Symptomatic treatment of idiopathic and rosacea-associated cutaneous flushing with propranolol

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Flushing has been associated with medications, rosacea, menopause, carcinoid syndrome, pheochromocytoma, polycythemia, and mastocytosis, although it can occur without known cause. There are no known specific treatments available, but β-blockers have suppressed flushing reactions in some patients, particularly when associated with anxiety. The medical histories and clinical characteristics of 9 patients with either idiopathic flushing or flushing associated with rosacea were reviewed. Eight patients experienced subjective improvement with propranolol therapy. (J Am Acad Dermatol 2005;53:881-4.)

Flushing, a periodic exaggeration of the normal blush response, has been associated with rosacea, menopause, alcohol or nicotinic acid ingestion, and with rare conditions, such as carcinoid syndrome, pheochromocytoma, polycythemia, and mastocytosis.[1,2] Flushing also occurs in the absence of any known cause. Despite its benign nature, some patients find their symptoms disabling. The β-blockers nadolol[3] and propranolol[1,4] have suppressed flushing reactions in some patients, particularly when associated with anxiety. We present our findings of 9 patients with flushing treated with propranolol.

METHOD

Medical records of patients with flushing treated with propranolol were reviewed retrospectively to compare age, sex, duration, distribution, aggravating factors, symptomatology, and co-occurring illnesses. All but one patient was treated initially with propranolol, 10 mg, by mouth 3 times daily, with doses increased as tolerated until symptoms improved. Success was measured by each patient's perception of improvement, based on decreasing flushing episodes, decreasing symptoms, and quality of life (Tables I and II).

RESULTS

All but one patient were female and all were Caucasian. They ranged in age from 31 to 69 years and had symptom duration between 1 and 10 years. Facial erythema or blushing on examination was noted in 8 patients. Heat was the most common aggravating factor, but sunlight induced flushing in 4 patients. One patient reported that fluorescent lights made her flushing worse. Eight patients had erythematotelangiectatic or papular rosacea and one had idiopathic flushing. Four patients with rosacea had associated symptoms that occurred with each episode: 3 with a burning sensation, and one with stinging. Medical histories revealed one patient with hypertension, 4 with allergic rhinitis or sinus allergies, 3 with headaches (2 migraine), and 3 patients had fibromyalgia.

Eight of the 9 patients reported diminished symptoms and fewer flushing episodes while taking propranolol. None had sufficient relief from the initial dosage of propranolol, 10 mg taken 3 times a day. This dosage was then increased and individualized. The dose of propranolol needed to achieve symptomatic control of flushing varied between 20 and 40 mg taken twice daily to 3 times a day (Table II). For patient 2, long-acting propranolol, 80 mg daily, was substituted for a calcium channel blocker that controlled her hypertension without affecting her flushing. This propranolol formulation controlled her blood pressure and decreased her flushing symptoms.

Patient 3, the only male patient in the study, did not have his flushing improve with propranolol. However, he only received 10 mg of propranolol 3 times a day for 1 month without side effects and then elected to discontinue propranolol altogether.

Two patients experienced adverse side effects that necessitated discontinuation of propranolol. Patient 1 had significant improvement of her flushing, but her pulse rate decreased and she experienced some dizziness. Patient 8 had mild improvement, but dizziness and a sensation of balance loss developed

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Table I. Summary of case presentations

