Extrafacial and Generalized Granulomatous Periorificial Dermatitis

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Background: Granulomatous periorificial dermatitis is a well-recognized entity presenting most commonly in prepubertal children as yellow-brown papules limited to the perioral, perinasal, and periorbital regions. The condition is self-limiting and is not associated with systemic involvement.

Observations: We reviewed the medical charts of 5 healthy children presenting with extrafacial granulomatous papules in addition to the typical periorificial papules. These extrafacial lesions were clinically and histologically identical to the facial lesions, were self-limiting, and were not associated with systemic involvement. Resolution seemed to be hastened with the use of systemic antibiotic therapy in 4 of the 5 patients.

Conclusions: Extrafacial lesions can occur in granulomatous periorificial dermatitis and do not appear to adversely affect the duration, response to therapy, or risk of extracutaneous manifestations. Overly aggressive evaluation and inappropriate systemic therapy should be avoided.

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In 1970, Gianotti et al described 5 children with monomorphic perioral papules that showed a granulomatous pattern when lesional biopsy sections were examined. Since then, several additional patients have been reported and the condition has been variably called Gianotti-type perioral dermatitis, sarcoidlike granulomatous dermatitis, facial Afro-Caribbean childhood eruption (FACE), granulomatous perioral dermatitis, and, most recently, granulomatous periorificial dermatitis (GPD). All affected patients have been healthy prepubertal children, and the eruption was confined to the skin surrounding the mouth, nose, and eyes in 56 of 59 patients described. The 3 patients with extrafacial involvement who were described in the literature had lesions on the neck, upper trunk, extensor wrists, and vaginal area.

We describe 5 prepubertal children with periorificial granulomatous dermatitis, but with extensive extrafacial involvement as well. The clinical characteristics of our 5 patients and the 3 cases from the literature are summarized in Table 1. Two of the cases are outlined herein.

REPORT OF CASES

CASE 1

A 23-month-old white boy with no history of skin disease developed lesions on his right leg at the injection site 2 weeks after varicella vaccination. During the subsequent month, lesions became widely disseminated, but were asymptomatic and had never been associated with fever, weight loss, cough, shortness of breath, or ocular complaints. He was otherwise healthy and there was no family history of similar skin lesions. The skin lesions were initially treated with 0.1% triamcinolone acetonide ointment for 3 weeks without improvement.

The findings from the physical examination 4 months after the onset of the rash showed an active boy with thousands of discrete 1- to 3-mm red to yellow-brown papules on his scalp, face, trunk, and extremities (Figure 3). The highest concentration of lesions was around his mouth, nose, and eyes (Figure 4). The rest of the physical examination findings were normal.

The examination of 3 serial lesional biopsy specimens showed noncaseating...
granulomas in the dermis, many alongside the hair follicles (Figure 5). The results of special stains for acid-fast bacilli and fungus were negative, and cultures yielded no organisms. A polarization test for foreign material was negative. A chest x-ray film and findings of an ophthalmologic examination were normal and a purified protein derivative test was nonreactive.

Because of the resemblance of the patient’s condition to GPD, oral erythromycin estolate, 125 mg 3 times daily, was administered. This treatment resulted in dramatic flattening of the lesions after 1 month of therapy and resolution of all lesions 6 months after the initiation of therapy and left mild atrophodermic scarring. The erythromycin regimen was tapered and discontinued after 9 months of treatment. Within 1 month after discontinuation of the erythromycin, the lesions began to recur, once again initially at the site of the varicella vaccination. Treatment with oral erythromycin estolate, 125 mg 3 times daily, was restarted and again resulted in flattening of the lesions within 1 month. The resolved lesions left shallow pitted scars that resembled follicular atrophodermia (Figure 6).

**CASE 2**

A 12-year-old white girl with no significant medical history had a 1-year history of diffuse hair thinning. Two months later, she also developed hundreds of nonpru-
ritic lesions on her face and neck. She denied fever, weight loss, cough, shortness of breath, or arthralgias. She had had recurrent episodes of blepharitis during the previous year, but had never experienced any visual disturbances. There was no family history of skin lesions, eye abnormalities, or hair loss.

