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SUPERINFECTION INDUCED BY ANTIBIOTICS IN FAMILIAL BENIGN CHRONIC PEMPHIGUS

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Abstract. Two patients with familial chronic benign pemphigus (FBCP) suffered relapses of their dermatitis after initial improvement with antibiotic therapy. New pathogens, resistant to the antibiotic employed, create a vacuum in the cutaneous microflora which can be filled by opportunistic pathogens. Sudden exacerbations during antibiotic therapy should alert the physician to such ecological disruptions. Frequent cultures provide the information necessary for optimal therapy.

Familial benign chronic pemphigus (FBCP) is a genodermatosis in which the skin is predisposed to acantholysis (5). Many stimuli can provoke this response, including ultraviolet irradiation (2), friction, cryotherapy (1), contact dermatitis (6) and other physical forms of trauma. Various pathogenic organisms, both bacteria and yeast-like fungi, may excite and propagate the lesions of FBCP. Consequently, topical or systemic therapy is often useful in management (12). In our experience initial improvement with antimicrobial therapy is often followed by relapse. The present report presents an explanation for such relapses: namely, superinfection by other organisms resistant to the antibiotic resulting in clinical exacerbation.

CASE HISTORIES

Case 1

A 54-year-old white man had had for 15 years a weeping, malodorous dermatitis of the axillae and inguinal folds and at times a similar dermatitis of the antecubital fossae and neck folds. His father had a similar dermatitis. By biopsy and physical examination a diagnosis of familial benign pemphigus was made (Fig. 1). Quantitative cultures revealed the average density of aerobic organisms to be 7.8×10^6 per cm^2; 97% of these were *S. aureus*. This organism was sensitive to ampicillin, chloramphicol, neomycin, penicillin and gramicidin. Topical treatment was instituted with 2.5% chloramphenicol in equal amounts of propylene glycol and ethanol. Within one week exudation had been eliminated and the general appearance greatly improved. Two weeks later, despite continued treatment, a severe relapse occurred. The patient again had a malodorous, weeping dermatitis of the groin and axillae. This time quantitative cultures yielded only *C. albicans*, albeit in enormous numbers. The treatment was changed to Castellani's paint t.i.d. Rapid regression of the dermatitis followed. In an attempt to avoid further superinfections, the treatment was changed to a high strength topical steroid cream which also contained 2% 5,7,dichloro-8-hydroxyquinoline. The latter possesses both antifungal and antibacterial capabilities. This therapy controlled the condition successfully. Several months later the patient travelled to a subtropical resort area in the Caribbean. Preoccupied with pleasures, he failed to use the medication regularly. A relapse occurred promptly. On return to our care, he again showed an oozing dermatitis of the groin and axillae. Cultures indicated a microbial density of 26×10^6 aerobes per cm^2 in the axilla with 85% *Proteus*, the remainder being lactose-fermenting enterobacteria. Castellani's paint again brought about rapid remission of the dermatitis. He was switched again to the steroid–hydroxyquinoline combination and the condition has since remained under control.

Case 2

A 48-year-old man had a recurrent dermatitis on both axillae for 20 years. Biopsy had established a diagnosis of familial benign chronic pemphigus. Prior to our examination he had been treated with ampicillin because cultures had shown large numbers of *S. aureus*. Clinical improvement occurred but after 3 weeks of treatment with 250 mg q.i.d. ampicillin, there was a relapse (Fig. 2). Cultures from both axillae yielded a heavy growth of *C. albicans*. His treatment consisted of topical compresses and a cream containing neomycin, triamcinalone acetonide and nystatin (Mycolog®—Squibb & Sons, New York, N.Y.). The dermatitis regressed within 2 weeks. There was no further follow-up on this patient.

COMMENT

The two patients demonstrate that bacterial successions may cause clinical relapses during antibiotic therapy of FBCP. Patient one had three

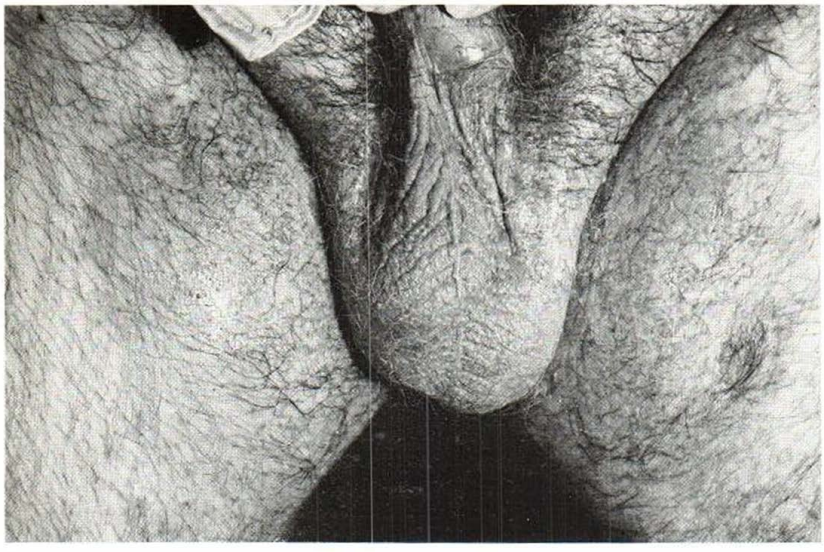

Fig. 1. Exacerbation of FBCP due to heavy overgrowth of *S. aureus*.

exacerbations, each one associated with a different organism, namely *S. aureus*, *Candida albicans* and *Proteus*. The second patient had a relapse of his dermatitis due to *Candida albicans* overgrowth as a consequence of the elimination of *S. aureus* by antibiotic therapy. The clinical picture was the same each time; the disease pattern is constant and clinical signs and symptoms cannot be related to specific pathogens. The selective effect of the antibiotic facilitates the emergence of a resistant pathogen in an essentially pure culture.

