

Acute Papulopustular Rosacea-like Eruption from Oral Parabens

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Sir,

Rosacea is a common chronic cutaneous disorder of unknown aetiology that affects approximately 10% of the population (1). The prevalence of rosacea is highest among fair-skinned 20–60-year-old individuals, particularly those of Celtic and northern European descent (1). Cutaneous manifestations include transient or persistent facial erythema, telangiectasia, oedema, papules and pustules that are usually confined to the central portion of the face (2). Rosacea can also be associated with ocular symptoms of redness, itching, tearing, dryness and eyelid fullness or swelling (3). Rosacea actually represents a spectrum of diseases, ranging from chronic skin hypersensitivity and flushing to rhinophyma. The National Rosacea Society's Expert Committee on the Classification and Staging of Rosacea identified 4 subtypes of rosacea: erythematotelangiectatic, papulopustular, phymatous and ocular (4). Differential diagnosis with 3 other acneiform facial eruptions (acne vulgaris, folliculitis, and perioral dermatitis) should be considered when assessing patients. Although the clinical features of the disease are well-recognized, the pathogenesis of rosacea is still poorly understood.

We describe here a patient with four episodes of an acute papulopustular rosacea-like eruption associated with systemic treatments containing parabens.

CASE REPORT

A 35-year-old woman was referred to our department for the evaluation of a papulopustular rash on the face. She reported that the manifestation had started one week prior to presentation, with a progressive worsening of the clinical course during treatment with a cough syrup. The patient, a dermatologist, had experienced the same skin reaction in three other occasions, after systemic treatment with two other kinds of cough syrups and some vitamins. Moreover, she explained that after discontinuing the systemic therapy she had observed complete remission of the papules and pustules in 2 days and the erythema in 4–5 days.

Examination of the skin revealed erythema, oedema, papules, some of which were surmounted by tiny pustules and the absence of comedones. These lesions were observed mainly on the face; however, some papulopustules could be detected on the chest and laterally on the neck (Fig. 1). A careful examination of the cutaneous manifestation in order to differentiate morphologically similar conditions was carried out and a clinical diagno-



Fig. 1. Examination of the skin revealed erythema, oedema, papules, some of which were surmounted by tiny pustules, and an absence of comedones. These lesions were observed mainly on the face; however, some papulopustules could be detected on the chest and laterally on the neck.

sis of papulopustular rosacea was made. Accordingly, when the treatment was discontinued, once again a rapid and complete remission of the papules, pustules and erythema was observed in 2–5 days.

The patient's medical history was significant for papulopustular and nodular acne at the age of 27 years, which had been treated with oral isotretinoin for 8 months. The patient had not had any rosacea-like cutaneous manifestations previously.

After a thorough evaluation of all the ingredients (active substances and excipients) in the syrups and the vitamins, the only common substances observed were the parabens (methyl-para-hydroxybenzoic acid, propyl-para-hydroxybenzoic acid and ethyl-para-hydroxybenzoic acid). However, the patient refused to undergo a paraben mix epicutaneous patch-test, since she had been using cosmetics (creams and make-up) containing parabens with no problems.

DISCUSSION

Parabens were first introduced in the 1930s and currently are the most widely used preservatives in cosmetic products, pharmaceuticals, and food processing (CEE list; E211–E219) (5). Parabens are a family of alkyl esters of para-hydroxybenzoic acid that differ at the para position of the benzene ring by various chemical substitutions. There are five widely marketed para-hydroxybenzoic acid esters: methylparaben, ethylpara-

ben, propylparaben, butylparaben and benzylparaben. Parabens have a broad spectrum of activity against yeasts, moulds, and some activity against bacteria. Products that commonly contain parabens preservatives are cosmetics, topical and systemic medicines, foods and industrial goods (6).

Topical parabens have been reported to cause allergic contact dermatitis, contact urticaria and to have a weak oestrogenic effect (7). Several cases of immediate hypersensitivity reactions to parenterally administered compounds containing parabens (antibiotics, corticosteroids, local anaesthetics, radiopharmaceuticals, vitamins, anti-hypertensives, diuretics, insulin, heparin, and chemotherapeutic agents) have been reported (7). Moreover, there are a few reports of a generalized eczematous eruption after ingestion of parabens-containing medications or foods (8, 9).

