of hyperparakeratosis with keratohyalin granules restricted to the horny layer.[3] This dermatosis is acquired and characterized by the presence of multiple brownish or red-brownish hyperkeratotic plaques ranging from three to four millimeters, occasionally forming plaques located in the intertriginous areas.[1,2] ALesions are asymptomatic or little pruritic, lasting for months or undergoing spontaneous involution. Regression of GP may occur with the use of numerous topic medications.[4] The first description was followed by others, of lesions in the axillae[1,3-6] and also in submammary and intermammary,[1,7] inguinal[1,2,13] and perianal[1] folds. The expression intertriginous granular parakeratosis seems the most adequate, since GO can occur in cutaneous folds other than the axillary.[4] In Brazil, the first reported case was in an adult female with lesions in the submammary region.[14]

The first pediatric case reported in literature was that of a child presenting with lesions bilaterally in the inguinal region, with a history of topical use of various products on the affected site.[2] Six other cases were reported in children ranging from 10 to 24 months of age.[9,11] The first case described in the pediatric age with lesions in left axilla had past history of use of roll-on deodorant.[10] Of the three more recent cases, two presented erythema under the scales, and authors have suggested two clinical patterns of presentation, one with linear scales and the other associated with erythema.[8]

Etiology of GP is still undetermined. There is an hypothesis that states that the basic defect is in the transformation of profilagrin into filagrin, resulting in failure to degrade keratohyalin granules and to aggregate keratine filaments during hornification. Abnormalities in cell surface structures and components of the horny envelope would then contribute to the formation of retention hyperkeratosis.[1]

Physical factors such as hyperhydrosis, obesity and friction could contribute to its onset because of mechanical irritation, which in its turn would provoke a protective response, determining epidermal proliferation with formation of abnormal granular cell layers.[6] Irritating substances and toxic agents seem to have an etiological implication in GP. The use of chemicals in soaps, deodorants (roll-on, stick), antiperspirants, shampoo, formulas, cosmetic and dermatological creams and ointments would increase the number of transitional cells.[1,7] Zinc oxide, which is a component of ointments with protective properties against diaper area dermatitis, would increase the rate of mitoses of cells in the basal layer.[12] Participation of microbial organisms and of *Candida albicans* has not been proven.[1]

On histology, GP presents a thick, paraketatotic and basophilic horny layer, as well as a discrete perivascular lymphocyte infiltrate, which may be due to irritating factors. Electronic microscopy demonstrates a great amount of keratohyalin granules, and infundibles present thick horny plugs with alterations similar to those occurring in the epidermis.[6] Also reported are epidermal hyperplasia with a preserved granulous layer, discrete perivascular T $CD4^+$ lymphocyte infiltrate in the upper dermis, absence of dendritic $CD1^+$ cells in the epidermis, as well as epidermal keratins (keratin 5/14,1/10) and normal involucrin expression. Horny layer cells are filled with basophilic granules which are immunoreactive to antibodies that recognize filagrin and its precursor, which is a feature of GP.[1]

Differential diagnosis in the infant must be made with keratotic affections which affect cutaneous folds, such as verrucous nevus, acanthosis nigricans, confluent and reticular papilomatosis, seborrheic dermatitis, fungal infections, inverted-form psoriasis, Darier's and Haley-Haley's disease, and contact dermatitis.

Several topic agents are used in the treatment of GP. Calciprotriene, pimecrolimus, topic steroids, topic and oral tretionine are all described.[5,8] Spontaneous disappearing is reported in five cases in literature.[1]

Including the ones here presented, there are 17 GP cases described in children (Chart 1). Cases reported here are similar to those in literature concerning clinical presentation, evolution, site of affection in the pediatric age range, histopathological features and past history of use of ointments containing zinc oxide. In the literature, eight cases had used zinc oxide in the perineum, and in other two there were no specifications concerning the use of topical substances.

The authors support the hypothesis that diaper friction, sweating and use of ointments containing zinc oxide, together are irritating factors that may explain the onset of perineal lesions. In axillary and cervical folds, the use of creams, soaps and talc powder, the latter already contraindicated for infants, could be implicated as triggering agents. Bilateral axillary and cervical affection (Cases 2 and 3) was up to our knowledge not described in pediatric literature.

In cases 3, 5 and 6, diagnosis was based on clinical data and on the presence of small depres-

sions in the site where scales over covered the skin, following curettage. It is important to highlight that, in the small children, diagnosis can be made by simple curattage instead of skin biopsy.[15] Scales are detached by using a curette, leaving tiny depressions in the base of the lesion, visible to the naked eye, facilitating clinical diagnosis. Five of the cases presented here were treated with salicylic acid, at concentrations going from 3 to 5%, with total remission of the lesions in a few days. Use of classical keratolytics such as salicylic acid seems sufficient for a complete resolution of the lesions.

Clinical presentation, use of ointments containing zinc oxide, curettage of the lesions and accurate histopathological examination of scales confirmed the diagnosis of this rare entity. ❑

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