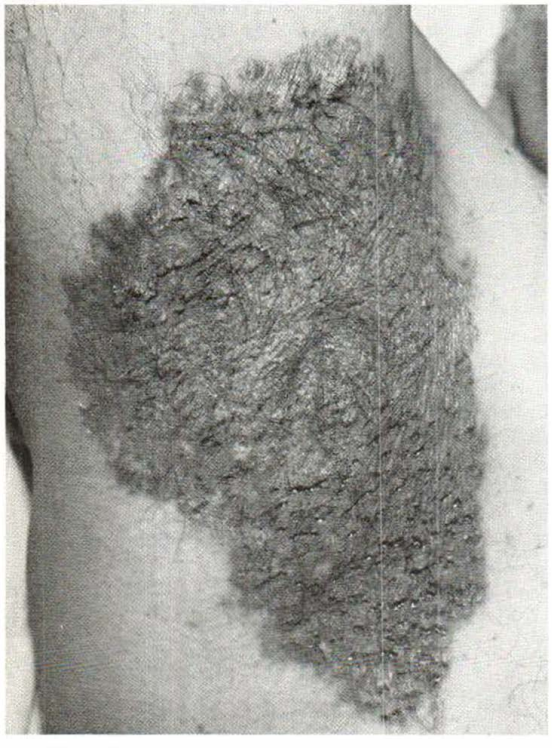

Fig. 2. A heavy overgrowth of *C. albicans* during antibiotic therapy provoked this severe flare of FBCP.

Recently, other examples have come to light in which antibiotics have induced superinfections. These include: 1) staphylococcal enteritis and candidiasis of the intestine following broad spectrum antibiotics (11); 2) gram-negative infections in newborns as a result of total body washing with hexachlorophene detergents (phisohex) (4); 3) mixed gram-negative and monilial intertrigo following intensive use of anti-microbial soaps (3) (Safeguard); 4) gram-negative folliculitis in acne patients under long-term treatment with tetracycline (7); *S. aureus* pyoderma following topical neomycin (8). These instances of cutaneous superinfections parallel a world-wide trend of an increased prevalence of systemic gram-negative infections complicating antibiotic therapy.

In his review of FBCP, Montes stresses the importance of recognizing bacterial infection (10). Presumably the temporary benefit of antibiotic therapy in some of his patients represents the phenomenon of superinfection.

The microflora, whether it be in the nasopharynx, the intestine or skin, exists as a delicately balanced, ecological community. The maintenance of the normal resident flora is important in preventing the intrusion of pathogens (13). Elimination of resident organisms creates an ecological void which may be filled by more virulent organisms. While this principle is self-evident with topical medicaments, it should be realized that oral antibiotics may reach the surface and transform the resident microflora into a resistant population (9).

A theoretical goal of anti-microbial therapy, topical or oral, is to curtail the growth of pathogens and promote the restoration of the resident microflora. We would emphasize the undesirability of total elimination of organisms which normally inhabit the site. A vacuum is almost certain to be repopulated by organisms, some of which may be exotic and dangerous.

We would offer the following guidelines for managing patients with FBCP. Pathogenic organisms are probably the chief exacerbating agents in this disease. The heat and moisture of the axillary and groin regions normally support a dense microflora. With the addition of a serous exudate to such a habitat, the growth of pathogens is greatly enhanced. In the absence of antibacterial therapy, *S. aureus* is the most frequent organism to colonize the area. Initial therapy should therefore include an antibiotic directed against *S. aureus*. The continuation of the antibiotic beyond its immediate benefit is unwise. Such prolonged therapy can lead to ecological escalation. If *S. aureus* is suppressed, the path is cleared for invasion by gram-negatives, notably *Proteus* or *C. albicans*. This process of supplanting one pathogen by another as a result of interference with the normal ecologic balance is apparently open-ended unless one could achieve suppression of all potential pathogens; the latter might include organisms that are for the most part harmless, such as many of the yeast-like fungi, various enterobacteria and even algae. At present, no means are at hand to keep intertriginous areas free of all opportunistic invaders. The goal, therefore, must be to restore the normal, protective microflora, dominantly cocci and diphtheroids, as quickly as possible.

Ideally, intelligent management demands cultures to allow selection of the appropriate antibiotic. When the disease process abates in a week or so, that antibiotic should be withdrawn and an attempt made to suppress the underlying bullous disease with topical corticosteroids. The patient is advised to do everything to avoid friction and sweating. Keeping the axillae dry is an important deterrent to microbial overgrowth, especially of *C. albicans* and gram-negatives. Exercise must be judiciously controlled.

Many practitioners will have to proceed without the benefit of cultures; an awareness of the above ecologic principles will enhance the likelihood of successful management. One might begin with a topical preparation containing a steroid and antibiotics active against the two chief pathogens, *S. aureus* and *C. albicans*. As soon as the disorder comes under control, no antibacterial therapy is permitted (save perhaps bacteriostatic soaps) and a simple low strength topical steroid becomes the mainstay of therapy. Minor flares, following exercise and sweating can be controlled with a few days' use of Castellani's paint.

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