A woman with rosy cheeks and erythematous facial lesions

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Test your diagnostic skills in our regular dermatology quiz. What is the cause of this patient's inflammatory facial lesions and background erythema?

Case presentation

A 57-year-old woman presents with a history of several months' duration of erythematous papules and pustules on her face with associated skin sensitivity and a stinging sensation. She reports frequent facial flushing, particularly with exercise or after ingestion of spicy foods, tea, coffee and alcohol. She does not have any medical history of note and does not take any regular medications.

On examination, background erythema and erythematous papules and pustules are observed to be affecting the central portion of the patient's face, including her forehead, cheeks, chin and infranasal region (Figure).

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Differential diagnoses

Conditions to consider among the differential diagnoses include the following.

Acne vulgaris

Acne vulgaris, an inflammatory disorder of the pilosebaceous unit, is one of the most common skin conditions, affecting about 85% of adolescents and 9.4% of the global population.[1,2] The pathogenesis involves a complex interplay between increased sebum production and follicular hyperkeratinisation, which results in comedone formation and subsequent proliferation of *Cutibacterium acnes* (formerly *Propionibacterium acnes*) and inflammation. Well-known predisposing factors include family history, androgen excess, insulin resistance and psychological stress.[3-5] There is limited evidence about the role of diet, but some studies have demonstrated an association between acne and dairy or foods with a high glycaemic load.[5-8]

Acne has a predilection for body sites that have a high concentration of sebaceous glands, such as the face, upper back and chest. The condition is characterised by comedones, both open (blackheads) and closed (whiteheads), as well as erythematous and inflamed papules, pustules, cysts and nodules. There may also be postinflammatory hyperpigmentation and scarring (atrophic, boxcar, ice pick, rolling, hypertrophic and keloid).

For the case patient, no comedones are observed on examination. The lesions are concentrated in the central portion of the face, whereas the lesions of acne vulgaris would be expected to be more widespread. Acne is not usually associated with facial flushing.

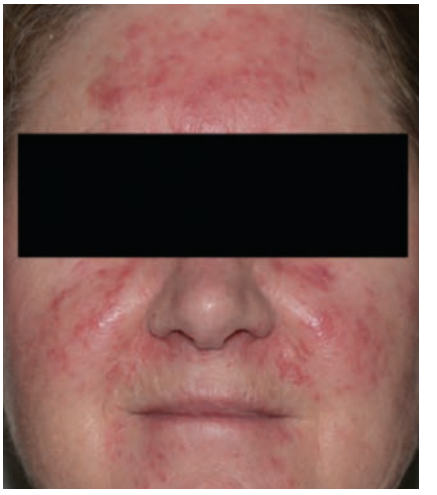

Figure. Centrofacial erythema with erythematous papules and pustules (case patient).

Folliculitis

Folliculitis (inflammation of the hair follicle) can be infectious or noninfectious. Infectious folliculitis is commonly caused by bacteria (*Staphylococcus aureus*, *Streptococcus* spp., Gram-negative bacteria such as *Pseudomonas aeruginosa*) but can also be brought about by fungi (dermatophytes, *Malassezia* spp. [discussed below], *Candida* spp.), viruses (herpes simplex virus, varicella zoster virus) and parasites (*Demodex* spp.). Hair removal (shaving, waxing, epilating, plucking) can inflame the hair

follicles during the removal process, increasing the risk of folliculitis. Other causes of noninfectious folliculitis include irritants (e.g. cutting oils, tar products, other chemicals), occlusion (e.g. by oils, ointments, adhesives) and drugs (e.g. corticosteroids, androgens) as well as immunosuppression (eosinophilic folliculitis in the setting of HIV infection) and inflammatory skin diseases (e.g. folliculitis decalvans). A swab can be taken for microscopy and culture to distinguish between infectious and noninfectious types of folliculitis.

Folliculitis affects body sites with hair. The condition is characterised by tender follicular papules or pustules on an erythematous base. Follicular lesions can be distinguished from their nonfollicular counterparts by the presence of hair piercing the lesions and spatial pattern, which follow the hair follicle distribution.

For the case patient, the erythema is more widespread than perifollicular and the papules and pustules do not have a folliculocentric distribution. Folliculitis is not associated with facial flushing.

Pityrosporum folliculitis

The pathogenesis of pityrosporum folliculitis (also known as *Malassezia* folliculitis) involves follicular occlusion followed by overgrowth of *Malassezia* in a sebaceous environment. Living in a hot, humid climate has been reported as a predisposing factor.[9,10] As *Malassezia* is part of normal skin flora in 90% of individuals, it has been postulated that altered host immunity and immunosuppression may play a role.[11,12] The incidence has been observed to be higher after antibiotic use.[13]

Pityrosporum folliculitis manifests as small, pruritic, monomorphic, folliculocentric papules and pustules on the upper back and chest. Other sites, such as the forehead, hair line and chin, can also be affected, albeit not as often.

Dermoscopic findings include perifollicular erythema, perilesional scales, and hair that is hypopigmented and coiled or looped.[14] Woods lamp examination may show a yellow-green fluorescence. A potassium hydroxide test performed on skin scrapings may show budding yeasts.

For the case patient, the lesions are not pruritic, folliculocentric or monomorphic. There is no associated flushing in pityrosporum folliculitis.

