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Perioral dermatitis

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Abstract Perioral dermatitis is a relatively common inflammatory facial skin disorder that predominantly affects women. It is rarely diagnosed in children. A typical perioral dermatitis presentation involves the eruption of papules and pustules that may recur over weeks to months, occasionally with fine scales. The differential diagnosis includes seborrheic dermatitis, systemic lupus erythematosus, acne vulgaris, lupus miliaris disseminatus faciei, polymorphous light eruption, steroid-induced rosacea, granulomatous perioral dermatitis, contact dermatitis (allergic and irritant), and even basal cell carcinoma. The histopathology is similar to that of rosacea, with a perivascular and perifollicular lymphohistiocytic infiltrate and sebaceous hyperplasia. The etiology of perioral dermatitis is unknown, but the uncritical use of topical corticosteroids often precedes skin lesions. Physical sunscreens with high sun protection factors may cause perioral dermatitis in children.

Definition

Perioral dermatitis (PD), which is also known as rosacea-like dermatitis, is an inflammatory and chronic papulopustular and vesicular dermatitis. In 1957, cyclic dermatitis that affects the skin of the perioral region, principally among young females, was described with the term *light-sensitive seborroeid.*[1,2] PD predominantly affects young and middle-aged women.[1] The clinical and histological features of PD lesions resemble those of rosacea. Patients require systemic or topical treatment (or both), the evaluation of underlying factors, and reassurance. Synonyms for perioral dermatitis include rosacea-like dermatitis, periorificial dermatitis, light-sensitive seborrheid, chronic papulopustular facial dermatitis, granulomatous perioral dermatitis, facial Afro-Caribbean childhood eruption, lupus-like perioral dermatitis, stewardess disease, and granulomatous periorificial dermatitis.[3]

Epidemiology

PD predominantly affects women, who account for an estimated 90% of cases. The number of men is assumed to be increasing as a result of changes in their cosmetic habits. PD may occur but is rarely diagnosed in children.[1,2,4] The vast majority of patients are women between the ages of 20 and 45 years.[1,5,6] The granulomatous form of PD is increasing among African-American children.[1,3]

Pathogenesis

There may be more than one cause of PD (Table 1).[1,3,6,7] The etiology of PD remains unknown, but the uncritical use of topical steroids for minor alterations of the face often precedes the manifestation of the disease.[1,5,7] The underlying cause cannot be detected in all patients.[1] After PD has developed, corticosteroid creams seem to help, but the disorder reappears when the treatment is discontinued. In fact, PD usually comes back even worse than it was before the use of steroid creams. The use of inhaled prescription steroid sprays applied into the nose and mouth can also

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Table 1 Etiology of perioral dermatitis

Drugs	• Topical steroids • Inhaled prescription steroid sprays (fluorinated and nonfluorinated)
Cosmetics	• Fluorinated toothpaste • Skin care ointments and creams • Mercury-containing dental fillings • Mint-flavored tooth-cleaning powder
Physical factors	• Ultraviolet light • Heat • Wind
Microbiologic factors	• Fusiform spirilla bacteria • Candida species • *Demodex folliculorum*
Miscellaneous factors	• Hormonal factors (oral contraceptives) • Gastrointestinal disturbances (malabsorption) • Emotional stress • Musical instruments • Latex gloves • Lipstick • Response to permethrin treatment

induce PD. Cosmetics and topical corticosteroids have been implicated in the pathogenesis of this condition.[8,9] Fluorinated toothpaste, the overuse of heavy facial creams and moisturizers (especially those with a petrolatum or paraffin base), and the vehicle isopropyl myristate are other common causes.

Physical factors such as ultraviolet light, heat, and wind worsen PD. Physical sunscreens with high sun protection factors may cause PD in children.[10] Many investigators have considered that infections may cause PD. Microbiologic factors such as fusiform spirilla bacteria, *Candida* species, *Demodex folliculorum,* and other fungi have been cultured from lesions, but their presence has no clear clinical relevance. The increased density of *D folliculorum* in patients with PD is a secondary phenomenon associated with topical steroid therapy.[11] Hormonal factors are suspected due to the premenstrual deterioration that has been observed. Oral contraceptive pills have been considered as well.[5,12] An impaired skin barrier and atopic diathesis are causative factors of PD.[13] PD has also been described in immunocompromised children, particularly in those with leukemia.[3]

Clinical

PD is limited to the skin. Skin lesions occur as grouped follicular reddish papules, papulovesicles, and papulopustules on an erythematous base with a possible confluent aspect (Figures 1 and 2). The papules and pustules have mainly perioral locations. The predominant locations of PD lesions are the perioral area, the nasolabial fold, and the lateral portions of the lower eyelids. With an extreme variant of the disease called *lupus-like PD,* granulomatous infiltrates have a yellowish aspect when viewed with diascopy. A frequently seen feature of PD is a border of normal skin that separates the lesional skin from the lips. With the perioral type of PD, discrete to moderate erythematous papules and pustules are found circularly, with a clear zone of 3 to 5 mm under the lower lip (Figures 2 and 3).

