Rosacea Fulminans

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Practice Points

- Rosacea's primary signs are flushing, persistent erythema, papules, pustules, and telangiectasia.
- There are 4 subtypes of rosacea: erythematotelangiectatic, papulopustular, phymatous, and ocular.
- Prompt and appropriate therapy, mainly with oral isotretinoin and a corticosteroid, is necessary for good results and scar avoidance.
- Rosacea is a disease that can be persistent, deforming, and stigmatizing without proper treatment, and may interfere with the self-esteem and quality of life of patients.

We review rosacea fulminans, a rare condition that may cause facial scarring and disfigurement. All physicians and health care professionals must be aware of this form of rosacea to treat or refer the patient. Early treatment of rosacea fulminans is essential to avoid scarring.

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Rosacea is a chronic skin disorder that affects the convex and central areas of the face (ie, nose, chin, zygomatic region, forehead) and is characterized by periods of remission and exacerbation. The primary signs of rosacea are flushing (transient erythema), persistent erythema (most common), papules, pustules, and telangiectasia. The presence of 1 or more of these signs in the central region of the face typically is indicative of rosacea. Secondary signs, which may appear in association with primary signs or occur independently, include burning, plaques, dry appearance of the face, edema, ocular manifestations, phymatous alterations, and extrafacial lesions.[1] Because extrafacial lesions most frequently occur on the neck, upper trunk, back, ears, and scalp, it can be difficult to make an accurate diagnosis in the absence of other clinical manifestations of rosacea.

In 2004, the National Rosacea Society's expert committee classified rosacea into 4 subtypes and 1 variant according to clinical presentation.[1] The subtypes defined were erythematotelangiectatic, papulopustular, phymatous, and ocular. Evolution from 1 subtype to another may or may not occur, and patients can demonstrate features of more than 1 subtype simultaneously.[1,2]

Granulomatous rosacea was considered a variant; however, rosacea fulminans, also known as pyoderma faciale, was not included as a subtype or variant by the National Rosacea Society in 2002.[2]

The erythematotelangiectatic subtype is characterized by flushing and persistent central facial erythema. Telangiectases are common, but their presence is not essential for diagnosis. In the papulopustular subtype, persistent central facial erythema and transitory papules and/or pustules in the central region of the face are present; a burning sensation also may be noted. This subtype can be distinguished from acne vulgaris by the absence of comedones. The phymatous subtype includes skin thickening, irregular nodules on the surface of the skin, and hypertrophy. Rhinophyma, or thickening of the skin of the nose, is the most common presentation; however, it also can occur in other locations such as the chin, malar region, forehead, and ears.[1,3-5] A diagnosis of ocular rosacea should be considered when a patient presents with 1 or more of the following signs and symptoms: interpalpebral conjunctival hyperemia, foreign body sensation, burning, dry eyes, itching,

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sensitivity to light, blurred vision, conjunctival telangiectasia of the palpebral edge, and palpebral and periocular erythema. Blepharitis, conjunctivitis, palpebral border irregularity, chalazion, and corneal complications also may occur.[1,6]

History

Rosacea fulminans was first described by O'Leary and Kierland[7] in 1940. The authors reviewed 1600 cases of acne in females older than 15 years and identified 13 atypical cases that they referred to as pyoderma faciale. They characterized the condition as a sudden and fulminant pyoderma with involvement of the face in young women around 20 years of age and linked the inflammatory process to the infection of the sebaceous glands and follicular structures of the skin.[7]

The term *pyoderma faciale* initially was given because the condition appeared to involve most of the face with countless fluctuant inflamed papules and nodules that frequently fused to form larger lesions.[7] In 1992, Plewig et al[8] reported 20 additional cases of pyoderma faciale and determined that the condition represented an aggressive variant of rosacea, not acne; therefore, they recommended the term *rosacea fulminans*. The authors also proposed a combination of oral isotretinoin and corticosteroids for the treatment of rosacea fulminans,[8] which is still recommended.

