Noninfectious facial papular granulomas can be the presentation of several conditions, including granulomatous periorificial dermatitis, granulomatous rosacea, lupus miliaris disseminatus faciei, and papular sarcoidosis. Although these entities are treated distinctly from one another, they share several clinical and histological characteristics. We present 2 cases of facial papular granuloma: one patient presented with granulomatous rosacea, and the other had a presentation consistent with sarcoidosis but also demonstrated features of granulomatous periorificial dermatitis and had a protracted course of treatment. Such cases exemplify heterogeneity in the evaluation and management of this cutaneous lesion and highlight the necessity of appreciating its various potential causes.

Case Reports

Patient 1—A 10-year-old Ethiopian girl with a history of atopic dermatitis presented with a facial rash of 4 months' duration. Her pediatrician initially treated the rash as pityriasis alba and prescribed hydrocortisone cream. Two months into treatment, the patient developed an otherwise asymptomatic, unilateral, papular dermatosis on the right cheek. She subsequently was switched to treatment with benzoyl peroxide and topical clindamycin, which she had been using for 2 months with no improvement at the time of the current presentation. The lesions then spread bilaterally and periorally.

At the current presentation, physical examination demonstrated fine, diffuse, follicular-based, flesh-colored papules over both cheeks, the right side of the nose, and the perioral region (Figure 1). A biopsy of a papular lesion revealed well-formed, noncaseating granulomas in the superficial and mid dermis with an associated lymphocytic infiltrate and highlight the necessity of appreciating its various potential causes.
Calcium and angiotensin-converting enzyme levels were normal.

The patient denied any fever, chills, hemoptysis, cough, dyspnea, lymphadenopathy, scleral or conjunctival pain or erythema, visual disturbances, or arthralgias. Hydroxychloroquine 200 mg twice daily was started with minimal improvement after 5 months. Methotrexate 20 mg once weekly was then added. Topical fluocinonide 0.05% also was started at this time, as the patient had required several prednisone tapers over the past 3 months for symptomatic relief. The lesions improved minimally after 5 more months of treatment, at which time she had developed inflammatory papules, pustules, and open comedones in the same areas as well as the glabella.

Repeat biopsy of a papular lesion demonstrated noncaseating granulomas and an associated chronic lymphocytic infiltrate in a follicular and perifollicular distribution (Figure 3). Biopsy of a pustule demonstrated acute *Demodex* folliculitis. Fluocinonide was stopped, and anti-mite therapy with ivermectin, permethrin cream 5%, and selenium sulfide lotion 2.5% was started, with good response from the pustular lesions.

The patient continued taking methotrexate 20 mg once weekly during this time, with improvement in the papular lesions. She discontinued methotrexate after 12 months with complete resolution. At follow-up 12 months after stopping the methotrexate (roughly 2 years after initial presentation), she showed sustained resolution, with small pitted scars on both cheeks and the nasal tip.

**Patient 2**—A 33-year-old Ethiopian woman presented with a facial rash of 15 years’ duration. The lesions had been accumulating slowly and were asymptomatic. Physical examination revealed multiple follicular-based, flesh-colored, and erythematous papules on the cheeks, chin, perioral area, and forehead (Figure 4). There were no pustules or telangiectasias. Treatment with tretinoin cream 0.05% for 6 months offered minimal relief.

Biopsy of a papule from the left mandible showed superficial vascular telangiectasias, noncaseating granulomas comprising epithelioid histiocytes and lymphocytes in the superficial dermis, and a perifollicular lymphocytic infiltrate.
infiltrate (Figure 5). No organisms were identified on Fite or Gomori methenamine silver staining.

Comment

The first step in differentiating cutaneous granulomatous lesions should be to distinguish infectious from noninfectious causes.1 Noninfectious cutaneous granulomas can appear nearly anywhere; however, certain processes have a predilection for the face, including GPD, GR, LMDF, and papular sarcoidosis.5-7 These conditions generally present with papular granulomas with features as described above.

