

Boyle (6) and Lansky et al. (5) the authors stress the possible confusion of the ONP with tuberous sclerosis. The present case gives rise to the question whether the ONP is a distinct entity as assumed by many authors (10, 11) or can perhaps be considered as a variation of tuberous sclerosis.

Skin lesions pathognomonic of tuberous sclerosis are "adenoma sebaceum" consisting of angiofibromatous proliferation, and subungual fibromas. These lesions are practically never present at birth. Rather, leaf-shaped white macules sometimes present at birth are the earliest diagnostically important cutaneous sign of tuberous sclerosis (2). Retinal phakomas are the most frequent ocular signs.

Computed tomography (CT) has become a useful investigative technique in the recognition of tuberous sclerosis also in cases without typical clinical signs (3).

Our patient did not show retinal phakomas. His neurological signs and CT findings might also lead to a diagnosis of tuberous sclerosis, especially when the bone defect, one leaf-shaped white macule and the radiologically confirmed calcification in the brain are considered together.

Can the present patient thus have simultaneously two phakomatoses? This possibility is not excluded, since case reports of the coexistence of tuberous sclerosis with Morbus Recklinghausen (8) and with Sturge-Weber syndrome (9) are to be found in the literature.

The picture of the ONP will be completed when CT findings in other patients are reported. Time will tell whether our patient will show further manifestations of the disease.

REFERENCES

1. Feuerstein, R. C. & Mims, L. C.: Linear nevus sebaceous with convulsions and mental retardation. *Am J Dis Child* 104: 675, 1962.
2. Fitzpatrick, T. B., Szabo, G., Hori, Y., Simone, A. A., Reed, W. B. & Greenberg, M. H.: White leaf-shaped macules. Earliest visible sign of tuberous sclerosis. *Arch Dermatol* 98: 1, 1968.
3. Gomez, M. R., Mellinger, J. F. & Reese, D. F.: The use of computerized transaxial tomography in the diagnosis of tuberous sclerosis. *Mayo Clin Proc* 50: 553, 1975.
4. Hornstein, O. P. & Knickenberg, M.: Zur Kenntnis des Schimmelpenning-Feuerstein-Mims-Syndroms. Organoide-Naevus-Phakomatose. *Arch Dermatol Forsch* 250: 33, 1974.
5. Lansky, L. L., Funderburk, S., Cuppage, F. E., Schimke, R. N. & Diehl, A. M.: Linear nevus sebaceous syndrome: Hamartoma variant. *Am J Dis Child* 123: 587, 1972.

6. Lovejoy, F. H. & Boyle, W. E.: Linear nevus sebaceous syndrome: Report of two cases and review of the literature. *Pediatrics* 52: 382, 1973.
7. Pinkus, H. & Mehregan, A. H.: A guide to dermatohistopathology. Appleton-Century-Crofts, New York, 2 Ed, 1976.
8. Ranneberg, K. M.: Gleichzeitiges Vorkommen von M. Pringle und M. Recklinghausen. *Med Welt* 23: 841, 1972.
9. Solomon, L. M. & Bolat, I. H.: Adenoma sebaceum in encephalofacial angiomas (Sturge-Weber syndrome). *Acta Dermatovener (Stockholm)* 52: 386, 1972.
10. Solomon, L. M., Fretizin, D. F. & Dewald, R. L.: The epidermal nevus syndrome. *Arch Dermatol* 97: 273, 1968.
11. Zaremba, J.: Jadassohn's naevus phakomatosis: 2. A study based on a review of thirty-seven cases. *J Ment Defic Res* 22: 103, 1978.

Effects of Topical Erythromycin on Aerobic and Anaerobic Surface Flora

Joel E. Bernstein¹ and Alan R. Shalita

¹Department of Medicine, Section of Dermatology, University of Chicago, Division of the Biological Sciences and the Pritzker School of Medicine, Chicago, Illinois 60637 and ²Division of Dermatology, Downstate Medical Center, Brooklyn, New York, USA

Received March 12, 1980

Abstract. The contents of acne lesions from 30 men with inflammatory acne vulgaris, obtained before and at the conclusion of 4 weeks of topical 2% erythromycin therapy, were cultured on aerobic and anaerobic plates. Sensitivity testing of cultures was performed with discs containing 50 mg erythromycin, in order to ascertain the prevalence of erythromycin-resistant strains of *Propionibacterium acnes* and aerobic micrococci. The percentages of patients in whom erythromycin-resistant micrococci could be isolated increased from 3 to 60% during topical erythromycin therapy, but no resistant *P. acnes* strains were isolated either before or after therapy. Considering the widespread use of topical antibiotics, long-term studies on their ecological effects are desirable.

