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Childhood granulomatous periorificial dermatitis: case report and review of the literature

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Abstract

Childhood granulomatous periorificial dermatitis (CGPD), considered a clinical variant of perioral dermatitis, typically affects prepubertal children of African descent. It is a condition of unknown etiology characterized by the presence of a monomorphic yellow-brown papular eruption limited to the perioral, perinasal, and periocular regions that histopathologically shows a granulomatous pattern. This disorder should be differentiated from other conditions as granulomatous rosacea, sarcoidosis, and lupus miliaris disseminatus faciei. We report a case of a 9-year-old boy who presented with flesh-colored perorificial papules on the face, evolving for two months. Upon treatment with topical tacrolimus for follicular eczema, an aggravation of the condition was observed. A skin biopsy confirmed the diagnosis of CGPD. Our patient was successfully treated with a combination of topical metronidazole and topical erythromycin.

Keywords: childhood granulomatous periorificial dermatitis, children, diagnosis, tacrolimus

Introduction

Childhood granulomatous periorificial dermatitis (CGPO) is an eruption that affects usually prepubertal children. Clinically, it is characterized by monomorphic papules grouped around the mouth, nose, and eyes without systemic involvement. The diagnosis can usually be made by assessment of the patient history and recognition of the classic clinical features. Skin biopsy showing granulomatous infiltrate is indicated to confirm the diagnosis in atypical presentations. Treatment is not mandatory if mild, since the eruption is self-limited.

Case Synopsis

A 9-year-old boy presented to our clinic for a mild itchy skin eruption on the face, evolving for two months. Past medical history was significant for atopic dermatitis. Physical examination revealed multiple, non-scaly, pinpoint whitish to flesh-colored papules distributed around the mouth and nose, and to a lesser extent around the eyes (**Figure 1A)**. The rest of the examination was unremarkable. A diagnosis of follicular atopic dermatitis was made. The patient received a low potent topical corticosteroid for 5 days, followed by topical tacrolimus 0.03% for 25 days. At the follow-up visit, the parents described an initial improvement after topical corticosteroid and then an exacerbation upon the switch to tacrolimus (**Figure 1B)**.

All treatments were stopped and a punch biopsy of a single papule was performed. Hyperkeratosis with parakeratosis, acanthosis, and focal spongiosis were noted. A granulomatous infiltrate composed of histiocytes, lymphocytes, and polymorphonuclear cells infiltrating the upper and mid dermis was observed. Some granulomas were also found around the hair follicles (**Figure 2**). A stain for fungi was negative. These findings were consistent with the

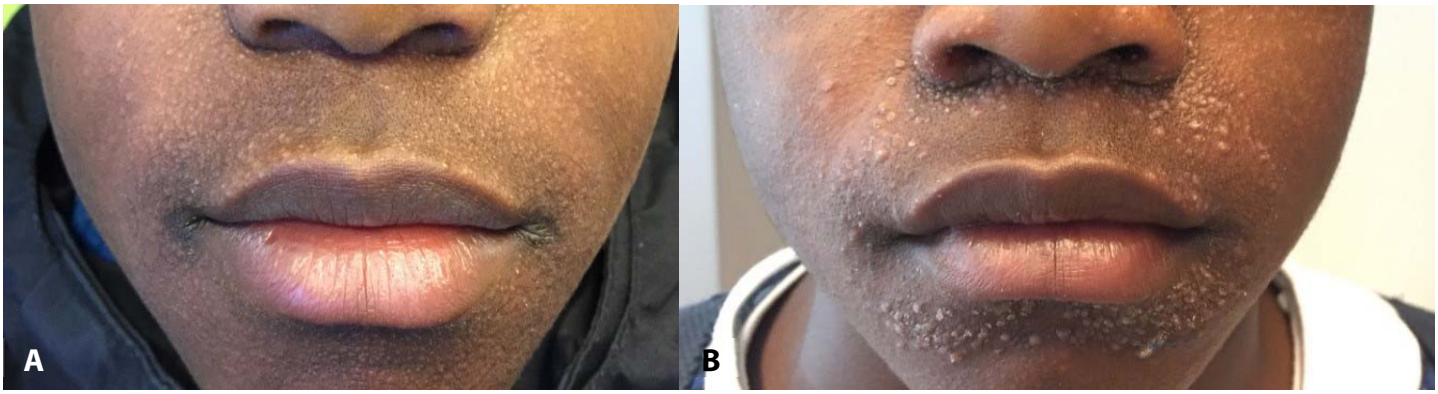

Figure 1. ***A)*** *Multiple pinpoint whitish to flesh colored papules distributed around the mouth.* ***B)*** *Exacerbation after treatment with tacrolimus.*

diagnosis of CGPD. The patient was treated with a combination of topical metronidazole 2% and topical erythromycin 2%. After two months, clearance of almost all skin lesions was noted (**Figure 3**).