Granulomatous Periorificial Dermatitis—In 1970, Gianotti and colleagues 8 briefly described the first possible cases of GPD in 5 children. The eruption comprised numerous yellow, dome-shaped papules in a mostly perioral distribution. Tuberculin and the Kveim tests were nonreactive; histopathology was described as sarcoid-type and not necessarily follicular or perifollicular.9 In 1974, Marten et al9 described 22 Afro-Caribbean children with flesh-colored, papular eruptions on the face that did not show histologic granulomatous changes but were morphologically similar to the reports by Gianotti et al.9 By 1989, Frieden and colleagues10 described this facial eruption as “granulomatous perioral dermatitis in children”. Additionally, the investigators observed granulomatous infiltrates in a perifollicular distribution and suggested follicular disruption as a possible cause. It was clear from the case discussions that these eruptions were not uncommonly diagnosed as papular sarcoidosis.10 The following year, Williams et al11 reported 5 cases of similar papular eruptions in 5 Afro-Caribbean children, coining the term facial Afro-Caribbean eruption.11 Knautz and Lesher12 referred to this entity as “childhood GPD” in 1996 to avoid limiting the diagnosis to Afro-Caribbean patients and to a perioral distribution; this is the most popular current terminology.12 Since then, reports of extrafacial involvement and disease in adults have been published.13,14

Granulomatous periorificial dermatitis often is seen in the perinasal, periorcular, and perioral regions of the face.2 It is associated with topical steroid exposure.5 Histologically, noncaseating granulomas around the upper half of undisrupted hair follicles with a lymphocytic infiltrate are typical.13 Treatment should begin with cessation of any topical steroids; first-line agents are oral tetracycline or macrolide antibiotics.5 These agents can be used alone or in combination with topical erythromycin, metronidazole, or sulfur-based lotions.13 Rarely, GPD presents extrafacially.13 Even so, it usually resolves within 2 weeks to 6 months, especially with therapy; scarring is unusual.5,13,15

Granulomatous Rosacea—A report in the early 20th century described patients with tuberculoid granulomas resembling papular rosacea; the initial belief was that this finding represented a rosacealike tuberculid eruption.5 However, this belief was questioned by Snapp,16 among others, who demonstrated near universal lack of reactivity to tuberculin among 20 of these patients in 1949; more recent evidence has substantiated these findings.17 Still, Snapp18 postulated that these rosacealike granulomatous lesions were distinct from classic rosacea because they lacked vascular symptoms and pustules and were recalcitrant to rosacea treatment modalities.

In 1970, Mullanax and colleagues19 introduced the term *granulomatous rosacea*, reiterating that this entity was
Granulomatous rosacea typically is seen in middle-aged women. Hallmarks of rosacea, such as facial erythema, flushing, telangiectasias, pustules, and rhinophyma, are not always present in GR. Lesions usually are distributed around the central face, although extension to the cheeks, total facial involvement, and extrafacial lesions are possible. Histologically, perifollicular and follicular-based noncaseating granulomas with dilatation of the dermal papillary vasculature are seen. As a whole, rosacea is comparatively uncommon in dark-skinned patients; when it does occur, GR is a frequent presentation.

First-line treatment for GR is tetracycline antibiotics. Unresponsive cases have been treated—largely anecdotally—with topical modalities (eg, metronidazole, steroids, immunomodulators), systemic agents (eg, dapson, erythromycin, isotretinoin), and other therapies. Granulomatous rosacea tends to have a chronic course.

First-potential documented case of sarcoidosis was by Hutchinson in 1869 in a patient seen in London. The author labeled purple plaques on the index patient’s legs and hands as “livid papillary psoriasis.” In 1889, Besnier described a patient with violaceous swellings on the nose, ears, and fingers, which he called “lupus pernio”; his contemporary, Tenneson, published a case of lupus pernio and described its histologic profile as comprising epithelioid cells and giant cells. It was not until 1899 that the term sarcoid was used to describe these cutaneous lesions by Boeck, who thought they were reminiscent of sarcoma. In 1915, Kuznitsky and Bitto described a patient with cutaneous lesions histologically consistent with Boeck’s sarcoid but additionally with hilar lymphadenopathy and pulmonary infiltrates. Around 1916 or 1917, Schaumann described patients with cutaneous lesions and additionally with involvement of pulmonary, osseous, hepatosplenic, and tonsillar tissue. These reports are among the first to recognize the multisystemic nature of sarcoidosis. The first possible case of childhood sarcoidosis might have been reported by Osler in the United States in 1898.

