Pediatric Rosacea

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PRACTICE **POINTS**

- Although rosacea is largely a diagnosis of adults, it also can begin in childhood and adolescence.
- Ocular rosacea and papulopustular disease are common clinical findings in younger patients.
- Usage of topical metronidazole and age-appropriate oral antibiotics are the mainstay of management.

Because rosacea is uncommon in the pediatric population, care must be taken to exclude other papulopustular disorders. Children can present with vascular, papulopustular, and/or ocular findings. Importantly, ocular symptoms can appear before the cutaneous symptoms of rosacea, leading to misdiagnosis. Rosacea is a clinical diagnosis, but histopathologic examination typically reveals dilated vessels, perivascular lymphohistiocytic infiltrates in the upper dermis, elastosis, and disorganization of the upper dermal connective tissue. Treatment involves avoiding known triggers and utilizing topical and/or systemic therapies. Although treatment can control flares, pediatric rosacea often persists into adulthood.

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Rosacea is a chronic skin disease characterized by flushing, erythema, telangiectasia, papules, and pustules in the central face region.[1] It most often affects middle-aged women (age range, 30–50 years).[2] Rosacea is rare in the pediatric population, especially before puberty.[3] There are 3 subtypes of pediatric rosacea: vascular, papulopustular, and ocular. Phymatous/rhinophymatous rosacea is only seen in the adult population.[3] Recommendations for the management of pediatric rosacea heavily rely on data from retrospective chart reviews and case series.

Etiology of Pediatric Rosacea

Rosacea is thought to be a consequence of vasomotor instability in both adults and children. A family history of rosacea is sometimes reported in patients with pediatric rosacea.[4] Patients often are sensitive to heat, sunlight, topical corticosteroids, spicy foods, hot liquids, and certain soaps and cleansers.[1,3,4] In a review of the literature by Vemuri et al,[5] the various reported triggers of rosacea include harsh climates that damage the blood vessels and dermal connective tissue, defects in the endothelium and dermal matrix, perivascular inflammation, orally ingested chemicals, changes in the flora of the hair follicles, excessive antimicrobial peptides, and the presence of free radicals. Overall, it is unclear which of these factors are triggers of pediatric rosacea.

The molecular basis of rosacea has been elucidated. It is well known that rosacea patients have higher levels of cathelicidins in the facial skin. Furthermore, they appear to have different processed forms of cathelicidin peptides compared to adults without rosacea, possibly due to changes in posttranslational processing.[6] One such peptide, cathelicidin LL-37, also has been implicated in atopic dermatitis[7] and psoriasis.[8] Its role in rosacea appears to be multifaceted. Cathelicidin LL-37 helps to attract neutrophils, monocytes, and T lymphocytes, and also has antimicrobial properties; therefore, it plays a role in both the innate and adaptive immune systems.[9] Cathelicidin LL-37 also has been implicated in inducing angiogenesis[10] and suppressing dermal fibroblasts.[11]

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Muto et al[12] found that there is an increased number of mast cells in the dermis of patients with rosacea. Mast cells contribute to vasodilation, angiogenesis, and the recruitment of other inflammatory cells.[12] Importantly, human mast cells are a source of cathelicidins including cathelicidin LL-37; these proteins play a vital role in the antimicrobial capabilities of mast cells.[13]

Clinical Presentation and Comorbidities

Vascular rosacea presents with characteristic flushing and erythema, which lasts more than a few minutes as compared to physiologic erythema,[1] and sometimes telangiectasia is seen.[3] The cheeks, chin, and nasolabial folds are most commonly involved.[2] In papulopustular rosacea, papules and pustules are seen overlying the erythema.[1,3] Open and closed comedones also have been documented in case reports but are not commonly seen.[2] Pediatric rosacea often begins with flushing of the face and then progresses to the development of papules and pustules.[4]

Ocular rosacea can occur with or without cutaneous findings. In a retrospective study of 20 pediatric patients (aged 1–15 years), 11 (55%) patients had both ocular and cutaneous rosacea, 3 (15%) only had ocular symptoms, and 6 (30%) only had cutaneous symptoms. The most common form of rosacea in this study was papulopustular rosacea.[14] Ocular symptoms often are bilateral[15] and can include blepharitis, conjunctival injection, recurrent chalazion, conjunctivitis,[2] and less commonly corneal ulceration and scarring.[16] Patients also may report photophobia or a foreign body sensation.[17] Importantly, ocular symptoms often precede the cutaneous symptoms and can delay the diagnosis of rosacea,[14,16,18] as these symptoms often are misdiagnosed as viral or bacterial infections.[15] Fortunately, ocular disease responds well to treatment if diagnosed early.

