Review

Perioral dermatitis: an update

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Perioral dermatitis is a distinct condition, first described as "light sensitive seborrhoeide" in 1957,[1] and recognized as a distinct entity in 1964.[2] It presents as a persistent erythematous eruption composed of tiny papules and papulopustules distributed primarily around the mouth, with a narrow zone of sparing around the vermilion border of the lips (Fig. 1). Without treatment, it tends to run a fluctuating course.

Epidemiology

Perioral dermatitis is a common dermatosis and is considered by most dermatologists to be increasing in incidence;[3] however, some authors have suggested that it has declined[4–6] since 1970–72.[4] Perioral dermatitis most often affects women between 16 and 45 years of age. Children may occasionally have perioral dermatitis;[7] the age ranges from 7 months to 13 years, the median being in the prepubertal period. Boys and girls, and black and white individuals, are equally affected.[8] In one study, a higher incidence was reported in boys.[9] The condition has been reported mainly in Western Europe, Scandinavia, North America, and Australia.

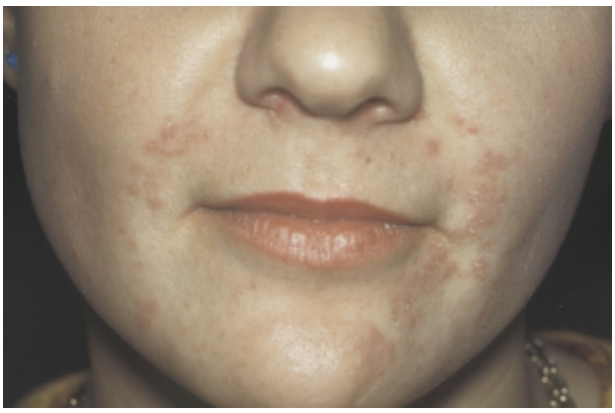

Figure 1 Papules with slight scale in a perioral distribution (courtesy of L. E. Gibson, MD, Mayo Clinic, Rochester, MN)

Etiology and pathogenesis

Despite its description as "light sensitive seborrhoeide,"[1] the light causation theory has not been substantiated either clinically or on phototesting.[2,4] A number of agents have been implicated in its pathogenesis, including infective agents, contact and hormonal factors, and glucocorticoids. Fluorinated steroids,[4,6,10] hydrocortisone butyrate,[11] contraceptive pills,[12] fluorinated and tartar control toothpastes,[13,14] moisturizing creams[15,16] and their occlusive effects which cause the proliferation of skin flora,[15] cosmetics,[15] and mercury sensitization from amalgam fillings[17] have been implicated. Perioral dermatitis has been caused by inhaled steroids in asthmatic children,[18,19] and also by systemic glucocorticoids.[20] Some patients have noted a premenstrual flare, or develop this eruption during pregnancy.[4,5]

Contact allergy to hydroxyisoflavans in cocus wood has been reported in a 15-year-old girl, who developed perioral dermatitis and swelling of the lips after playing a cocus wood flute for 2 years.[21] Perioral dermatitis and mucosal edema due to contact allergy to proflavine in mouthwashes has also been reported.[22] In a single case report, a 32-year-old woman had positive scrapings for *Candida* from her perioral lesions.[23] Mycologic examination of pustular lesions in a series of 73 patients,[6] as well as in another series of seven children with perioral dermatitis,[24] however, failed to demonstrate *Candida*.

In a study of 329 patients, allergens detected by patch testing included cosmetics, dental pastes, washing powders, chloric water, mohair, synthetics, and flowers. *Demodex* was detected in 80 patients.[25] A series of 400 cases compared with controls stressed that the presence of fusiform bacteria was a

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sine qua non in the diagnosis, and that a bacterial cause was consistent with a favorable response to tetracycline.[15] Other studies, however, did not confirm this high prevalence.[4]

Histopathology and laboratory examination

The lesions resemble those of mild eczema with minimal spongiosis, often in proximity to or affecting the pilosebaceous follicle. Most histologic reports have shown mild, nonspecific, subacute inflammation with a variable perifollicular or perivascular lymphohistiocytic infiltrate and occasional papillary dermal edema.[4,25] Infrequently, plasma cells are predominant.[25]

No granulomatous changes have been reported.[25] In other studies, granulomas, some sarcoid-like, have been described.[4,7,26–29] In five infantile cases, a sarcoid-like infiltration with little relation to vessels or follicles, extending into the deep dermis, was noted.[7]

Investigations reported in perioral dermatitis include patch testing,[4,30] bacteriology,[4,30] mycology for *Candida*,[23,31] and a search for *Demodex*.[4,30,32] Sporadic reports of routine hematology and biochemistry[27,33] and Kveim tests[7,26] exist.

Clinical features

The perioral area is affected, with a narrow zone of sparing around the vermilion of the lips. Erythematous, scaly papulopustules occur around the mouth, chin, upper lip, and nasolabial folds, and may involve the periorbital areas as well. The eyelids may be involved as part of a more widespread facial eruption or in isolation. The severity of the condition varies widely between individuals and has a chronic, fluctuating course. Pruritus is variable and mild, but an irritant or burning sensation in the affected areas is common.[1,2,5] This condition is often intolerant to sunlight. Soaps and cosmetics cause irritation, and even simple topical preparations are badly tolerated.