Key words: Surface flora; Topical erythromycin; Acne vulgaris

Ecological disturbances in surface microflora have been well documented with the use of systemic

antibiotics for the treatment of acne vulgaris (8). Recently, Crawford et al. (2) demonstrated that topically applied clindamycin and erythromycin induced the development of resistance to these antibiotics in strains of *Propionibacterium acnes*. Since the therapeutic effectiveness of topical antibiotics has been at least partially attributed to their antibacterial activity against *P. acnes* (10), the development of such antibiotic-resistance might substantially reduce their clinical value.

Along with *P. acnes*, coagulase-negative micrococci comprise almost all of the follicular flora (8). High levels of resistance in such cocci are induced by short (3 week) systemic courses of clindamycin, tetracycline and erythromycin (8). These micrococci seem to play a minor role in acne pathogenesis, and have long been viewed as relatively innocent commensals. Recent literature on central nervous system infections (3) and endocarditis (5) caused by *Staphylococcus epidermidis* indicate that this organism can act as a dangerous pathogen in immunologically suppressed patients or patients possessing a surgical prosthesis.

The purpose of this investigation was to ascertain the prevalence of erythromycin-resistant strains of *P. acnes* and aerobic micrococci in patients treated with topical erythromycin for moderate inflammatory *Acne vulgaris*.

MATERIALS AND METHODS

Specimens for microbiological evaluation were collected from open and closed comedones and pustules of 30 men, aged 18–30 years, with moderate inflammatory *Acne vulgaris*, who consented to participate in this study. All subjects were in good health and none had received any systemic or topical antibiotic within 4 weeks preceding this investigation.

After thorough cleansing of the skin surface with 70% alcohol, the contents of the various lesions were obtained on sterile lancets and these were used to inoculate trypticase soy broth for aerobes and thioglycollate broth for anaerobes. Samples for bacteriological testing were obtained before and at the conclusion of 4 weeks of topical 2% erythromycin therapy for acne vulgaris. The aerobic plates were incubated for 72 hours at 35°C and the anaerobic plates in N₂ 10% CO₂ for 168 hours at 35°C. Bacterial identification employed standard methods (1, 6, 12).

Sensitivity testing was performed with antibiotic discs containing 50 mg erythromycin. A strain was called resistant if there was no inhibition of growth with such erythromycin discs.

RESULTS

Aerobic micrococci were isolated from 93% (28 of 30) of the subjects whose acne lesions were sampled and *P. acnes* was isolated from the acne lesions of all 30 patients. Prior to treatment, samples of micrococci resistant to erythromycin were isolated from one patient. After 4 weeks of topical erythromycin therapy, samples of cocci resistant to erythromycin were obtained from 18 patients. No *P. acnes* strains resistant to erythromycin were isolated either before or after the topical erythromycin therapy.

DISCUSSION

Topical antibiotics are currently finding wide usage by dermatologists for the treatment of papulo-pustular acne vulgaris. The two most popular of these topical antibiotic preparations are topical clindamycin and topical erythromycin (11).

Although topical antibiotics may be efficacious in the majority of acne patients, many patients show little response to such treatment. The development of resistance by *P. acnes* to such antibiotics has been proposed as a reason for therapeutic failure (7). The current investigation, as well as previous studies (7, 9), failed to demonstrate the induction of erythromycin resistance in *P. acnes* after short-term topical therapy. Crawford et al. (2), nevertheless, isolated *P. acnes* resistant to erythromycin from 4 of 21 patients treated with topical 1% erythromycin for 8 weeks. All of these erythromycin-resistant strains of *P. acnes* were also resistant to clindamycin (2). If such results prove to be commonplace, they would provide at least a partial explanation for frequent failures with topical antibiotics, especially during long-term administration.

The safety of topical antibiotic therapy for *Acne vulgaris* appears to be greater than that of systemic antibiotic therapy. Erythromycin is perhaps the safest of the topical antibiotics, since it possesses a very low sensitizing potential (4) and is not associated with severe adverse reactions such as the pseudomembranous colitis occasionally observed with clindamycin. The ability of short-term topical erythromycin therapy to induce a high degree of resistance in aerobic micrococci raises questions concerning this safety. These micrococci are usually harmless, but can produce life-threatening infections in patients with a surgical prosthesis or an impaired immune response.