Weston and Morelli[19] conducted a retrospective study of 106 children (46 males; 60 females) 13 years and younger with steroid rosacea; 29 children were younger than 3 years. A family history of rosacea was present in 20% of participants, and prior use of class 7 steroids was reported in 54%, whereas only 3% had used class 1 topical steroids. Ninety-eight participants had perinasal involvement, 94 had perioral involvement, and 44 had periorbital involvement of the lower eyelids.[19]

Rosacea fulminans (also known as pyoderma faciale) is a rare acute-onset eruption typically found in young women in their 20s and 30s.[20] Rosacea fulminans is characterized by papules, pustules, nodules, cysts, draining sinuses, communicating sinus tracts, and less commonly comedones.[20,21] The skin can appear erythematous, cyanotic, or dull red.[21] Most of the lesions are found on the face, particularly on the forehead, cheeks, nose, and chin,[21] but lesions on the chest and back have been documented in adult patients.[20] In an examination of prior case series, most patients were otherwise healthy. There are case reports documenting rosacea fulminans in teenagers,[20] but the youngest patient recorded was an otherwise healthy 3-year-old girl who developed a sudden onset of erythematous papules, pustules, cysts, and purulent discharging sinuses on the cheeks that spread to the chin, perioral, and paranasal areas.[21]

Differential Diagnosis

Rosacea is rare in children, so other papulopustular disorders must be ruled out, including acne vulgaris, periorificial/perioral dermatitis, sarcoidosis, systemic lupus erythematosus, steroid-induced rosacea, ataxia telangiectasia, and demodicosis.

Acne vulgaris commonly presents in older adolescents and teenagers with open and closed comedones, inflammatory papules, and pustules.[2] Intense facial flushing and telangiectasia usually is not seen.

In perioral dermatitis, skin lesions often are clustered around the mouth, nose, and eyes. Typically there are no telangiectases or ocular complications.[3] Facial flushing and telangiectases are uncommon, except in steroid-induced perioral dermatitis.[2]

The cutaneous findings of sarcoidosis include red-brown papules on the face and lips, and patients also may have ocular involvement such as uveitis and iritis.[3] However, there are typically other systemic findings such as pulmonary symptoms, weight loss, fatigue, lethargy, fever, and erythema nodosum.[2,3] Chest radiograph findings (eg, bilateral hilar lymphadenopathy), ophthalmologic examination, and laboratory data (eg, elevated alkaline phosphate and/or elevated angiotensin-converting enzyme) can help confirm or rule out the diagnosis of sarcoidosis.[2,3]

Unlike systemic lupus erythematosus, patients with rosacea will have involvement of sun-protected areas of the skin. Patients with systemic lupus erythematosus typically report arthralgia and severe photosensitivity and will have elevated antinuclear antibody titers. Skin biopsies and immunofluorescence can help confirm the diagnosis.[3] Importantly, some patients with rosacea will have a positive lupus band test.[22,23]

Steroid-induced rosacea typically occurs 2 weeks after discontinuing therapy with topical fluorinated glucocorticosteroids.[24] Children present with monomorphic papules, pustules, and telangiectases[4] on the eyelids and lateral face as opposed to the central face regions.[24]

Ataxia telangiectasia can present with telangiectases, skin atrophy, café au lait spots, and premature graying.[25] A 15-year-old adolescent girl with ataxia telangiectasia presented with granulomatous acne rosacea that improved after 4 weeks of treatment

with isotretinoin 0.5 mg/kg daily. The lesions cleared almost completely after 5 months.[25]

Demodicosis is a disorder of the pilosebaceous units caused by the human *Demodex* mite.[26] It typically involves the periorificial regions in adults and the elderly population. Patients can present with fine, white-yellow, scaly changes of the sebaceous hair follicles, with minimal erythema and inflammation. Papules and pustules also can be present.[26]

Diagnosis and Histopathology

Because rosacea is rare in children, it is important to thoroughly evaluate other possible diagnoses. The diagnosis of pediatric rosacea is clinical and biopsies are rarely performed. Laboratory tests such as cultures generally are not useful.