Patient no.	Age (y)	Ethnic origin/ Sex	Duration of symptoms (y)	Distribution of flushing	Aggravating factors	Presence of blush on exam	Other symptoms
1	42	Caucasian/F	3	Nose, cheeks, chin, ears, anterior neck	Cold or hot weather, alcohol ingestion, stress	Yes	None
2	53	Hispanic/F	10	Malar cheeks and nose	Sun and heat exposure	Yes	None
3	31	Caucasian/M	1	Nose, cheeks, chin, lower forehead	Heat, alcohol ingestion	No	None
4	35	Caucasian/F	2	Diffuse background erythema on face	Anger, heat, nervousness, sun, wind, or cold exposure	Yes	None
5	52	Caucasian/F	2	Forehead, medial cheeks, chin, nose	Heat, stress, sun exposure	Yes	Burning sensation
6	31	Caucasian/F	2	Cheeks, chin, nose	Mowing the lawn	Yes	None
7	69	Caucasian/F	10	Face and anterior neck	Heat, stress	Yes	Burning sensation
8	43	Caucasian/F	2	Face, neck, ears, chest, scalp; left side more than right	Heat, fluorescent lights, stress, and sun exposure	Yes; preferred to sit in a dark room	Burning sensation
9	35	Caucasian/F	1	Cheeks, chin	Exercise; sometimes flushing wakes her at night	Yes	Stinging

when her propranolol dose reached 40 mg 3 times a day. Patient 4 attributed her mild weight gain to propranolol, but she continued it because propranolol was effective in treating her flushing and headaches. The two patients with known histories of migraine headache also experienced the positive side effect of decreased severity of headaches while taking propranolol.

DISCUSSION

Flushing of the face, chest, and neck occurs most commonly in individuals with fair complexion, particularly those of Celtic or northern European ancestry. The redness is often transient, but it may become persistent, and telangiectasia can occur. Patients are not only distressed by the visual redness; many also complain of symptoms such as burning, stinging, and heat associated with each episode. These symptoms even caused several patients to carry handheld or battery-operated fans and spray bottles with cold water for relief. Patient 5, whose symptoms were aggravated by light, preferred to remain in a darkened room.

Flushing that is accompanied by other symptoms, including abdominal pain, dyspnea, palpitations, and frequent stools, should prompt further work-up for an underlying systemic cause. Once systemic diseases and medications are excluded, flushing is most commonly associated with rosacea and menopause, although it may also be idiopathic. Flushing that accompanies menopause is usually amenable to estrogen replacement therapy. On the other hand, flushing associated with rosacea commonly fails to respond to standard therapies for rosacea. Idiopathic flushing tends to occur in women and the symptoms persist for a long duration.[2]

Treatment of flushing is difficult primarily because it has been associated with multiple etiologies. Improvement in transient flushing is also difficult to quantitate, although attempts to provoke flushing and to measure the responses to medications have been performed. Even so, only small series and case reports are found in the literature. Friedman et al[2] described 10 patients with idiopathic flushing. These patients failed to respond to one or more therapies including H_1 and H_2 antihistamines, aspirin and nonsteroidal anti-inflammatory drugs, systemic steroids, calcium channel blockers, danazol, and cromolyn sodium. In another report, clonidine reduced malar temperature in patients with erythematotelangiectatic rosacea, despite the failure to reduce redness after provocative maneuvers.[5] Although

Table II. Diagnoses, treatment, and side effects

Patient no.	Other medical diagnoses	Systemic medications	β Blocker dose*	Side effects
1	Rosacea, fibromyalgia	None	Propranolol, 10 mg, 20 mg q afternoon and 10 g qhs	Decreased heart rate, fatigue, dizziness
2	Rosacea, contact dermatitis, migraines, depression, sinus allergies, hypertension	Estrogen Sertraline Rabeprazole Fexofenadine	Propranolol LA 80 mg qd	Controlled migraine headaches
3	Psoriasis, rosacea, hypertension, peptic ulcer disease	Tetracycline Valsartan	Propranolol 10 mg tid for 1 mo gave no relief of symptoms; patient discontinued drug	None
4	Allergic rhinitis, seborrheic dermatitis, headaches	Fexofenidine Aspirin 81 mg Cetirizine	Propranolol 20 mg tid	Weight gain, less headaches
5	Rosacea, atopic dermatitis	Aspirin 81 mg	Propranolol 40 mg tid	None
6	Fibromyalgia, atopic dermatitis, rosacea, migraine headaches	Cetirizine Tetracycline Oral contraceptive pills	Propranolol 40 mg bid	Less migraine headaches
7	Rosacea	Aspirin 81 mg	Propranolol 20 mg bid	None
8	Fibromyalgia, chronic pain syndrome, allergic rhinitis, rosacea	Morphine Alprazolam Lorazepam Cyclobenzaprine Lansoprazole Gabapentin Amitriptyline Oral contraceptive pills	Propranolol 40 mg tid	Transient dizziness and sense of balance loss
9	Hypothyroidism, rhinitis, rosacea	Levothyroxine	Propranolol 20 mg tid	None