An important factor in determining the impact of the development of resistance of *P. acnes* and aerobic micrococci to topical antibiotics, is the kinetics of reconstitution of an antibiotic-sensitive surface microflora. Our investigation did not include any follow-up after treatment was concluded. However, there is some preliminary evidence (2) that normally sensitive strains of *P. acnes* repopulate comedones 1–2 months after topical clindamycin or erythromycin is discontinued.

The widespread usage of topical antibiotics for the treatment of acne has profound effects on the resident microbial flora of the skin. Further study of the long-term ecological effect of these agents is warranted, particularly in view of their widespread use.

REFERENCES

1. Baird-Parker, A. C.: The classification of staphylococci and micrococci from world wide sources. *J Gen Microbiol* 38: 262, 1965.
2. Crawford, W. W., Crawford, I. P., Stoughton, R. B. et al.: Laboratory induction and clinical occurrence of combined clindamycin and erythromycin resistance in *Corynebacterium acnes*. *J Invest Dermatol* 72: 187, 1979.
3. Crowe, J. J. & Ward, O. C.: *Staphylococcus epidermidis* as a cause of meningitis. *Ir Med J* 146: 113, 1977.
4. Fisher, A. A.: Erythromycin, a nonsensitizing topical antibiotic. *Arch Dermatol* 112: 732, 1976.
5. Hammond, G. W. et al.: Combination antibiotic therapy in an outbreak of prosthetic endocarditis caused by *Staphylococcus epidermidis*. *Can Med Assoc. J* 118: 524, 1978.
6. Izumi, A. K., Marples, R. R. & Kligman, A. M.: Bacteriology of acne comedones. *Arch Dermatol* 102: 397, 1970.
7. Leyden, J. J.: Antibiotic resistant acne. *Cutis* 17: 593, 1976.
8. Marples, R. R. & Kligman, A. M.: Ecological effects of oral antibiotics on the microflora of human skin. *Arch Dermatol* 103: 148, 1971.
9. Mills, O. H., Kligman, A. M. & Stewart, R.: The clinical effectiveness of topical erythromycin in acne vulgaris. *Cutis* 15: 93, 1975.
10. Resh, W. & Stroughton, R. B.: Topically applied antibiotics in acne vulgaris. *Arch Dermatol* 112: 182, 1976.
11. Stoughton, R. B.: Topical antibiotics for acne vulgaris. *Arch Dermatol* 115: 486, 1979.
12. Voss, J. G.: Differentiation of two groups of *Corynebacterium acnes*. *J Bacteriol* 101: 392, 1970.

Superficial Actinic Porokeratosis in a Patient Undergoing Long-term PUVA Therapy

Jean Louis Reymond, Jean Claude Beani and Pierre Amblard

Department of Dermatology, University of Grenoble, F-38043 Grenoble Cédex, France

Received May 12, 1980

Abstract. A patient who was treated with PUVA for psoriasis developed disseminated superficial actinic porokeratosis. The significance of this complication is discussed.

Disseminated superficial actinic porokeratosis (DSAP) might be expected as a side effect of PUVA therapy.

CASE REPORT

Patient G. M. L., female, 67 years old, skin type III, has had psoriasis vulgaris since 1942. She has never been treated with arsenic for her disease. Her brother has psoriasis. There is no known family history of porokeratosis.

Standardized PUVA conditions had been used since November 1977, with 40 mg 8-MOP tablets (Meladinine; Promédica, France) and total irradiation 2 h later. The cumulative UVA dose was 611 j/cm². Localized PUVA therapy was also given to the legs after application of 8-MOP 1% solution. The UVA dose was 350 j/cm². Up to December 1979 the total dose applied to her legs was 961 j/cm².

At that time the psoriasis was under control, but various lesions appeared, localized essentially on the anterior surface of both legs. Clinically there were multiple superficial keratotic lesions surrounded by a slightly raised keratotic border. These small circinate lesions enlarged in a centrifugal fashion, the older central portion becoming atrophic and less keratotic (Fig. 1). A histological study of the keratotic rim of this lesion showed a well delimited parakeratotic zone above the spinous layer which displayed several isolated dyskeratotic cells (Fig. 2).

A diagnosis of DSAP was made.

DISCUSSION

This case of actinic porokeratosis during PUVA therapy is the first one observed, to our knowledge.

Disseminated superficial actinic porokeratosis (1) is a dominant autosomic genodermatosis, with some sporadic cases recorded. The disease begins