Childhood variants share many characteristics of the adult form. Children often have perioral, periocular, and perinasal lesions that are often iatrogenic and respond rapidly to treatment.[8] In one study, five children, aged 3–11 years, developed a distinct perioral, perinasal, and periorbital eruption, consisting of tiny, closely spaced, flesh-colored "micronodules." Histopathologic examination in all five cases revealed upper dermal and perifollicular granulomas, admixed with lymphocytes. The lesions resolved after months to years, leaving no scars. It was proposed by the authors that the condition was a form of perioral dermatitis with granulomatous histologic features that could be distinguished clinically and histologically from sarcoidosis and other facial eruptions of childhood.[29] Childhood granulomatous perioral dermatitis with involvement of the neck and upper trunk has also been reported.[34]

Table 1 Differential diagnosis

Rosacea
Contact dermatitis
Seborrheic dermatitis
Acne
Lip-licking cheilitis
Glucagonoma syndrome[36]
Xanthomas[37]
Acne agminata
Papular sarcoid
Syringomas (eruptive forms)

Granulomatous perioral dermatitis was diagnosed in a young woman with a persistent eruption around the mouth and chin. As she was unresponsive to conventional therapies, 20 weeks of oral isotretinoin treatment was eventually given and the lesions cleared and left pitted, atrophic scars.[35] Some authorities consider perioral dermatitis to be a circumscribed variant of rosacea.[35]

Diagnosis and differential diagnosis (Table 1)

The typical appearance of perioral dermatitis usually allows no confusion with any other facial dermatosis. Rosacea, contact dermatitis, acne, lip-licking cheilitis, seborrheic dermatitis, glucagonoma syndrome (florid, more extensive eruption around the mouth[36]), xanthomas[37], acne agminata, and papular sarcoid have differentiating clinical and histologic features.

A number of other perioral eruptions have been described which lack the special features of perioral dermatitis. A biotin-responsive, multiple carboxylase deficiency syndrome in infancy has been described.[38] *Demodex* granulomas, which are expected to respond to antimicrobials, have been reported.[39] Recently, perioral dermatitis-like lesions have been reported in a 71-year-old undergoing psoralen plus UVA treatment for mycosis fungoides. Its histology showed a specific infiltrate of the latter.[40]

Treatment (Table 2)

Without adequate treatment, perioral dermatitis can be quite persistent, especially when patients have been applying topical steroids. The cessation of topical glucocorticoids forms a major part of treatment, and rebound flare can be prevented by reducing their potency over several weeks.[4,41] Rebound flare usually occurs when corticosteroids are stopped and, in order to prevent this phenomenon, the substitution of potent steroids by less potent steroids is emphasized, before they are discontinued altogether. This regimen tends to reduce the likelihood of rebound, which often encourages the patient to go back to the potent steroid. The discontinuation of all other

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Table 2 Treatment options

Topical
Substitution of potent steroids by less potent steroids (before they are discontinued)
Erythromycin solution (1.5–2%)
Metronidazole gel (0.75%) or cream (1% or 2%)
Isotretinoin (granulomatous perioral dermatitis)
Sulfacetamide or erythromycin with 1% hydrocortisone
Tetracycline
Clindamycin
Systemic
Tetracycline
Doxycycline
Minocycline
Erythromycin (children, pregnant women, or those with intolerance to tetracyclines)
Cotrimoxazole

topical applications is also advised. Oral tetracyclines have been found to be the most effective. Tetracycline, 250 mg twice daily[5,6,41] (four times daily in severe cases[5]), or doxycycline 100 mg or minocycline 100 mg, once daily for 2–3 weeks,[42] may be given. Regimens may be less than[4,43] or longer than[5,44] 6 weeks. For children and pregnant women, or if tetracyclines cannot be tolerated, erythromycin, 250 mg two to three times daily for 4–6 weeks, is prescribed. It has been reported to be less effective than the tetracyclines.[41]

Topically, 1.5–2% erythromycin solution can be applied twice daily for several months; however, the systemic administration of erythromycin has greater efficacy.[41] Topical metronidazole as a gel (0.75%)[45] or cream 1%[46] has been found to be effective when patients are treated for 14 weeks[45] or 8 weeks,[46] respectively. The latter was a double-blind study in which oral tetracycline, 250 mg twice daily, and metronidazole cream (twice daily application) were compared. It was concluded that oral tetracycline provided greater clinical improvement than topical metronidazole; 2% metronidazole cream has also been used.[24] Topical metronidazole has been effective in children[45] and in adults, but less effective than the tetracyclines.[41] Isotretinoin has been used in granulomatous perioral dermatitis.[35]

Topically, a combination of sulfacetamide and hydrocortisone is effective,[43] as well as erythromycin and hydrocortisone.[41] Cotrimoxazole has also been found to be helpful.[4]

A number of miscellaneous treatments have been reported in the literature, but few have been generally embraced. Some of these include liquid nitrogen,[25] nightly washings with soap and water,[34] benzoyl peroxide or tretinoin,[41] control of seborrhea of the scalp,[1] awaiting spontaneous improvement,[47] radiotherapy,[3] and psychotherapy.[30]

Prevention, course, and prognosis

Although numerous factors have been discussed in the etiology of perioral dermatitis, there is no doubt that, in many patients, topical glucocorticoids may aggravate or precipitate the condition. Their use on the face,[13] even hydrocortisone, should be discouraged.[48]

The untreated disease usually persists over a number of years. There is constant low-grade activity; the course is punctuated by unpredictable episodic exacerbation,[1,2] but the condition can also resolve spontaneously. The prognosis is excellent when the appropriate treatment is given. It has been reported that the incidence of recurrence after treatment is low.[4,5,49]

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