The results of a physical examination 14 months after the onset of hair loss showed diffuse thinning of her scalp hair that was most pronounced on the vertex of the scalp, with widening of the central part. Scarring was not apparent. She had hundreds of discrete flesh-colored papules with varying amounts of surrounding erythema and scale on her scalp, face, ears, and neck. The facial lesions were predominantly located periorally. The results of the examination also disclosed erythema and scale along the margins of her eyelids and shotty posterior cervical lymphadenopathy.

Four lesional skin biopsy specimens were obtained from the scalp and neck; all showed granulomas in the dermis, mostly around the hair follicles (Figure 7). Focal epidermal spongiosis overlay some of the hair follicles. The results of special stains and cultures were negative for mycobacteria and fungus.

Laboratory evaluation, including a complete blood cell count, chemistry panel, calcium level, erythrocyte sedimentation rate, VDRL test, thyroid function tests, and serum levels of antinuclear antibody and testosterone, showed no abnormalities. A chest x-ray film, results of pulmonary function tests, and an electrocardiogram were also normal.

The patient was initially treated with desonide lotion for 2 weeks, with worsening of the skin lesions. A presumptive diagnosis of sarcoidosis was made and oral hydroxychloroquine sulfate, 200 mg daily, and oral cyclosporine, 150 mg daily, were administered. Medications were discontinued after 2 months of therapy when no improvement occurred. Because of the resemblance to granulomatous perioral dermatitis, oral minocycline hydrochloride, 100 mg twice daily, and topical 0.75% metronidazole, administered twice daily, were initiated, leading to resolution of all skin lesions within 6 weeks without scarring. The minocycline was tapered during a
Granulomatous periorificial dermatitis is thought to be a less common variant of perioral dermatitis. Perioral dermatitis is an eruption characterized by grouped red papules, pustules, or papulovesicles and diffuse erythema and scaling around the mouth, nose, and eyes that can be seen in children. The lack of pustules and the presence of discrete yellow-brown papules, less prominent erythema and scaling, and a perifollicular granulomatous infiltrate on examination of a biopsy specimen can differentiate GPD from perioral dermatitis. Most reported cases have occurred in prepubertal children. The disease affects both sexes almost equally. According to the literature, GPD is seen more commonly in dark-skinned patients, but this observation may reflect population bias and, in fact, all but 1 of our cases occurred in white patients.

**Figure 7.** Small, well-formed dermal perifollicular granulomas on histologic examination of a papule from the scalp of patient 2 (hematoxylin-eosin, original magnification ×200).

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Clinical Characteristics</th>
<th>Extracutaneous Manifestations</th>
<th>Histologic Features</th>
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<tr>
<td>Sarcoïdosis</td>
<td>Red to yellow-brown papules on face; violaceous plaques on trunk; ichthyosis</td>
<td>Constitutional symptoms, uveitis, arthritis, lymphadenopathy, pulmonary involvement</td>
<td>Noncaseating epithelioid granulomas</td>
</tr>
<tr>
<td>Infection (fungal, mycobacterial)</td>
<td>Papules, nodules, pustules on face or body</td>
<td>Constitutional symptoms, multiorgan involvement</td>
<td>Caseating granulomas, giant cells, epithelioid macrophages, neutrophils</td>
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<tr>
<td>Granulomatous rosacea</td>
<td>Diffuse red or brown papules; erythema, pustules, telangiectasias</td>
<td>Blepharitis, conjunctivitis</td>
<td>Perifollicular granulomas, diffuse lymphohistiocytic infiltrate</td>
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<tr>
<td>Familial juvenile systemic granulomatosis (Blau syndrome)</td>
<td>Translucent skin-colored papules on trunk and extremities</td>
<td>Uveitis, synovitis, arthritis</td>
<td>Noncaseating epithelioid granulomas</td>
</tr>
<tr>
<td>Granulomatous periorificial dermatitis</td>
<td>Small red to brown papules clustered around mouth, nose, eyes, genital region</td>
<td>Blepharitis</td>
<td>Perifollicular noncaseating granulomas, diffuse granulomatous infiltrate</td>
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The primary lesion is a discrete 1- to 3-mm dome-shaped papule that is red or yellow-brown. In some instances erythema surrounds the papule and overlying scale is present. As in classic periorificial dermatitis, the face is always involved, with lesions concentrated around the mouth, nose, and eyes. Some cases of GPD have described prominent involvement of the helices of the ears as an important diagnostic feature.