Complications

Although PD is limited to the skin and is not a life-threatening condition, emotional problems may occur as a result of the disfiguring character of facial lesions and the possibly prolonged course of the disease. Most PD is resolved without sequelae after relapse. An initial rebound effect frequently occurs during the weaning of the steroid, but this phenomenon is rare when no underlying cause can be identified. A chronic course is not uncommon. The development of a lupoid dermal infiltrate is considered to be a feature of the maximal variant of the disease. The diagnosis of lupus-like PD is made on the basis of yellowish discoloration after diascopy. Scarring may be a problem with the lupoid form of PD.

Histopathology

The histopathologic appearance of PD biopsy specimens is similar to that of rosacea.[1,5,7] According to most authors, changes in the follicular epidermis are quite marked,[1,6,14,15] which suggests that the disorder may be provoked by some external irritants.[14] Biopsies should be taken from the chin or the nasolabial groove and should include at least one papule.

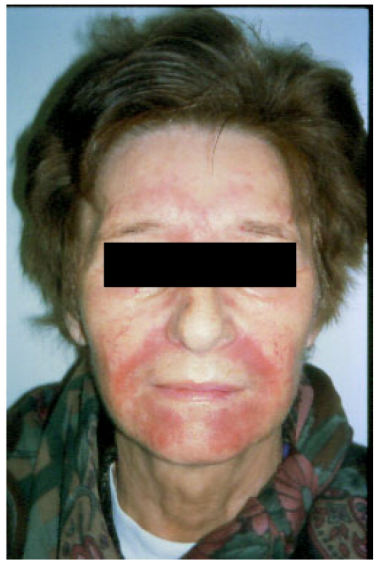

Fig. 1 Perioral dermatitis provoked by topical corticosteroid ointment.

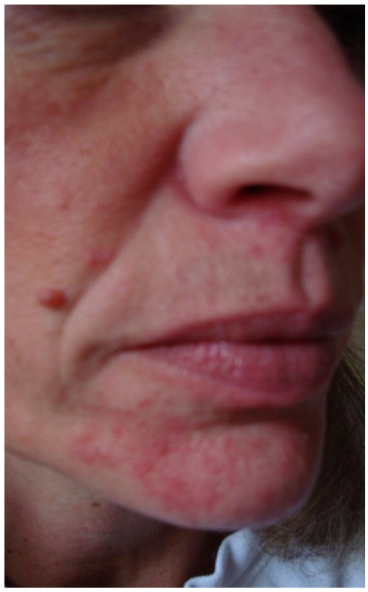

Fig. 2 A patient with perioral dermatitis provoked by corticosteroids.

Usually, the clinical picture and the history of the disease determine the diagnosis.[1,6,7] The histopathologic examination of early papular lesions demonstrates eczematous changes that consist of mild acanthosis, epidermal edema, and parakeratosis. There are mainly ectatic venules and lymphocytes, mild edema, and sparse lymphatic perivascular infiltration. Usually, small peripheral areas of the hair follicles are edematous and then invaded by inflammatory cells. Sometimes, follicular abscesses can be seen. Abscess cavities related to PD contain many polymorphonuclear leukocytes, and elastic fibers confirm the presence of elastic degeneration. Demodex mites can sometimes be demonstrated as an incidental finding. The examination of late papular lesions reveals diffuse hypertrophy of the connective tissue that is accompanied by hyperplasia of the sebaceous follicles. In the dermis, there is occasionally discrete epithelioid cell granuloma of the noncaseating type with perifollicular predominance and scanty Langerhans giant cells. Caseating granuloma is a characteristic feature of granulomatous PD.[1,6]

Diagnostics

Clinical diagnosis

Usually the clinical picture and the history of the disease determine the diagnosis.[1] A thorough patient history that reveals the prolonged use of local corticosteroids or contact with other potential causal factors (Table 1) is enough. The clinical picture is also characteristic, with a predominance of erythematous papules and papulopustules that are usually localized in the perioral region. In more than 98% of patients, a rebound phenomenon occurs.[1,6] There is gradual disappearance of all symptoms, and relapses are rare unless corticosteroids are repeatedly administered.[1,6]

