Granuloma Glutaeale Infantum: A Re-emerging Complication of Diaper Dermatitis

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Granuloma gluteale infantum is a rare nodular complication of irritant diaper dermatitis. The association of this condition with the widespread use of nondisposable cloth diapers has been increasingly recognized. We present the case of an 18-month-old girl with granuloma gluteale infantum. Our aims are to emphasize the importance of clinical recognition of this re-emerging complication of diaper dermatitis and to point out the potential role of topical calcineurin inhibitors as a treatment option.

abstract

Irritant diaper dermatitis (DD) is a common condition, estimated to occur in 25% of children seeking care from a pediatrician in the first 4 weeks of life.[1] The diagnosis and therapeutic management of this condition are usually straightforward. DD usually follows a benign clinical course and resolves without complications. Chronic severe forms of DD are rare, have atypical presentations, and should be addressed specifically.

CASE REPORT

An 18-month-old girl was referred to our dermatology clinic with a 9-month history of severe relapsing DD. The child was otherwise healthy, and family history of skin conditions included only a maternal grandfather with psoriasis. Her parents used nondisposable cloth diapers. She was initially prescribed topical clotrimazol and zinc oxide cream for the rash, resulting in temporary improvement. However, subsequently, she developed a persistent rash unresponsive to multiple treatments that included barrier creams, topical antibiotics and antifungal agents, and various topical corticosteroids (TCS), including betamethasone valerate 0.1% and hydrocortisone butyrate 0.1% creams.

At the time of our observation, the patient had multiple, either irregularly shaped or oval-shaped and rounded, red, infiltrated, nontender nodules and plaques, located in the convexities of the gluteal region and major labia. All lesions had surrounding erythema, some had a central ulceration, and others had an intact surface yet slightly elevated borders (Fig 1). General examination was otherwise unremarkable; the child was well, but some unspecific scaling of the right temporal scalp area was noted.

A clinical diagnosis of granuloma gluteale infantum (GGI) was suspected. A skin biopsy of one of the nodules was performed to rule out other conditions. Histologic examination disclosed irregular acanthosis with prominent hypergranulosis. There was mild ectasia of the superficial vascular plexus, surrounded by a perivascular lymphocytic infiltrate but no vascular necrosis (Fig 2). Periodic acid–Schiff staining did not reveal any fungal elements. Correlation of these histologic findings with a typical clinical presentation of GGI supported the diagnosis.

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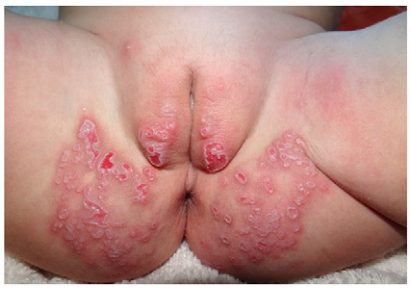

FIGURE 1
Clinical presentation with multiple red-to-purple, deep, firm nodules and plaques distributed over the gluteal region. Some had central ulceration. The dimensions of the lesions varied from 0.5 to 3 cm.

Because the parents decided to continue use of nondisposable cloth diapers, general measures concerning alleviating DD were reinforced, and frequent diaper-free periods (as long-lasting as possible) were also suggested. All previous topical treatments were discontinued. A 1-month trial of daily pimecrolimus 0.1% cream application was initiated. Because it was well tolerated, treatment with the more potent tacrolimus 0.03% ointment followed. After 4 weeks, a complete regression of the ulcerated lesions was observed. Subsequently, there was a gradual thinning of the lesions. After 8 weeks, only transient postinflammatory hyperpigmentation remained, evolving to hypopigmented residual patches at the last examination (Fig 3).

Treatment of the patient was subsequently maintained with only the same general measures, including the application of barrier creams. At follow-up in 9 months, she developed a mild relapse, presenting with 3 nodules located on the gluteal region. There was a rapid and complete regression of the lesions after 1 week of topical tacrolimus treatment.

DISCUSSION

GGI was first described in 1971 by Tappeiner and Pfleger[2] as a rare complication of DD with a

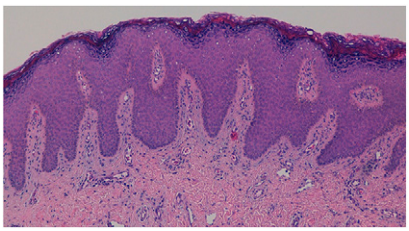

FIGURE 2
Histology of one of the nodules revealed a perivascular dermal lymphocytic infiltrate with prominent irregular acanthosis of the overlying epidermis. (Hematoxylin and Eosin stain ×50.)

characteristic presentation consisting of multiple inflammatory papules and nodules. GGI typically occurs in infancy (especially between 4 and 9 months of age).[3] Irrespectively of age group, GGI is particularly common in the setting of chronic diarrhea or fecal or urinary incontinence[4] associated with conditions such as short gut syndrome, inflammatory bowel disease, Hirschsprung disease, or spina bifida. Additionally, GGI occurring in peristomal locations in both children and adults with urostomies or colostomies should be recognized as having a particularly refractory presentation.[4]

The etiology of GGI is not fully understood, but a few contributing factors have been proposed. GGI occurs in the setting of severe irritant contact DD[5,6] related to prolonged occlusion from diapers, resulting in increased exposure to feces and urine. This has not only a direct contributory role but also renders local skin more sensitive to other proposed etiologic factors. These factors include candidiasis,[5,6] foreign material[3] such as starch, and topical preparations, especially potent and moderate fluorinated TCS.[3,5] However, *Candida* and positive polarized examination have not been consistently found in the majority of case reports: an argument against its etiologic role.[3] Remarkably, the increased absorption of TCS through inflamed skin of the diaper area can induce alterations in dermal collagen, which may, in turn, be responsible