Case Discussion

Childhood granulomatous periorificial dermatitis is also known as granulomatous periorificial dermatitis and facial Africo-Caribbean childhood eruption (FACE), [1-4]. Gianotti et al. were the first to report this entity in 1970 [5]. In 1974, Marten et al. reported 22 cases of black children with flesh-colored papules on the central face [6]. In 1989, the eruption was named "granulomatous perioral dermatitis in children" by Frieden et al., then FACE by Williams et al. in 1990 [7]. Knautz and Lesher finally called the eruption CGPD [8].

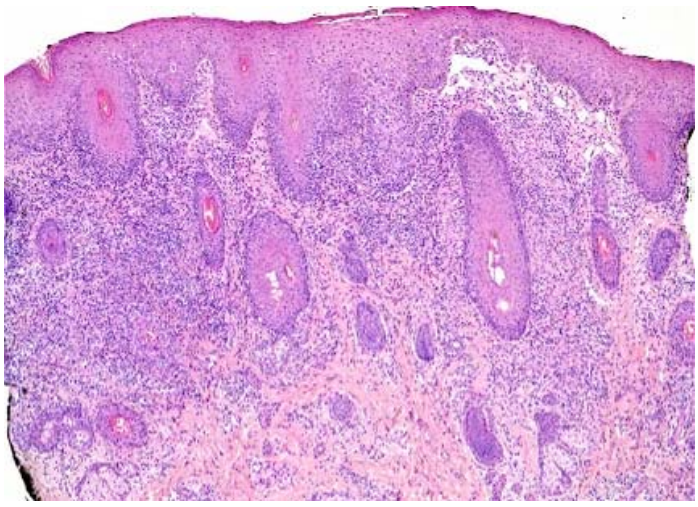

Figure 2. *Histopathological examination showing upper and mid dermis granulomatous infiltrates. H&E, 10×.*

Childhood granulomatous periorificial dermatitis usually affects prepubertal children [9]. A few cases have been reported in adults [10]. Involvement of areas other than the face has been observed [11]. Basically, CGPD is limited to the skin with no systemic involvement [12]. Occasionally, it may be associated with blepharitis or conjunctivitis [13]. Histologic examination shows upper dermal non-caseating granulomas with prominent perifollicular involvement associated with a lymphohistiocytic infiltrate [12].

The differential diagnosis may include periorificial dermatitis, granulomatous rosacea, sarcoidosis, lupus miliaris disseminatus faciei, and acne (**Table 1**). Periorifical dermatitis, more common in women aged 20-45, is characterized by clustered papulopustules and papulovesicles sparing the narrow zone around lips [14]. Granulomatous rosacea shares similar histologic findings with CGPD and some authors consider them to be the same

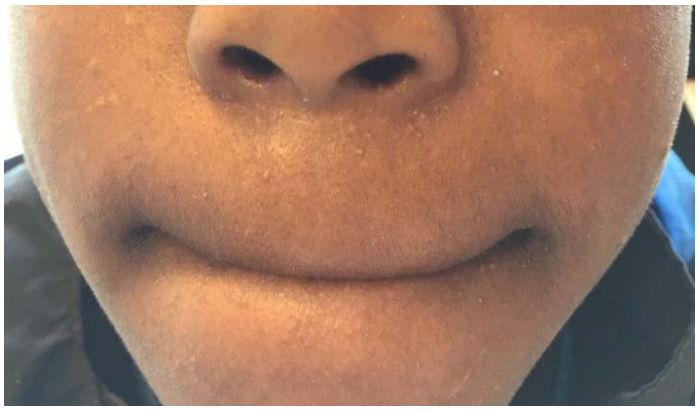

Figure 3. *Remission, two months after treatment with topical erythromycin and topical metronidazole.*

disorder. However, classical rosacea typically presents with signs of telangiectasias and erythema [12]. Childhood granulomatous periorificial dermatitis has also been suggested as a variant of sarcoidosis [15]. The limited skin involvement and spontaneous resolution noted in CGPD helps to differentiate these two conditions. Lupus miliaris disseminatus faciei, presenting as papular lesions over the central face in adolescents and adults of both sexes, might be a challenge to differentiate form CGPD [16].