Laboratory diagnosis

No laboratory abnormalities can be expected.[1,6,7,12] Prick testing and specific immunoglobulin E testing against a mixture of aeroallergens have been used to test for skin barrier dysfunction. In a German study, patients with PD experienced significantly increased transepidermal water loss as compared with patients with rosacea and a control group, which indicated a skin barrier function disorder. This type of testing is not routinely used.[16]

Differential diagnosis

PD is usually a straightforward clinical diagnosis.[1,6] As part of the differential diagnosis, a few facial skin diseases should be excluded (Table 2). Facial demodicosis (ie, infestation with *D folliculorum*) clinically resembles PD and should be excluded, especially when anti-inflammatory therapies fail. Patients who are prone to acne or rosacea may experience worsening while undergoing topical immunomodulating therapy (eg, with tacrolimus ointment). Haber syndrome or familial rosacea-like dermatosis with intraepidermal epitheliomas, keratotic plaques, and scars is a rare genodermatosis that begins during childhood. Granulomatous periorificial dermatitis manifests most commonly in prepubertal children as yellow-brown papules that are limited to the perioral, perinasal, and periocular regions.[17] The condition is self-limiting, and it is not associated with systemic involvement.

Periocular dermatitis is a variant of PD. The elimination of topical corticosteroids and the gradual reduction of the use of skin-care products regularly leads to clearing of the condition. Acne agminata (ie, lupus miliaris disseminatus faciei, acnitis, and papular tuberculid) is a rare form of necrotizing granulomatous inflammation of the dermis on the eyelids; in one case, it disappeared in the vicinity of a steroid

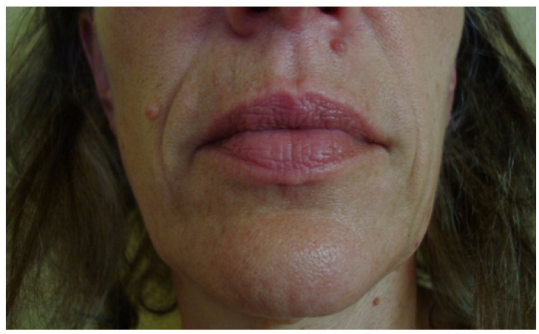

Fig. 3 Perioral dermatitis after "null (zero) therapy."

Table 2 Differential diagnosis of face rashes that resemble perioral dermatitis

Rosacea	• Usually a centrofacial disease • No comedones • Rhinophyma is usually present
Seborrheic dermatitis	• Predominantly retroauricular • Nasolabial region, eyebrows, and scalp are affected • Main symptom is scaling
Acne vulgaris Acneiform eruption	• Comedones, papules, pustules, nodules, and cysts • Affects younger population
Facial demodicosis	• Mycology isolation of *Demodex folliculorum*
Lupus miliaris disseminatus faciei, with or without extrafacial involvement	• Scars are present • Discrete red-brown, dome-shaped papules • Spontaneous regression
Polymorphous light eruption	• Itchy red papules, vesicles, or plaques • Occurs after sun exposure
Contact dermatitis (allergic and irritant)	• Border of the rash emerges into normal skin
Haber syndrome (familial rosacea-like dermatosis)	• Intraepidermal epitheliomas, keratotic plaques, and scars • Begins during childhood
Granulomatous periorificial dermatitis	• Yellow-brown papules limited to the perioral, perinasal, and periocular regions • Occurs in prepubertal children
Lip-licking cheilitis	• Scale with a well-demarcated border • Common in children
Ectropion	• Dermatitis and ectropion with a preexisting loss of elasticity
Contact urticaria	• Persisting dermatitis
Facial Afro-Caribbean eruption syndrome	
Oral and perioral pigmented lesions	• Endogenous pigmented lesions in the mouth
Primary cutaneous follicle center lymphoma	• Reddish nodules, plaques, and tumors of the head, neck, back, scalp, and so on

injection site.[18] In another case, periocular exanthema associated with chronic rejection after kidney transplantation diminished rapidly without any treatment after the renal allograft was extracted.[19] Children with dry skin developed PD after using sunscreens with micropigment bases.[10] Oral and perioral endogenous pigmented lesions are important for a positive diagnosis of endogenous pigmented lesions and to facilitate early detection, particularly of the malignant ones.[20] PD occurs in patients with myasthenia gravis and in patients with pemphigus after systemic corticosteroid treatment.[9,21] Persistent dermatitis of the lips can occur immediately after dental treatment with a mint-flavored tooth-cleaning powder; it will resolve after the toothpaste type is changed.[22] Dermatologists should be aware of the variants and the peculiar clinical presentation of primary cutaneous follicle center lymphoma so that patients are treated promptly and properly.[23]