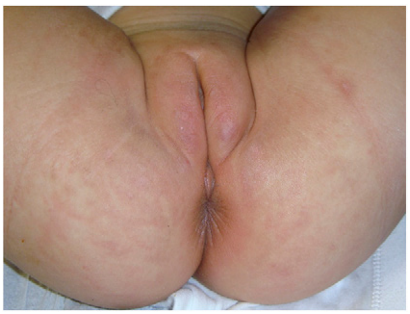

FIGURE 3
Clinical presentation at the last consultation. Only slightly hypopigmented residual patches were observed.

for some of the unique clinical features of GGI. Temporal association between the first GGI descriptions and the widespread use of potent TCS supports their etiologic role. Lastly, the increasing use of cloth reusable diapers has been implicated in the recent re-emergence of papulo-nodular DD complication reports.[7] Reusable diapers are generally considered to be more ecological and economical, but they are purportedly less absorbent than disposable ones.[7]

The clinical appearance of an asymptomatic eruption of red-purple to red-brown, round to oval, deep, firm nodules with central ulceration is typical. This characteristic, along with the classic distribution over the convexities of the gluteal region, sparing the inguinal folds, points to the clinical diagnosis of GGI.

Nonetheless, when the number of nodules is limited or the dermatitis has atypical clinical features, other conditions must be clinically considered. These include infectious diseases (such as scabetic nodules, genital molluscum contagiosum, and candidiasis) and neoplastic disorders (namely Kaposi sarcoma, mastocytomas, Langerhans cell histiocytosis, and leukemic infiltrates), among others. In addition, other complications of irritant DD may exhibit overlapping clinical features, including extensive and confluent ulcers in Jacquet's erosive DD and pseudoverrucous

papules and nodules.[8] These complications are deemed to be in the same clinical spectrum of GGI. They probably result from different individual susceptibilities producing polymorphous local presentations as a response to the same pathophysiological mechanisms.[8]

Histologic findings are neither specific nor consistently diagnostic, but their correlation with clinical features allows exclusion of other conditions clinically considered in the differential diagnosis. Histology reveals a nonspecific perivascular dermal infiltrate with lymphocytes, plasma cells, histiocytes, eosinophils, and aggregates of neutrophils forming microabscesses. The overlying epidermis shows prominent acanthosis and parakeratosis.

Removal of the precipitating factors is the key aspect of the treatment.[9] When this removal is difficult or not possible, such as in the setting of peristomal GGI or chronic medical conditions associated with persistent diarrhea and incontinence, a particular emphasis should be put on local skin care. In these situations, secondary bacterial infections are a common aggravating factor, so swabs for microbiological examination should be obtained routinely specifically from peristomal skin. Prevention of secondary infection and recovery of skin barrier function should be attempted by using gentle antiseptic cleansers and barrier creams, such as zinc oxide or petrolatum-based preparations. Apart from these special settings, specific treatment is generally not needed because the removal of the predisposing factors leads to a spontaneous yet slow-paced resolution.[9] To minimize morbidity and potential complications arising from this protracted clinical course, many authors have proposed the use of low-potency TCS (such as hydrocortisone).[9] However, this option is controversial[5] given the potential etiologic role of corticosteroid preparations in GGI etiology. Additionally, some authors recommend that TCS should not be used in the diaper area, because its application in the locally sensitive and inflamed skin may induce prominent atrophy and other adverse effects, arising from significant local absorption.[5,10]

For our patient, we prescribed once-daily application of tacrolimus 0.03% for 8 weeks, resulting in complete resolution of the dermatitis. The clinical remission was maintained for 6 months. Use of topical calcineurin inhibitors (TCIs) for children <2 years of age has not been formally approved; however, large population studies have failed to identify any safety concerns in this population. A recent extensive review concluded that TCIs are safe and effective for the treatment of infants of at least 3 months of age, especially in sensitive skin areas.[10] TCIs do not carry the risk of skin atrophy, impaired barrier function, or enhanced percutaneous absorption, in contrast to TCS. Tacrolimus was well tolerated by our patient and potentially led to a prompt resolution of the initial GGI presentation and its subsequent relapse. We cannot, however, exclude the potential role that may have been played by strict and adequate obedience to the DD general treatment measures that were recommended (although this child's parents chose to continue using nondisposable diapers). Additionally, we must recognize that a short, tapering course of low-potency TCS may be considered safe and perhaps a good option as a transition therapy to a longer TCI course in patients with protracted disease.

Our patient's case fits the classic clinical and histologic descriptions of GGI. Additionally, this report emphasizes the emergent etiologic role of reusable diapers in recent reported outbreaks of papulo-nodular DD complications. To the best of our knowledge, this is the first case reporting the use of TCIs in GGI treatment.

DD is a common condition initially presented to pediatricians. The prompt recognition of its complications and appropriate management is crucial for all pediatric physicians. Considering the current increase in GGI reports related to the widespread use of cloth diapers, we aim to alert pediatricians to consider this diagnosis. In particular, physicians should be aware that GGI has a typical presentation that may clinically simulate a granulomatous or a neoplastic disease. Additional studies are required to assess if TCIs might be an option to minimize morbidity and more promptly resolve GGI, without major adverse events.

ABBREVIATIONS

DD: irritant diaper dermatitis
GGI: granuloma gluteale infantum
TCI: topical calcineurin inhibitor
TCS: topical corticosteroids

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