bid, Twice daily; *q,* every; *qd,* daily; *qhs,* at bed time; *LA,* long-acting; *tid,* 3 times a day.
*The dose required for subjective relief of symptoms.

β-blockers have also not demonstrated objective laboratory evidence for direct effects on cutaneous blood vessels during flushing episodes, some patients have reported fewer symptoms.[1,3,4] Single case reports exist for improvement of resistant flushing with thoracoscopic sympathectomy[6] and injection of botulinum toxin A.[7,8] Biofeedback training also failed to show objectively measured decreases in flushing.[9]

Cutaneous flushing is frequently associated with anxiety reactions.[10] Nonselective β-blockers are known to decrease sympathetic activity and to reduce the symptoms of anxiety in normal subjects.[3,11,12] According to Abelson, Nesse, and Vinik,[10] there is a significant overlap between patients with panic disorder and idiopathic flushing. In addition, β-blockers may reduce episodes of tachycardia that are known to intensify flushing symptoms.[3]

Beta-blocker therapy should be monitored for side effects. Fatigue, somnolence, and dizziness are reported by approximately 10% of patients. Dyspnea, vivid dreams, confusion, and bradycardia can occur in up to 3% of patients, although only 1% experience hypotension. Sexual dysfunction can occur in male patients, especially with the nonselective β-blockers propranolol and pindolol.[13] Caution should be exercised in prescribing β-blockers to patients with asthma[14] and psoriasis,[15] whose diseases may worsen.

Symptomatic idiopathic flushing and flushing associated with rosacea deserve separate treatment, since the flushing does not respond to conventional rosacea treatment. Although the perceived improvement of flushing and its symptoms in 8 of our 9 patients treated with propranolol is encouraging, prospective randomized studies with control subjects and standardized quality of life data are necessary to better determine the efficacy of propranolol therapy.

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Dermoscopy of the nail bed and matrix to assess melanonychia striata

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Melanonychia striata represents a diagnostic dilemma for dermatologists. The use of dermoscopy to assess the nail has advantages over clinical examination. However, when compared to skin lesions, it gives fewer details. We describe two cases of melanonychia striata submitted to dermoscopic examination of the nail bed and matrix. This is a new procedure that enables observing dermoscopic characteristics that are not visualized in the nail plate, thus, providing additional information. (J Am Acad Dermatol 2005;53:884-6.)

Melanonychia striata can be neoplastic or benign in nature.[1] This represents a diagnostic dilemma for dermatologists, as it is often impossible to identify the cause of these lesions using clinical examination alone.

There are advantages to the adjuvant use of dermoscopy in assessing nail abnormalities.[2-4] However, as opposed to the dermoscopic assessment of skin lesions in which melanin distribution and structure are examined directly at the site of origin, fewer details can be seen dermoscopically in the nail.[5] Examination of nail lesions is limited to the pigment that is deposited in the nail plate as a result of melanocytic activity that occurred in the nail matrix, bed, or both. Therefore, dermoscopic characteristics observed in the nail plate can misrepresent the underlying lesion.

Two cases of melanonychia striata (melanoma and hypermelanosis/racial melanonychia) are described to exemplify the difficulty faced when making a diagnosis. Both patients were submitted to dermoscopic examination of the nail plate, bed, and matrix. Dermoscopic examination of the nail bed and matrix enables visualizing pigmentation directly in its original site, revealing aspects not observed when the nail plate is interposed between the pigmented lesion and the Dermatoscope (Dermlite, 3 Gen, LCC, Dana Point, Calif).

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