Erythermalgia Involving the Face Alone: Two Case Reports

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Erythermalgia is a rare cutaneous disease characterized by episodic attacks of burning pain, erythema, and increased temperature. It primarily involves the extremities, with possible extensions to the ears, face, neck, and scrotum; in rare instances, it may afflict the ears, face, or the scrotum alone. Although various medications alone or in different combinations have been tried with significant variations in response, no recommended therapeutics have been established until very recently. This report presents two case histories of a 20-year-old and a 46-year-old woman, respectively, who displayed intermittent facial erythema associated with warmth and pain during the episodes and who presented normal between episodes. Both had good response to combinative treatments of systemic medication and topical lidocaine compounds. The younger was disease-free after more than 4 years of follow-up, and the older had recurrence after stopping the treatment. **Conclusion:** Erythermalgia may involve the face alone, and combinative approaches may be of choice for its treatment. Topical lidocaine compounds are considered to be a good option for palliative treatment. *J Oral Facial Pain Headache 2019;33:e15–e18. doi: 10.11607/ofph.2139*

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Erythermalgia (EM), also called erythromelalgia, is a rare cutaneous disorder presenting as episodic cutaneous erythema associated with increases in temperature and pain. These conditions can be provoked by warmth or exercise and can be prevented or relieved by cooling. EM primarily involves the extremities, particularly the hands and feet, and may infrequently extend to other parts of the body, including the head, neck, and scrotum.[1–3] In rare instances, localized extra-extremity conditions have also been described, including the thigh,[4] vulva,[5] scrotum,[6–8] cheeks,[9] isolated auricular variants,[10,11] and involvement of both the face and ears.[12] The treatment of EM is still difficult. In this case history report, two case histories of women with facial involvement alone are reported.

Case Presentations

Case 1

A 20-year-old woman was referred for a month-long history of intermittent attacks of red cheeks associated with a marked burning sensation and warmth. The patient noticed that each episode presented with reddening, increased temperature, and burning on her cheeks without any other associations. The flare occurred several times a week and lasted for hours each time. When the flare stopped, no abnormality was present. Warmth, movement, or excitement could trigger or worsen the attack, while cold water or a cold facial mask relieved the flare rapidly. The patient had a habit of sitting in a chair with her head lowered to read information on a mobile phone for hours a day. Her past medical and family histories were unremarkable. Headache, increased heart rate, and/or lesions on the extremities were not present.

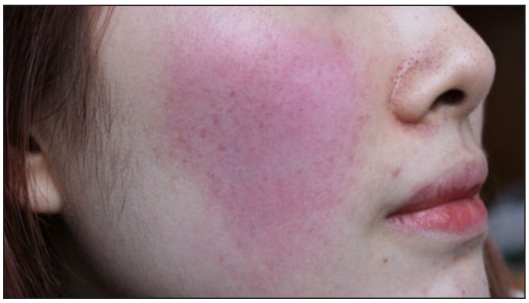

Fig 1 Evident erythema on the cheek during the episode of flaring.

Cutaneous examination showed that evident erythema presented on both cheeks when the attack was occurring (Fig 1) and was associated with marked warmth and tenderness, but there appeared to be no relationship with the trigeminal innervation pattern. The temperature over the lesions was higher than the peri-lesion area during the episodes and than the cheeks between episodes. No other areas, including the limbs and ears, had similar involvement. The heart rate and blood pressure were within normal ranges when the flare was attacking. Laboratory tests for complete blood cell counts, biochemistry profiles, anti-nuclear antibodies, and auto-antibodies were either within normal limits or negative. Biopsy and gene analysis were refused. The patient was then diagnosed with erythermalgia and was treated with combinative therapeutics of gabapentin, celecoxib, and topical lidocaine compounds. She was also asked to correct the harmful reading posture, resulting in an excellent response after 1 month of treatment. She also noted that topical lidocaine compounds resulted in excellent remission for facial pain. However, recurrence occurred after the treatment was stopped. Then treatment was administered for 6 months, and no relapse occurred for more than 4 years of follow-up until the present publication.