Marks and Harcourt-Webster[27] reviewed the biopsies of 108 adult patients with rosacea. The biopsies of patients with predominantly erythema and telangiectasia showed evidence of vascular dilatation with a perivascular infiltrate composed predominantly of lymphocytes and 39 specimens that were compared to controls showed more solar elastosis. Biopsies of papular rosacea contained inflammatory infiltrates in the upper and mid dermis composed primarily of lymphocytes and histiocytes. In some patients, neutrophils, plasma cells, and giant cells also were observed. Hair follicle abnormalities were present in 20% of the biopsies, with 19% showing evidence of the *Demodex* mite. Vascular dilatation also was common. Overall, common findings included lymphohistiocytic infiltrates around the blood vessels of the upper dermis, dilated vessels, edema, elastosis, and disorganization of connective tissue in the upper dermis.

Helm et al[28] reviewed histopathologic patterns from 53 patients with granulomatous rosacea. Findings included a mixed lymphohistiocytic infiltrate (predominantly lymphocytic in 40% of patients and predominantly histiocytic with occasional giant cells in 34% of patients), epithelioid granulomas (11% of patients), and epithelioid granulomas with caseation necrosis (11% of patients).

The histopathology of rosacea fulminans is characterized by dense perivascular and periadnexal infiltrates composed of granulocytes, eosinophils, and epithelioid granulomas, as well as panniculitis.[20]

Treatment and Clinical Outcomes

Certain lifestyle recommendations are integral components of disease management, including avoidance of triggers such as extreme temperatures, hot drinks, spicy food, and topical agents that could be irritating (especially topical corticosteroids).[29] Patients should be advised to use daily sunscreen containing physical blockers such as titanium dioxide or zinc oxide. Teenagers should avoid the use of cosmetics and makeup, especially products containing sodium lauryl sulfate, menthol, and camphor. Daily use of emollients can help some patients.[29]

There are both topical and systemic therapies available for pediatric rosacea; however, most of the data are based on the use of these treatments in the adult population. Patients with mild to moderate disease often can be managed using topical agents. Metronidazole (0.75% cream, 1% gel, or 0.75% lotion) has been studied extensively in adult patients, and when used once daily for 12 weeks, it has been able to control moderate to severe disease.[30,31] In one study conducted in adult patients, topical metronidazole was able to maintain remission in adults who had previously been treated with a combination of oral tetracycline and metronidazole gel.[31] Sodium sulfacetamide 10%–sulfur 5% (cleanser or lotion) has been successful in adult patients and often is used in combination with other therapies such as topical metronidazole.[32-34] Azelaic acid cream 20%,[35] benzoyl peroxide (wash or gel),[29] topical clindamycin,[36] topical erythromycin,[29,37] tacrolimus ointment 0.1%,[38] and tretinoin cream also have been studied in adults.[3,39] Several of these topical agents can cause irritation on application (eg, metronidazole, sulfur-based agents, azelaic acid, benzoyl peroxide, erythromycin, tretinoin).[3]

The use of systemic treatments in pediatric patients is heavily based on case reports and case series.[2,14,16,40] Therapies have included tetracycline (500 mg twice daily tapered to 250 mg daily),[29] minocycline (50–100 mg twice daily), doxycycline (50–100 mg twice daily or 4 times daily), erythromycin (30–50 mg/kg daily), clarithromycin (15 mg/kg twice daily for 4 weeks and then daily for 4 weeks), and azithromycin (5–10 mg/kg daily).[3] Tetracycline antibiotics should not be used in children 8 years or younger.

In a case series by Drolet and Paller,[2] an 11-year-old girl was treated with tetracycline 500 mg (later tapered to 250 mg daily) and metronidazole gel 0.75%, both used twice daily. Previously, she had not responded to topical steroids, tretinoin cream 0.05%, benzoyl peroxide 5%, or systemic prednisone. After 6 weeks of treatment, the pustules and chalazion had resolved and she had only minimal erythema of the skin and conjunctiva. Sixteen months after the start of treatment, a regimen of tetracycline 250 mg daily and metronidazole gel resulted in disease clearance on the face.[2]

A 9-year-old girl with concurrent systemic lupus erythematosus was treated with tetracycline 250 mg and topical erythromycin 2%, both used twice daily.[2] After 4 weeks her face was clear. Four months later she developed new telangiectases and topical erythromycin

was replaced with topical metronidazole. Eventually the dose of tetracycline was reduced to 250 mg daily.[2]