Scarring is variable. The initial cases described by Gianotti et al and several subsequent authors in 1,11,14 reported the occurrence of small pitted scars after resolution of the papules. This same type of scarring was seen in one of our patients (patient 1) and is likely a result of the inflammatory process.

Although the histologic appearance alone is not diagnostic, cases in which skin biopsy was performed have shown a dermal granulomatous infiltrate, usually concentrated around the upper half of normal, nondisrupted hair follicles. In some biopsy specimens, the infiltrate has been more diffuse, with multiple epithelioid macrophages, lymphocytes, and giant cells; in others, well-formed noncaseating granulomas are surrounded by lymphocytes. Focal epidermal spongiosis is occasionally described. The results of special stains and cultures for acid-fast bacilli and fungi are always negative.

The etiology of this condition is unknown. In some cases the eruption was linked to an external allergenic or irritant contactant. The essential oils in bubble gum, antiseptic solution, formaldehyde, and black synthetic mesh were among the incriminated agents. Topical fluorinated corticosteroids have been incriminated in triggering and exacerbating GPD. In patient 1, the eruption was temporally and positionally related to varicella vaccination. Granulomatous periorificial dermatitis may represent a nonspecific granulomatous response to a variety of topical or systemic agents.

Granulomatous periorificial dermatitis is a benign and self-limited condition without any systemic manifestations. Occasionally, blepharitis or conjunctivitis is an associated finding, and blepharitis occurred in patients 2 and 3. Results of routine laboratory studies and ophthalmologic examination are usually normal; a chest radiograph is likewise usually normal. Spontaneous resolution usually occurs by a few months to 3 years after onset. The administration of oral macrolides or tetra-
cyclines, alone or in combination with topical erythromycin, metronidazole, or sulfur-based lotions, hastens resolution in most patients.

The differential diagnosis of small papules with granulomatous histologic features in children includes sarcoidosis, fungal or mycobacterial infection, familial juvenile systemic granulomatosis (Blau syndrome), and granulomatous rosacea (Table 2). In typical cases of GPD, these entities can be differentiated clinically. In cases with extracutaneous involvement, other disorders can be differentiated by a thorough history and physical examination, a review of symptoms, examination of a chest radiograph, an ophthalmologic examination, and the use of special stains and cultures of tissue specimens for fungal or mycobacterial organisms.

The diagnosis of granulomatous rosacea deserves special consideration. Both GPD and granulomatous rosacea present with red or yellow-brown, dome-shaped facial papules and a perifollicular lymphohistiocytic or granulomatous infiltrate. Other similarities include the occurrence of blepharitis or conjunctivitis, extracutaneous lesions, and a response to the tetracycline class of antibiotics and topical metronidazole. Lesions have been described as involving the ears, neck, axillae, trunk, and groin in granulomatous rosacea.17 The major distinguishing features of granulomatous rosacea are the lack of a concentration of periorificial lesions and the association of erythema, telangiectasias, pustules, and edema, which are features of more typical rosacea.17 Rosacea and granulomatous rosacea have been reported in children, but are uncommon.17 A case of GPD was reported in a girl who later developed a more acineiform and telangiectatic form of rosacea (Judith Schifferner, MD, oral communication, February 2001).19 Arguably, GPD may actually be a variant of granulomatous rosacea and, in a subset of patients, the first manifestation of a rosacea diathesis.

The 8 cases summarized in Table 1 extend the clinical spectrum of GPD; all of these children had the classic facial periorificial papules, but also developed extracutaneous lesions that were clinically and histologically indistinguishable from the facial lesions. Extensive involvement did not appear to change the duration of the eruption, the response to treatment, or the risk of extracutaneous manifestations. The diagnosis of GPD is important to consider in the child who presents with grouped papules around the mouth, nose, and eyes as is typical of GPD, but also in those with similar lesions in nonfacial areas. Overly aggressive evaluation and inappropriate systemic therapy should be avoided. Just as perioral was expanded to periorificial because lesions could occur around the nose and eyes, it may be necessary to further expand this entity to include extracutaneous lesions as well.

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