Childhood Granulomatous Periorificial Dermatitis

Abhijit S. Chakraborty, Rashmi Agarwal, Pellakuru Preethi, B S Chandrashekar

Department of Dermatology, Cutis Academy of Cutaneous Sciences, Bengaluru, Karnataka, India

Introduction

Childhood granulomatous periorificial dermatitis (CGPD) is a rare, benign, self-limited papular eruption of unknown pathogenesis that occurs commonly in prepubertal dark-skinned children.[1] Clinically, it is characterized by multiple flesh-colored to yellow-brown papules, often accompanied by erythema and desquamation, that are typically grouped around the mouth, nose, and eyes without systemic involvement.[1] The current review was conducted with the objective of determining the various presentations of CGPD and its treatment options.

Two of the authors (AC and RA) searched PubMed independently using the terms "childhood granulomatous periorificial dermatitis or CGPD" and used the filters of "case reports" and "the age limit of birth to 18 years". The case reports with a confirmed diagnosis of CGPD were included in the current review. The data extracted were analyzed for gender predominance, age at presentation, duration of rashes, and treatment regimens. Continuous data were described as mean (±SD) or median [range], and categorical data were expressed as a proportion.

Cases

A total of 22 cases were described in the 20 case reports that were included in this study.[1-20] The details of the cases are described in Table 1.

In these 22 cases, 12 (55%) were male and 10 (45%) were female. The median age at presentation was 10 [range 2–18] years. The median duration of rashes at diagnosis was 3.5 [range 0.5–24] months. The majority of the cases were asymptomatic (77%), while four (18%) cases presented with pruritus, and only one (5%) case presented with blepharitis. The number of cases presented with monomorphic papules were 20/22 (91%), while only one case presented with papules and pustules, and one case presented with desquamating papules along with erythema. The distribution of the papules was observed in perioral and/or perinasal and/or periorbital regions in all cases. Extra-facial involvement (such as scalp, ears, neck, trunk, upper extremities, and perineum) was observed in six (27%) cases [Figure 1]. Treatment was provided in 20/22 (91%) cases [Figure 2], and the resolution was obtained in 17/20 (85%) cases. The median duration to resolution was 2 [range 0.75–12] months.

Discussion

The authors conducted a review of case reports of CGPD to determine various presentations and treatment options. A total of 20 case reports were included in this study, which described 22 cases of CGPD.

In this study, the authors found that CGPD is equally predominant in males and females with a slightly higher incidence in males. The median age of presentation of CGPD was 10 [range 2–18] years. This finding reinforces the fact that CGPD presents in the first two decades of life (especially in prepubertal children).

The authors observed that the median duration of rashes at diagnosis was 3.5 months. The clinical similarity of CGPD with other conditions such as periorificial dermatitis, granulomatous rosacea, sarcoidosis, lupus miliaris disseminatus faciei, and acne may lead to a delay in diagnosis [Table 2].

The distribution of rashes was mainly found to be perioral, perinasal, and periorbital.[1-20] In a few cases, extra-facial regions such as the neck, scalp, ears, trunk, upper extremities, and perineum were

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Address for correspondence:
Dr. Abhijit S. Chakraborty, Department of Dermatology, Cutis Academy of Cutaneous Sciences, Bengaluru - 560 040, Karnataka, India.
E-mail: abhijitchakraborty.ac1985@gmail.com

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Table 1: Details of the case reports of CGPD reviewed with respect to clinico-epidemiological parameters, histopathological findings, treatment modalities, and resolution time