Rosacea

This is the correct diagnosis. Rosacea, a chronic inflammatory dermatosis with centrofacial distribution, has a predilection for women aged between 30 and 50 years, particularly those of Celtic and northern European descent and skin phototype I or II.[15] However, men, darker-skinned individuals and other age groups can also be affected. The global prevalence is estimated to be 5.5%.[16]

The exact pathogenesis of rosacea is unknown but multiple factors are thought to be contributory, including a genetic predisposition and immune and neurocutaneous dysregulation in response to internal and external triggers, which lead to hyperinflammation and the resultant characteristics of rosacea.[17] Common triggers include exposure to ultraviolet radiation, spicy foods, hot beverages, exercise, alcohol, temperature change and psychological stress.[18]

Rosacea has been associated with systemic diseases, including cardiovascular, respiratory and metabolic disorders, neurological diseases (such as Parkinson's disease) and autoimmune disorders (such as rheumatoid arthritis, coeliac disease and multiple sclerosis).[18,19] Further studies are needed to confirm these associations.

Diagnosis

The diagnosis of rosacea can pose a challenge because the condition shares many common features with other facial dermatoses that may be present concurrently, such as those listed above. Traditionally, rosacea was divided into four subtypes: erythematotelangiectatic, papulopustular, phymatous and ocular. However, the global ROSacea COnsensus (ROSCO) panel recently created a new diagnostic and classification system (see Box), to reduce the subtype overlaps frequently seen in clinical practice.[20,21] The case patient fulfils the diagnostic requirement for rosacea with background ongoing centrofacial erythema (diagnostic feature), and the intensification by known triggers further supports the diagnosis. She also has centrofacial flushing, inflammatory papules and pustules (two major features) and a stinging sensation of the skin (minor feature).

DIAGNOSIS OF ROSACEA[20,21]

In accordance with the diagnosis and classification system published by ROSacea COnsensus (ROSCO) in 2019, a diagnosis of rosacea requires the presence of at least one diagnostic feature or two major features. Minor features might also be present with diagnostic and/or major features.

Diagnostic features

- Background ongoing centrofacial erythema, which may intensify in response to triggers
- Phymatous changes: skin thickening, sebaceous glandular hyperplasia, rhinophyma

Major features

- Flushing/transient centrofacial erythema
- Inflammatory papules and pustules
- Telangiectasia (excluding perinasal)
- Ocular manifestations: lid margin telangiectasia, blepharitis, keratitis, conjunctivitis, sclerokeratitis

Minor features

- Burning sensation of skin
- Stinging sensation of skin
- Dry sensation of skin
- Localised facial oedema

TABLE. TREATMENT OPTIONS FOR ROSACEA

Treatment	Notes
General measures	
Photoprotection	
• SPF 50+ sunscreen, preferably tinted • Other photoprotective measures (e.g. wearing a broad-brimmed hat)	• Advised for all patients
Skin care	
• Gentle cleansers and moisturisers, consider products that contain ceramides • Avoidance of exfoliants and products containing alcohol, menthols, camphor, witch hazel, fragrance, eucalyptus oil or peppermint • Avoidance of procedures such as chemical peels and dermabrasion	• Advised for all patients
• Avoidance of triggers, where practical	• Advised to reduce flushing
Medical treatments	
Topical	
• Metronidazole 0.75% gel or cream twice daily	• One of the most commonly prescribed topical agents for rosacea
• Ivermectin 1% cream once daily	• Shown to be more effective and to produce longer remission than topical metronidazole[22,23]
• Azelaic acid 15% gel or 20% lotion once daily	• Shown to have at least equivalent or superior efficacy to topical metronidazole in some studies[24-27]
• Topical alfa2-adrenergic receptor agonist, e.g. brimonidine tartrate 0.33% gel	• Used rarely for erythema/flushing with rapid result; used for special occasions • Can cause rebound erythema; long-term use should be avoided
Systemic	
• Oral antibiotics, e.g. doxycycline 50 to 100 mg daily, minocycline 50 to 100 mg daily, erythromycin 250 to 500 mg twice daily	• Patients should be advised about risk of photosensitivity, particularly with doxycycline (reported risk 3 to 16% at 100 mg daily)[28-30]
• Isotretinoin 10 to 20 mg weekly	• Consider for patients with refractory disease (off-label use)
Procedural management	
• Surgery	• For patients with phymatous changes
• Laser therapies, e.g. pulsed dye laser (for erythema/telangiectasia), ablative laser (for phymatous changes)	• Laser choice depends on main issue to be addressed
Specialist referral	
• Referral to dermatologist	• If there is diagnostic uncertainty or failure of multiple treatment lines; consideration of laser therapy
• Referral to ophthalmologist	• For patients with ocular involvement

Management

Current treatment options for rosacea are outlined in the Table.[22-30] Management requires a holistic approach, and should be individualised according to the main presenting features. The condition is not curable, but it can 'burn out' after several years. It is important that patients are educated about the chronicity of rosacea and its remitting/relapsing nature.

Outcome

The case patient was reviewed by a dermatologist and diagnosed with rosacea. She was advised about the chronicity of the disease and the importance of general skincare measures, photoprotection and trigger avoidance. She had previously tried topical metronidazole cream for a few months with no improvement in her symptoms. Therefore, she was commenced on oral doxycycline 100 mg daily. At one month follow-up, her facial eruption was almost completely cleared. To maintain remission, the doxycycline dosage was reduced to 100 mg every two days, and then further reduced to three times a week. It should be noted that the aim was to reduce the dose of doxycycline to the lowest possible dose that maintains remission (e.g. 50 mg three times a week) but this can vary between patients. In the presented case, the patient developed gastrointestinal discomfort with doxycycline after some time, and her maintenance treatment was changed to low-dose isotretinoin 20 mg twice a week, which has maintained disease remission and been well tolerated. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

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