Epidemiology

Rosacea fulminans is a rare disease, with approximately 60 published articles since 1978 and only 14 from the past 5 years according to a PubMed search of articles indexed for MEDLINE using the terms *rosacea fulminans* and *pyoderma faciale*. It once was thought that rosacea exclusively affected individuals of Celtic descent and therefore has been nicknamed "the curse of the Celts"; however, its impact on other ethnicities has since been acknowledged.[3] Although rosacea is no longer considered exclusive to the Celts, fair skin individuals with a tendency to blush and color are at a higher risk for the disease.[1] Rosacea fulminans affects women almost exclusively,[7-9] generally between 20 and 40 years of age.[10] In 2001, Firooz et al[11] reported a case of a 3-year-old girl with rosacea fulminans, though occurrence in this age group is rare. There have been a few cases described in men,[6,12,13] but they tend to present in the most serious stages, probably because they may take more time to seek treatment.[1]

Physiopathology

Although the etiology of rosacea fulminans remains unknown, it is multifactorial and is considered to be partly related to vascular hyperactivity.[14,15] The National Rosacea Society has encouraged studies on the etiology and pathophysiology of rosacea, as well as potential markers of the disease, its genetic expression profile, and the role of peroxisome proliferator-activated receptor 2 and its activators.[1]

Several immunologic, hormonal, and vascular factors have been implicated as triggers.[14,15] Alcohol and ingestion of hot and spicy foods generate flushing, which in some patients can worsen or trigger rosacea.[1]

The occurrence of rosacea fulminans during pregnancy[16,17] and in women taking oral contraceptives[16] partially may be due to hormonal factors. Cisse et al[18] reported a case of rosacea fulminans in pregnancy generated after hormonal stimulation with recombinant follicle-stimulating hormone and a luteinizing hormone-releasing hormone inhibitor.

Emotional stress,[14,19] seborrhea,[12,14] and drugs also can be triggering factors. There are 2 reported cases of rosacea fulminans associated with pegylated interferon alfa-2b and ribavirin therapy.[20,21] Jansen et al[14] linked the appearance of rosacea fulminans to a high intake of vitamins B_6 and B_{12} 2 weeks prior to the facial rash eruption. Associations with erythema nodosum[10] and inflammatory bowel disease (Crohn disease or ulcerative colitis) also have been described.[12,19,22]

Clinical Presentation

Rosacea fulminans is characterized by an acute onset of inflamed papules; yellow pustules; nodules with fluctuation; intercommunicable fistulas; erythema; and facial edema on the nose, malar region, chin, and temporal and frontal regions.[1,2,7] Seborrhea prior to onset is typical. Rosacea fulminans is neither pyodermic nor infectious, and it is not a variant of acne conglobata.[8] Facial flushing frequently precedes rosacea fulminans,[9,12,16] and the sometimes impressive plaques of the centrofacial area can occur from coalescence of various papules and pustules.[16]

There are no signs prior to the onset of the lesions (eg, fever, burning) and constitutional symptoms are rare.[11,16] Patients typically present in good general health. Pain is not characteristic of the disease.[11] However, patients sometimes present with low-grade fevers and/or myalgia. There are few reports of extrafacial lesions.[23,24] Ocular manifestations such as keratitis and conjunctivitis may be associated with rosacea fulminans.[6]

Recurrence is rare and generally evolves with hypertrophic to keloidal or atrophic to varioliform scars.[11,15] Severe scarring may occur in untreated cases and can be avoided with early diagnosis and treatment.[25]

Histopathology

In cases of rosacea fulminans, histopathology generally is nonspecific and rarely is performed because of the classic clinical presentation. Mild parakeratosis, edema of the superficial papillary dermis, telangiectases, collagen destruction, and deep papillary and reticular skin fibrosis typically are observed. A deep and superficial inflammatory infiltrate of perifollicular distribution surrounding sebaceous glands usually is present, consisting of lymphocytes, polymorphonuclear cells, plasmocytes, eosinophils, histiocytes, foreign body–type multinucleated giant cells, and epithelioid granulomas.[11,14,15,19] In the earliest stages of rosacea fulminans, an intense neutrophilic infiltrate can be observed.[17,26] Direct immunofluorescence was negative for IgA, IgG, IgM, C3, and fibrinogen in one case.[19]