Study identifier	Age/sex	Duration (months)	Symptoms	Morphology	Distribution	Histopathology	Treatment duration (weeks)	Time to resolution (months)
Kim *et al.* (2011)[1]	9/F	2	Asymptomatic	Monomorphic papules	Perioral + periorbital	Noncaseating granulomatous infiltrate of Langhans cells and few epithelioid cells in the dermis	None	No resolution
Faikh *et al.* (2020)[2]	9/M	2	Pruritus	Monomorphic papules	Perioral + perinasal	Noncaseating granulomatous infiltrate of lymphocytes/histiocytes in the upper and mid-dermis	Metronidazole 2% + erythromycin 2%	2
Lacarrubba *et al.* (2020)[3]	16/M	3	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Noncaseating epithelioid granulomas and lymphocytes in the upper and mid-dermis	Pimecrolimus 1%	5
Hatanaka *et al.* (2018)[4]	11/M	12	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital + forehead + malar	Perifollicular noncaseating epithelioid granulomas and lymphocytes in the upper and mid-dermis	Tacrolimus 0.1% + erythromycin 800 mg	1.5
Zalaudek *et al.* (2004)[5]	14/M	11	Asymptomatic	Papules + pustules	Perioral + perinasal + periorbital	Perifollicular noncaseating epithelioid granulomas	Tetracycline 500 mg BD + metronidazole 0.75%	0.75
Knautz *et al.* (1996)[6]	9/F	3	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Not done	Metronidazole 0.75%	3
Zhang *et al.* (2020)[7]	4/M	10	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital + neck	Noncaseating granulomatous infiltrate of lymphocytes/histiocytes in the upper and mid-dermis	Clarithromycin 125 mg (32)	8
Tiengo *et al.* (2013)[8]	4/M	24	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Noncaseating granulomatous infiltrate of lymphocytes/histiocytes in the upper and mid-dermis	Clindamycin 1% + BPO 5% (16)	4
Caruncho *et al.* (2013)[9]	9/F	3	Pruritus	Papules + erythema + desquamation	Perioral + perinasal + periorbital	Perivascular/perifollicular noncaseating epithelioid cell granulomas	Metronidazole 0.75% + metronidazole 250 mg BD (4)	1
Misago *et al.* (2005)[10]	11/M	1	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Perifollicular noncaseating epithelioid cell granulomas	Tacrolimus 0.3% + minocycline 100 mg (3)	0.75
Choi *et al.* (2006)[11]	11/M	7	Asymptomatic	Monomorphic papules	Perioral	Perifollicular, interfollicular, and upper dermal noncaseating epithelioid granulomas	Erythromycin 500 mg (52)	12
Garijo *et al.* (2019)[12]	18/F	4	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Perifollicular and upper dermal noncaseating epithelioid granulomas	Isotretinoin 10 mg/20 mg alternate days (12)	6
Antony *et al.* (2002)[13]	8/F	10	Asymptomatic	Monomorphic papules	Perioral + cheeks	Circumscribed noncaseating epithelioid granulomas in the dermis	NBUVB + HCQS 100 mg (16)	No resolution
Ahmed (2007)[14]	2/F	10	Pruritus	Monomorphic papules	Perioral + left upper extremity	Perifollicular noncaseating epithelioid cell granulomas	Oral erythromycin and topical metronidazole	4
Lucas *et al.* (2009)[15]	13/M	24	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Perifollicular noncaseating epithelioid cell granulomas	Erythromycin 400 mg/day + pimecrolimus 1% (6)	2

Contd...

Table 1: Contd...

Study identifier	Age/sex	Duration (months)	Symptoms	Morphology	Distribution	Histopathology	Treatment duration (weeks)	Time to resolution (months)
Gutte *et al.* (2011)[16]	6/M	1	Pruritus	Monomorphic papules	Perioral + perinasal + periorbital + neck + trunk + upper limb	Perifollicular noncaseating epithelioid cell granulomas containing lymphocytes, histiocytes, and giant cells	Amoxicillin–clavulanic acid + chlorpheniramine (4)	1
Choi *et al.* (2020)[17]	10/F	4	Asymptomatic	Monomorphic papules	Perioral + perinasal + forehead	Perifollicular noncaseating granulomas	Tacrolimus 1% + oral roxithromycin (10)	No resolution
Choi *et al.* (2020)[17]	11/F	8	Asymptomatic	Monomorphic papules	Perioral + perinasal	Perifollicular noncaseating granulomas	Tacrolimus 1% + oral roxithromycin (8)	No resolution
Urbatsch *et al.* (2002)[18]	2/M	0.5	Asymptomatic	Monomorphic papules	Face + scalp + trunk + extremities	Perifollicular noncaseating granulomas	Erythromycin 125 mg TDS (4)	1
Urbatsch *et al.* (2002)[18]	12/F	2	Blepharitis	Monomorphic papules	Face + scalp + neck + ears	Perifollicular noncaseating granulomas	Minocycline 100 mg BD + metronidazole 0.75% BD (16)	6
Thomas *et al.* (2005)[19]	10/F	3	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital + perineum	Perifollicular noncaseating granulomas	Not mentioned	Not mentioned
Hussain *et al.* (2007)[20]	11/M	1.5	Asymptomatic	Monomorphic papules	Perioral + perinasal + periorbital	Not done	Tacrolimus 0.1% BD (3)	0.75

BD: twice daily; BPO: benzoyl peroxide; HCQS: hydroxychloroquine sulphate; NBUVB: narrow band ultra-violet B therapy; TDS: thrice daily