Formerly, it was thought that parabens absorbed by the body were metabolized by esterases in the liver and kidney, excreted in the urine, and not accumulated in the body; however, recently some researchers found that para-hydroxybenzoic acid, the main metabolite of parabens, was detected in all patient blood and breast milk samples tested (7, 10). Moreover, a study demonstrated that a portion of parabens can be absorbed and retained in human body tissues without hydrolysis by tissue esterases (7, 11).

In our patient, we observed progressive worsening of the clinical course during systemic treatments containing parabens, although there was no evidence of an allergic contact dermatitis to this substance. Furthermore, the worsening of the cutaneous lesions seemed to be related to a regular and constant intake of medicine containing parabens. Since the patient did not suffer from cutaneous symptoms after occasional ingestion of products containing parabens, we believe that the cutaneous manifestation described could be dosage dependent and to some extent related to the accumulation of the substance.

Certain systemic medications can induce an exacerbation of rosacea or produce rosacea-like dermatoses. Amiodarone, etretinate (Tigason), nicotinic acid, and high doses of vitamins B6 and B12 have been reported to induce rosacea, flushing and acneiform eruptions (12–15). Yet, to our knowledge, there are no other case reports in the literature regarding rosacea-like eruption caused by parabens.

In conclusion, our observation suggests that parabens may represent an aetiological factor in rosacea-like eruptions; however, further studies are needed to support this hypothesis.

REFERENCES

1. Gupta AK, Chaundhry MM. Rosacea and its management: an overview. *J Eur Acad Dermatol Venereol* 2005; 19: 273–285.
2. Buechner SA. Rosacea: an update. *Dermatology* 2005; 210: 100–108.
3. Zug KA, Palay DA, Rock B. Dermatologic diagnosis and treatment of itchy red eyelids. *Surv Ophthalmol* 1996; 40: 293–306.
4. Wilkin J, Dahl M, Detmar M, Drake L, Feinstein A, Odum R, Powell F. Standard classification of rosacea: report of the national rosacea society expert committee on the classification and staging of rosacea. *J Am Acad Dermatol* 2002; 46: 584–587.
5. Richardson EL. Up-date frequency of preservative use in cosmetic formulas as disclosed to FDA. *Cosmetic and Toiletries, FDA Report* 1977; 92: 85.
6. Ngan V. Allergy to paraben. *DermNet NZ*, 2002. Available from: URL: <http://dermnetnz.org/dermatitis/parabens-allergy.html>.
7. Cashman AL, Warshaw EM. Parabens: A review of epidemiology, structure, allergenicity, and hormonal properties. *Dermatitis* 2005; 16: 57–66.
8. Kaminer Y, Apter A, Tyano S, Livni E, Wijzenbeek H. Delayed hypersensitivity reaction to orally administered methyl paraben. *Clin Pharmacol* 1982; 1: 469–470.
9. Veien NK, Hattel T, Laurberg G. Oral challenge with parabens in paraben-sensitive patients. *Contact Derm* 1996; 34: 433.
10. Nakazawa H, Oda H, Fujisima H. Analysis of chlorobenzenes, para-hydroxybenzoic acid esters and herbicide in human subjects using GC/MS. A report of the Research Fund of Health and Welfare of Japan. Tokyo: Ministry of Health and Welfare of Japan; 1999: 16. (in Japanese).
11. Oishi S. Lack of spermatotoxic effects of methyl and ethyl esters of p-hydroxybenzoic acid in rats. *Food Chem Toxicol* 2004; 42: 1845–1849.
12. Crawford GH, Pelle MT, James WD. Rosacea: I. Etiology, pathogenesis, and subtype classification. *J Am Acad Dermatol* 2004; 51: 327–341.
13. Reifler DM, Verdier DD, Davy CL, Mostow ND, Wendt VE. Multiple chalazia and rosacea in a patient treated with amiodarone. *Am J Ophthalmol* 1987; 103: 594–595.
14. Crivellato E. A rosacea-like eruption induced by Tigason (Ro 10-9359) treatment. *Acta Derm Venereol* 1982; 62: 450–452.
15. Jansen T, Romiti R, Kreuter A, Altmeyer P. Rosacea fulminans triggered by high-dose vitamins B6 and B12. *J Eur Acad Dermatol Venereol* 2001; 15: 484–485.