Laboratory Findings

There is no specific laboratory alteration for rosacea fulminans, but mild anemia, mild leukocytosis, increased hemosedimentation rate, and increased C-reactive protein can be observed.[10,15,17] Cultures of purulent secretions typically are negative for pathogenic bacteria.[12,14,26]

Differential Diagnoses

The differential diagnoses of rosacea fulminans include acne fulminans, acne conglobata, gram-negative acne bacteria, fungal and mycobacterial infections, bromoderma, iododerma, and even Sweet syndrome with only facial lesions.[8,15,27,28] Although ocular impairment associated with a skin rash is rare in cases of rosacea fulminans, it can be a clue in diagnosing this condition because it does not occur in acne fulminans.[6]

Cosmetic Implications

Rosacea, as with many other causes of severe facial lesions, can have a substantial impact on a patient's quality of life, and its effects are in part mediated by psychologic aspects related to self-perception and self-presentation.[29] Rosacea fulminans typically affects young and middle-aged adult women who experience easy facial flushing, as well as papules, pustules, and nodules on the face. Because of the location of the lesions, it is important to teach patients proper camouflaging techniques using cosmetics during the consultation. Nevertheless, due to the severity of rosacea fulminans, it is unlikely that cosmetics alone will disguise the lesions.

Treatment

Treatment of rosacea fulminans begins with a fast course of oral corticosteroids to reduce inflammation, followed by oral isotretinoin (0.5–1 mg/kg daily).[13,14,30,31] The duration of retinoid therapy can vary but usually is 4 to 6 months.[10] Strauss[31] recommended reaching a target dose of 150 mg/kg; others do not mention this goal. In some cases, high-potency topical corticosteroids are administered at the beginning of the manifestation.[14] Rosacea fulminans is probably the only indication for steroid use in the management of rosacea.[11] Patients have responded well to isotretinoin in combination with topical and systemic corticosteroids, and the response is superior and much more rapid than in patients treated with oral antibiotics.[32] Fender et al[9] described a 40-year-old woman who presented with localized pyoderma faciale that worsened during treatment with oral and topical antibiotics and corticosteroids. Subsequent treatment with isotretinoin for 5 months resulted in dramatic and sustained improvement.[9] Bettoli et al[21] did not use systemic corticosteroids in the management of a case of rosacea fulminans that occurred following treatment of hepatitis C virus given that this medication usually is not recommended in cases of viral infection. The author obtained a good clinical response with a low dosage of isotretinoin (0.2 mg/kg daily).[21]

Oral antibiotic therapy does not present good results in the management of rosacea fulminans.[13] Minocycline combined with corticosteroids for 4 weeks also has been studied but showed no clinical improvement.[19] Treatment with dapsone also can be useful and is justified by the presence of a dense neutrophilic infiltrate at the initial stage of the disease. Ormond and Rogers[15] obtained therapeutic success with the combination of dapsone and minocycline. After an initial treatment course of corticosteroids with isotretinoin, Bormann et al[26] and Patterson et al[13] obtained good clinical evolution with dapsone as monotherapy.

For cases of rosacea fulminans that are associated with pregnancy, isotretinoin, tetracycline, and dapsone are contraindicated; systemic steroids and topical and/or oral antibiotics are recommended.[33] Physicians should assess the pros and cons of corticosteroid treatment, especially in pregnant women, as there is a possibility of side effects for both the mother and the fetus (eg, intrauterine growth retardation, maternal diabetes mellitus, hypertension). Oral erythromycin is safe during pregnancy; however, there are fewer anti-inflammatory effects with erythromycin versus tetracyclines.[34]

Conclusion

Rosacea fulminans can be frightening for patients, as its onset often is sudden and intense. Early and proper treatment, particularly with oral isotretinoin

and an oral corticosteroid, is essential to obtain good short-term and long-term results and avoid scarring that can be persistent, deforming, and stigmatizing, thereby deteriorating the patient's self-esteem.

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