In the past century or so, an ongoing effort by researchers has focused on identifying etiologic triggers for sarcoidosis. Microbial agents have been considered in this role, with Mycobacterium and Propionibacterium organisms the most intensively studied; the possibility that foreign material contributes to the formation of granulomas also has been raised. Current models of the pathogenesis of sarcoidosis involve an interplay between the immune system in genetically predisposed patients and an infection that leads to a hyperimmune type 1 T–helper cell response that clears the infection but not antigens generated by the microbes and the acute host response, including proteins such as serum amyloid A and vimentin. These antigens aggregate and serve as a nidus for granuloma formation and maintenance long after infection has resolved.

Cutaneous lesions of sarcoidosis include macules, papules, plaques, and lupus pernio, as well as lesions arising within scars or tattoos, with many less common presentations. Papular sarcoidosis is very common on the face but also can involve the extremities. Strictly, at least 2 organ systems must be involved to diagnose sarcoidosis, but this is debatable. Among 41 patients with cutaneous sarcoidosis, 29 (58.5%) had systemic disease; cutaneous lesions were the presenting sign in 87.5% (21/24) of patients. Histologic analysis, regardless of the lesion, usually shows noncaseating so-called “naked” granulomas, which have minimal lymphocytic infiltrate associated with the epithelioid histiocytes. Perifollicular granulomas are possible but unusual.

Treatment depends on the extent of cutaneous and systemic involvement. Pharmacotherapeutic modalities include topical steroids, immunomodulators, and retinoids; systemic immunomodulators and immunosuppressants; and biologic agents. Isolated cutaneous sarcoidosis, particularly the popular variant, usually is associated with acute disease lasting less than 2 years, with resolution of skin lesions. That said, a recent report suggested that cutaneous sarcoidosis can progress to multisystemic disease as long as 7 years after the initial diagnosis.

Clinical and Histologic Overlap—Despite this categorization of noninfectious facial granulomatous conditions, each has some clinical and histologic overlap with the others, which must be considered when encountering a granulomatous facial dermatosis. Both GPD and GR tend to present with lesions near the eyes, mouth, and nose, although GR can extend to lateral aspects of the face,
below the mandible, and the forehead and has different demographic features.\textsuperscript{13} Granulomas in both GPD and GR generally are noncaseating and form in a follicular or perifollicular distribution within the dermis.\textsuperscript{7,13} Lupus miliaris disseminatus faciei and GR share a similar facial distribution in some cases.\textsuperscript{17,20} Even papular cutaneous sarcoidosis has masqueraded as GR clinically and histologically.\textsuperscript{4}

\textbf{Diagnosis and Treatment Difficulty}—Our cases illustrate the range of difficulty in evaluating and managing patients with facial papular granulomas. On one hand, our adult patient's clinical and histologic findings were highly consistent with GR; on the other hand, our younger patient had clinicopathologic features of both sarcoidosis and GPD at varying times. Both conditions are more common in dark-skinned patients.\textsuperscript{11,42}

Juvenile sarcoidosis is comparatively rare, with a reported annual incidence of 0.22 to 0.27 for every 100,000 children younger than 15 years; however, juvenile sarcoidosis commonly presents around 8 to 15 years of age.\textsuperscript{43}

It is unusual for saroid granulomas to be isolated to the skin, much less to the face.\textsuperscript{4,7,13,44} Patient 1 initially presented in this manner and lacked convincing laboratory or radiographic evidence of systemic sarcoidosis. Bilateral hilar calcifications in sarcoidosis are more typical among adults after 5 to 20 years; there were no signs or symptoms of active infection that could account for the pulmonary and cutaneous lesions.\textsuperscript{45}

The presence of perifollicular granulomas with associated lymphocytic infiltrates on repeat biopsy, coupled with the use of topical steroids, made it difficult to rule out a contribution by GPD to her clinical course. That her lesions resolved with pitted scarring while she was taking methotrexate and after topical steroids had been stopped could be the result of successful management or spontaneous resolution of her dermatosis; both papular sarcoidosis and GPD tend to have a self-limited course.\textsuperscript{7,13}

\textbf{Conclusion}

We present 2 cases of papular facial granulomas in patients with similar skin types who had different clinical courses. Evaluation of such lesions remains challenging given the similarity between specific entities that present in this manner. Certainly, it is reasonable to consider a spectrum upon which all of these conditions fall, in light of the findings of these cases and those reported previously.

\textbf{REFERENCES}