Case 2

A 46-year old woman presented with a 6-year history of painful attacks of facial erythema associated with warmth. The attacks occurred several times a week, lasted for 10 minutes to hours each time, and had poor response to systemic antihistamines, hydroxychloroquine, and steroids, as well as topical steroids. The episodes could be triggered by warmth, movement, or excitement, and could be relieved by cold water or stopping the movement. No lesions presented between episodes. Cutaneous examination showed no abnormality between episodes; however, erythema associated with increased temperature and burning pain, as well as tenderness, presented on her cheeks after a rapid walk or going upstairs. The attack lasted for an hour and disappeared after stopping the movement. No extremities were involved. No pathogenic mutation on the SCN9A gene for the patient or her family was detected. Considering the diagnosis of erythermalgia, the patient was treated with systemic amitriptyline, gabapentin, and ibuprofen, as well as topical lidocaine compounds, leading to an excellent improvement after about 3 weeks of treatment. She also found that topical lidocaine compounds were much more effective for pain relief than systemic treatment. The medications were used for 2 months before being stopped; however, recurrence occurred 1 month after stopping treatment. The medications mentioned above were re-used, with milder response from the patient this time. Afterward, paroxetine combined with gabapentin was added, and the patient was lost to follow-up later.

Discussion

The name "erythermalgia" originates from the clinical features of the disease: red (erythro), heat (therme), and pain (algos). It is also called "erythromelalgia" (red, extremity [melos], and pain).[1,3] Although erythromelalgia is the term most commonly used at present, the authors prefer to use erythermalgia, as it is a more accurate word to describe such a syndrome. EM occurs most often between the fifth and sixth decades of life and has a predilection towards women.[2] Interestingly, the present two cases were women under 50 years of age. The diagnostic criteria for EM include: intermittent (occasionally continuous) burning pain associated with erythema and increased temperature, and pain worsened by warmth and relieved by cooling.[13] However, no identifiable diagnostic or laboratory tests were available until recently, although SCN9A mutation may present in primary genetic form.[2,3,14] The diagnosis for EM is mainly based on a carefully taken history, physical findings during the episodes, and ruling out any other possible causes of symptoms.[1–3,13] As clinical manifestations may be absent between episodes, it is beneficial for the diagnosis if the patient is able to take an image or a record of the flare in progress. Although the present two patients did not have extremity involvement, their cheek presentations shared diagnostic criteria typical of EM that were similar to previous cases[5,9,12] and showed excellent response to the therapeutics similarly prescribed for EM,[1,2] and so it was considered that both were a variant of classic EM involving the face alone. Such a condition is also called "erythroprosopalgia" in the German literature, derived from prosopon (face).

EM is classified into primary and secondary subtypes. The primary subtype is diagnosed in patients in whom no objective cause is found and includes genetic and idiopathic forms. The potential factors for secondary EM may

Table 1 Differential Diagnoses for Erythermalgia

Diseases	Etiology	Presentations	Treatment
Seborrheic dermatitis[15,16]	Unknown; possibly includes genetic and environmental factors	Afflicting anywhere on the skin rich in oil-producing glands, including the scalp, face, and chest Presenting as red, scaly, greasy, itchy, and inflamed skin	Antifungals, antihistamines, anti-inflammatory treatments, phototherapy, topical immunosuppressants
Contact dermatitis[16,17]	Skin exposure to allergens or irritants	Affecting any part of the body with clear exposure to the triggering substance before the occurrence of lesions, presenting as itchy, burning skin with red rash and/or blisters or weals	Avoiding cause; alleviative treatments, including antihistamines and steroids.
Photosensitivity[18]	Abnormal reactions of skin to ultraviolet rays from the sun and other light sources, especially visible light, including photoallergy and phototoxicity	Usually following exposure to certain oral or topical drugs or to other sensitizing chemicals, resulting in accelerated reddening and blistering of the skin with exposure to sunlight, always with associations of itching or burning	Sun protection, sunscreens, steroids or pain medications, oral beta-carotene.
Facial flushing[12,16,19]	Various physiologic conditions and psychologic reasons	Sudden facial reddening, hot face, generally restricted to the face, cheeks, or ear without association of skin pain. Triggering factors including underlying disease and reaction to certain substances such as alcohol or drugs, allergy, emotions, exercise, etc.	Treating the underlying disease. Aspirin and antihistamines are sometimes helpful.
Harlequin syndrome[20]	Hemifacial cutaneous sympathetic denervation; congenital or acquired; plausible causes, including damage of preganglionic or postganglionic cervical sympathetic fibers, but exact mechanisms remain unknown	Sudden onset of unilateral facial flushing and hyperhidrosis induced by exercise, heat, or emotional stress, possibly involving arms and trunk	No medical treatments required for most patients; however, psychologic support and/or surgical sympathectomy (ipsilateral) are alternatives in conditions with significant embarrassment or with underlying diseases.
Rosacea[16,19]	Unknown; genetic and environmental factors playing important roles	Early presentations, including recurrent flushing and facial redness	Medical treatments including metronidazole, azelaic acid, ivermectin, or sulfur preparations; oral antibiotics and retinoids for severe conditions.
Erythermalgia[1–12]	Familial form caused by SCN9A mutation; sporadic remains unknown; some underlying diseases are responsible for the secondary form	Intermittent burning pain associated with erythema and increased temperature; pain worsened by warmth and relieved by cooling.	No recommended therapeutics established; avoidance of triggering factors and symptomatic treatment are important managements; treating the underlying disorder is the best method for the secondary form.