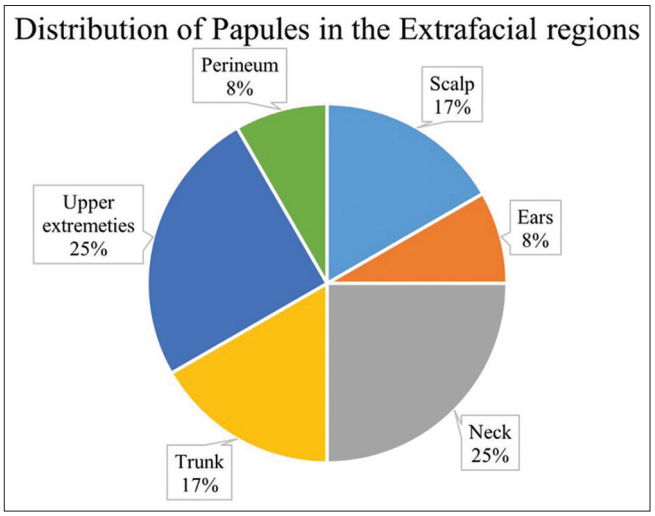

Figure 1: Distribution of papules at extra-facial sites

involved.[7,14,16,18,19] Most of the cases were asymptomatic at presentation. Occasionally, it was associated with blepharitis or pruritus.[2,9,14,16,18]

Histopathological examination is the only confirmatory investigation. In this study, it was observed that most of the cases showed perifollicular noncaseating granulomas with upper dermal and mid-dermal infiltration with lymphocytes and histiocytes.[1-5,7-19] The exact etiology of CGPD remains unknown. It can result from an exaggerated inflammatory response to allergens and irritants. Fakih *et al*. suggested that the initial allergen causes an inflammatory process, and then a focal disruption of the follicular wall creates a granulomatous reaction.[2] Some reports have implicated reactions to essential oils in bubble gum, formaldehyde, cosmetic preparations, black synthetic mesh, and antiseptic solutions.[2] A possible association between chronic CGPD and hormone growth therapy has been reported recently.[17]

In this study, the authors observed that the management of CGPD lacks consensus and guidelines. Multiple studies report the prior use of topical and systemic steroids for the management of this condition.[7,15] This can have dangerous consequences as children are particularly prone to develop both local and systemic side effects of steroids.[21] The authors noted improvement with topical treatment modalities, which included tacrolimus and pimecrolimus, and systemic agents, which included erythromycin/roxithromycin, metronidazole, tetracycline/minocycline, clarithromycin, and isotretinoin.[1-12,14-16,18] Topical agents are preferred over oral therapy for mild disease, characterized by small areas of involvement with no significant emotional distress.[2]

This study is limited by the small number of cases reported and the lack of uniformity in the treatment regimens prescribed.

Conclusion

The current study concludes that CGPD is a self-limited inflammatory dermatosis affecting children which resolves

Table 2: Differential diagnosis of childhood granulomatous periorificial dermatitis (CGPD)

Diagnosis	Age	Clinical features	Histopathology	Comments
CGPD	Childhood, prepubertal	Monomorphic papules	Perifollicular noncaseating granulomatous infiltration	Self-limiting
Rosacea	Adults (usually over 30 years of age)	Centro-facial erythema Papules Pustules Flushing Telangiectasias	Perivascular and perifollicular inflammatory infiltrates Demodex in 20–50% of cases Vasodilation involving dermal capillaries	Chronic condition
Papular sarcoidosis	Children and adults	Papules (1–10 mm in size)	Sarcoidal noncaseating epithelioid cell granulomas	May be associated with systemic sarcoidosis
Lupus miliaris disseminatus faciei	Adolescents and adults	Multiple reddish-brown 2 to 5 mm papules over the face	Perifollicular epithelioid caseating granulomas	Chronic course with scarring
Acne	Preadolescents, adolescents, and adults	Comedones Papules Pustules Nodules	Follicular keratin plugs Dermal mononuclear inflammatory infiltrate	Chronic or recurrent episodes
Periorificial dermatitis	Young women	Perioral monomorphic papules and pustules	Perifollicular and perivascular mononuclear inflammatory infiltrates	Exacerbated by steroid application

(Adapted from Fakih *et al*., 2020[2])

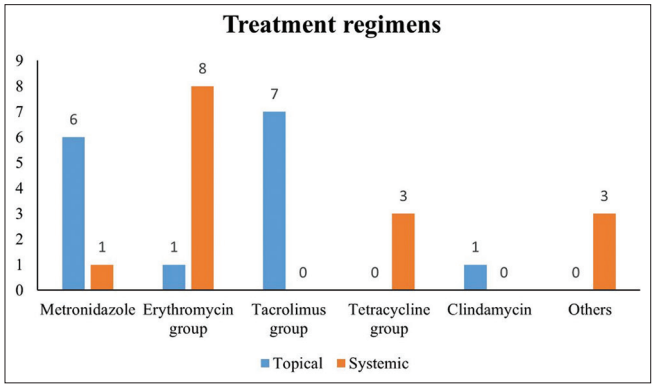

Figure 2: Treatment modalities used in CGPD

spontaneously without any significant sequelae. Parents need to be reassured regarding the benign nature of the condition as the skin lesions may persist unchanged for months. Consensus guidelines for the management of CGPD need to be developed as inadvertent topical steroid application only exacerbates this disorder and leads to dangerous sequelae, particularly in the pediatric age group.

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Conflicts of interest

There are no conflicts of interest.

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