An 11-year-old boy with likely granulomatous rosacea was treated with erythromycin 250 mg 4 times daily, alclometasone dipropionate cream 0.05% twice daily, and topical clindamycin twice daily.[2] Marked improvement was noticed after 3 weeks of treatment. Metronidazole gel 0.75% was added and 3 months later the patient's face was clear, without evidence of scarring. The dose of erythromycin was later reduced to 500 mg daily, and eventually the patient experienced clearance with the use of metronidazole gel daily.[2]

In another case series, 4 female patients (age range, 4–12 years) were treated with systemic erythromycin 20 mg/kg daily (ocular involvement only) or doxycycline 2.2 mg/kg daily used in two 12-year-old patients with ocular and cutaneous involvement for at least 12 months. All 4 patients showed considerable improvement within 1 month and remained free of disease throughout a mean follow-up period of 25.5 months.[40]

As evidenced by these case reports, there is a wide array of treatments that have been used for pediatric rosacea. Although there are no formal evidence-based guidelines, there are certain considerations that must be taken into account when choosing treatment plans. Doxycycline and minocycline are known to cause less gastrointestinal upset than tetracycline with similar efficacy.[41] Importantly, the tetracyclines are contraindicated in children younger than 9 years, as they can cause teeth staining and possibly affect skeletal growth.[3,4] When used in older children (age range, 9–12 years), patients must be advised not to take their medication with calcium or antacids.[3] Clarithromycin and azithromycin tend to have fewer gastrointestinal side effects than erythromycin. Erythromycin and other macrolides can be used in children of all ages and in patients who are allergic to tetracyclines.[3]

Children with mild ocular symptoms often can control their disease with bacitracin and topical ocular antibiotics such as erythromycin.[2,15] For patients who require systemic antibiotics, various tetracyclines and macrolides have been used with success.[2,14-16,40]

Adults with rosacea fulminans can require treatment with isotretinoin, oral antibiotics, and topical or even systemic corticosteroids.[42] The 3-year-old girl with rosacea fulminans initially was treated with oral erythromycin (250 mg 4 times daily), oral prednisolone (0.5 mg/kg daily tapered over 2 weeks), fluocinolone acetonide cream 0.025%, and warm compresses with only moderate improvement.[21] She was then started on oral isotretinoin (0.75 mg/kg daily) and within 4 weeks marked improvement was noted. After 8 weeks, the lesions had disappeared completely with only a few pitted scars remaining. Isotretinoin was continued for 24 weeks. One year after completion of treatment, she was still disease free.[21]

Weston and Morelli[19] recommended the following treatment regimen for children with steroid rosacea: abrupt cessation of topical steroid use (as opposed to gradual withdrawal) and initiation of oral erythromycin stearate (30 mg/kg daily) in 2 daily doses for 4 weeks. Children who were unable to tolerate erythromycin (n=6) were told to use topical clindamycin phosphate twice daily for 4 weeks. Within 3 weeks 22% of patients had resolution, while 86% had resolution within 4 weeks. All of the patients cleared within 8 weeks. Importantly, there was no significant difference in duration of time until clearance between children who used the oral antibiotic or topical antibiotic.[19]

Conclusion

We know that the skin of rosacea patients contains higher levels of cathelicidins, which have been implicated in amplifying and contributing to the inflammatory response in several ways. Mast cells, which are a source of cathelicidins, also are increased in the skin of these patients. Children can present with vascular rosacea (characterized by flushing, erythema, and/or telangiectasia), papulopustular rosacea, or ocular rosacea. Common ocular symptoms include blepharitis, conjunctivitis, and recurrent chalazion. It is important to refer pediatric rosacea patients with ocular symptoms to an ophthalmologist to prevent ocular sequelae.

Rosacea is a clinical diagnosis but biopsy can be performed to rule out other diagnoses. Treatment consists of lifestyle modifications such as avoiding known triggers and the use of topical and/or oral agents. Common topical therapies include metronidazole and erythromycin. Systemic antibiotics include tetracycline, doxycycline, minocycline, azithromycin, and erythromycin. Some children are able to taper systemic agents and maintain disease control with topical therapy, while others may need to continue a low-dose antibiotic. Although flares can be controlled within weeks to months, rosacea is a chronic disorder and childhood rosacea tends to persist into adulthood.

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