include myeloproliferative diseases, blood disorders, drugs, infectious diseases, food ingestion (mushrooms), neoplasms, connective tissue disease, physiologic conditions (pregnancy), and neuropathies.[3] However, as the real pathogenesis for the secondary subtype remains unknown, the relationship of many underlying disorders to EM may be a coincidental comorbidity rather than an underlying disease. In genetic EM, mutations in the SCN9A gene encoding the sodium channel protein Na(v)1.7 subunit have been identified and are considered to be responsible for its pathogenesis.[3,14] These mutations have rarely been detected in sporadic cases,[1,3] as in the present case 2; the pathophysiology in such conditions is not fully understood, and both neuropathologic and microvascular functional alterations are considered to play important roles.[3] Previous studies found that more dilated vessels presented when the episode was flaring, and the dilated vessels were considered to be responsible for both the increased temperature and the pain.[3,9,12] The authors of the present report also speculate that the reading gesture might have played a role in the episodes in case 1, as the long time spent lowering the head might result in abnormal carotid dissection, causing abnormal blood supply for the head.

The differential diagnoses for the present condition include seborrheic dermatitis, contact dermatitis, photosensitivity, rosacea, and especially facial flushing, as well as Harlequin syndrome[1–12,15–19] (Table 1). Based on the clinical features, it is not hard to exclude a diagnosis of seborrheic dermatitis, contact

dermatitis, or photosensitivity. Facial flushing, mimicking EM, is characterized by a sudden facial reddening and hot face and is always accompanied by other symptoms relating to the nosogenesis. This reddening may extend to the neck and upper chest, or even to the whole body, with absence of skin pain. The triggering factors include underlying medical conditions, reaction to certain substances (such as alcohol or drugs), allergy, emotions, exercise, etc. Harlequin syndrome is present as a sudden onset of unilateral facial flushing and sweating[20] that is not difficult to differentiate from the present condition.

The treatment and management of EM are still difficult. Various medications alone or in different combinations have been tried with significant variations in response. Treating the underlying disease may sometimes bring complete relief from the symptoms; however, no recommended therapeutics have been established until now.[1–3] Lumbar sympathetic block was reported to show excellent response in a refractory case.[21] Based on the literature, combinative modalities, such as those prescribed to the present patients, seem to be optimal for providing effective management.[1–3,9,12] Unfortunately, the previous two cases reported by some of the present authors[9,12] recurred after stopping the treatment for about 1 year, suggesting that it is hard to prevent the relapse for EM despite how long relief with treatment has been achieved.

As these authors have met four cases[9,12] (including the present two) of EM who had facial involvement but lacked limb lesion within 4 years, this suggests that EM with sole extra-extremity involvement is not as rare as anticipated. The reason for its rarity of report is likely because the disease is underestimated and misdiagnosed.

Conclusions

Erythermalgia may involve the face alone. Its response to therapeutics is varied, and combinative approaches may be the optimal choice for its treatment. Topical lidocaine compounds seem to be a good palliative for pain relief.

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