The exact etiology of CGPD remains unknown. It can result from an exaggerated inflammatory response to allergens and irritants. Frieden et al. suggested that the initial allergen causes an inflammatory process, then a focal disruption of the follicular wall creating a granulomatous reaction [7]. Some reports have implicated reactions to essential oils in bubble gum, formaldehyde, cosmetic preparations, black synthetic mesh, and antiseptic solutions [17]. A possible association between chronic CGPD and hormone growth therapy has been reported recently [18]. Childhood granulomatous periorificial dermatitis is generally considered a benign and self-limited disorder with no long-term sequelae. In some patients, active lesions may persist for several years [19].

There is no consensus for management of CGPD. We noted an exacerbation after use of calcineurin inhibitor that is not consistent with other reports in the literature. The reason for the exacerbation remains to be elucidated. It could have related to lack of efficacy of tacrolimus in this patient or facial irritation caused by the tacrolimus. Although improvement may be noted early with the prescription of topical corticosteroids, chronic use may exacerbate or perpetuate the disorder [20]. Therefore, the discontinuation of topical corticosteroids and the avoidance of cosmetics products may be helpful.

Topical agents are preferred over oral therapy for mild disease, characterized by small areas of involvement with no significant emotional distress. Options include pimecrolimus, tacrolimus, erythromycin, and metronidazole.

We also report excellent therapeutic result with a topical combination of metronidazole and erythromycin [21–23]. Oral agents such as tetracycline, clarithromycin, and erythromycin are used in moderate to severe cases [10,21]. Efficacy of isotretinoin therapy for resistant CGPD has been mentioned in case reports [24]. In addition, oral metronidazole may represent an option in recalcitrant cases [25].

Conclusion

Childhood granulomatous periorificial dermatitis is a benign self-limited inflammatory process that resolves spontaneously without serious sequelae. Patients and parents should be reassured that complete resolution usually occurs. Treatment is indicated in cases of emotional and quality of life issues. Physicians should be alert to this uncommon disorder in children.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 1: *Differential diagnosis of childhood granulomatous dermatitis [10], [23], [26-31].*

Diagnosis	Age	Origin	Gender	Clinical features	Histopathology	Treatment	Comments
Childhood granulomatous periorificial dermatitis [10]	Childhood, prepubertal	Afro-Caribbean	M>F	-Numerous small, yellow-brown, inflammatory papules -Perioral, perinasal or periocular areas	Perifollicular non-caseating granulomatous infiltration	-Topical antibiotics -Oral antibiotics - Topical calcineurin inhibitors [23]	-Benign -Self-limited -Exacerbated by topical corticosteroids
Rosacea [26]	Adults over the age of 30	Celtic and Northern Europe	F>M	-Centrofacial erythema -Papules -Pustules -Flushing -Telangiectasias -Ocular features	-Perivascular and perifollicular inflammatory infiltrates -Superficial blood vessels dilation -Demodex mites detected	Inflammatory lesions: topical metronidazole, topical ivermectin, oral antibiotics, low dose isotretinoin	-Chronic -Associated with CAD, HTN, IBD
Papular Sarcoidosis [27,28]	Children and adults	All ethnic groups	M=F	-1 to 10 mm papules -nasolabial and eyelids	Sarcoidal noncaseating epithelioid cell granulomas	-Topical calcineurin inhibitors -Oral tetracyclines	-Spontaneous resolution is possible -Atrophic macules -Associated with acute systemic sarcoidosis
Lupus miliaris disseminatus faciei [29]	Adolescents and adults	All ethnic groups	M=F	multiple red-brown 2 to 5 mm papules on the face	Perifollicular epithelioid caseating granulomas	-Topical tacrolimus -Dapsone -Low dose prednisone -Minocycline	-Chronic scarring -Variant of granulomatous rosacea
Acne [30]	Preadolescent, adolescent and adults	All ethnic groups	Preadolescent: F>M Adolescent: M>F	-Comedones, papules, pustules -Face, neck, chest, back	-Dilated follicle with a plug of keratin -Dense inflammatory skin infiltrate	-Topical retinoids -Topical antimicrobials -Oral antibiotics -Isotretinoin	-Risk of scarring -Chronic or recurrent episodes
Periorificial dermatitis [31]	Young women	All racial and ethnic backgrounds	F>M	-Erythematous papules, pustules, vesicles -Perioral	Perifollicular and perivascular lymphocytic infiltrates	-Topical antibiotics -Topical calcineurin inhibitors -Oral antibiotics	-No scars -Benign -Exacerbated by topical steroids

F, female; M, male; CAD, coronary artery disease; HTN, hypertension; IBD, inflammatory bowel disease.