Treatment

The first step in the therapeutic management of PD should be the discontinuation of all suspected topical treatments, although this usually leads to relapse of the skin lesion. The physician should insist on the abandonment of all cosmetics, soaps, detergents, moisturizers, abrasives, astringents, day or night creams, and skin conditioners.[1] The patient should be told to wash with mild water only; some authors suggest the use of fingers. This "null (zero) therapy" is hard for many patients to follow, so local neutral treatments involving neutral local creams and compresses (eg, chamomile tea, physiologic solution) may be used.[1,7] The duration of treatment is shorter for men, because they give up on the idea of ever being cured sooner than women do. Sometimes, the physician must supply a great deal of psychological support during office visits. If they become dependent on corticosteroids, some patients may need medical help, including psychological support, to break their habits.[24]

Patients have to be told that exacerbations are to be expected, that it may take many weeks for the skin to clear, and that the disease slowly regresses when exogenous factors are stopped. Some investigators treat patients with rebound phenomena with hydrocortisone, which reduces the violence of the rebound reaction while allowing the atrophic collagen to recover.[25] Others taper the dose of topical corticosteroids by reducing the frequency of administration.[25]

The second part of treatment is the suppression of bacterial infection in the hair follicles with systemic antibiotics. The population of *Propionibacterium acnes* within the follicles is markedly elevated among patients who apply local corticosteroids. *P acnes* directly inflames follicles by producing agents that are chemotactic for polymorphonuclear leukocytes. *Fusobacterium spp* are often found in PD that has been induced by fluorinated corticosteroids. In addition to these two bacteria, gram-negative *Staphylococci* and sometimes even *Streptococci* have been found. Preferences for pharmacological treatment include lipophilic erythromycin (400 mg three times daily);

tetracycline (250 mg two times daily); oxytetracycline or minocycline (50-100 mg two times daily); and doxycycline (50-100 mg two times daily for 3-4 months, rarely longer).[1]

To prevent poststeroid flare, oral tetracyclines are contraindicated for children who are less than 11 years old. Acceptable treatment for children includes oral and topical erythromycin as well as topical metronidazole.[26] If there is no response to the full dose of tetracyclines, the patient may need to be treated with isotretinoin. Quite low doses are effective; usual dose is 0.2 mg/kg orally initially; this can be reduced to 0.1 mg/kg or 0.05 mg/kg with notable clinical improvement. Precautions must be taken for women with child-bearing potential. In less severe cases only, a neutral local therapy in combination with anti-inflammatory agents can be used; this will usually be localized erythromycin and metronidazole, neomycin, or clindamycin and oxytetracycline administered in a nongreasy base (eg, gel, lotion, cream). Such preparations have both moisturizing and antibiotic effects.

The response of PD to metronidazole is the result of the drug's anti-inflammatory and immunosuppressive effects rather than any direct antimicrobial action.[1,3] Topical antiacne medications (eg, adapalene and azelaic acid applied two to three times a day) have been used in open studies. Ointments should be avoided. Local immunomodulatory creams (eg, tacrolimus, pimecrolimus) can be used in patients with severe PD, but caution is advised given the occasional reports of granulomatous eruptions after the use of these preparations.[1,3,27,28] Photodynamic therapy with topical 5-aminolevulenic acid is a promising alternative to antibiotics for the treatment of PD.[1,3,29] Successful treatment with minimal thermal damage makes the erbium:YAG laser an ideal tool for the treatment of the delicate periocular region, where even minimal scarring can be problematic.[30] An evidence-based review of PD therapies strongly supports the efficacy of zero therapy, topical pimecrolimus, oral tetracycline, and topical erythromycin.[1]

Topical antipruritics that contain no corticosteroids (eg, liquid pramoxine hydrochloride) offer excellent symptomatic relief. The response to local treatment with sulfur, resorcin, and ichthyol was very unsatisfactory. Topical metronidazole is the recommended first-line treatment for PD.[1,7]

Prevention

The best way to prevent PD is for persons who are predisposed to the condition to avoidance topical corticosteroid preparations.

Conclusions

The possible causes of PD include topical corticosteroids, physical factors, microbiologic factors, and miscellaneous factors. An initial worsening of the symptoms may occur with treatment, especially if topical steroids are withdrawn. Topical treatment of PD includes antibiotics such as metronidazole and erythromycin, and antiacne drugs such as adapalene and azelaic acid have been used in noncontrolled studies. Systemic treatment includes antiacne medications such as doxycycline, minocycline, and isotretinoin.

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