

TRICHOPHYTIN SENSITIVITY OF THE IMMEDIATE WHEEL TYPE

REPORT OF A CASE WITH UNUSUAL MANIFESTATIONS AND RESPONSE TO HYDROCORTISONE

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INTRODUCTION

TISSUE responses arising as a result of hypersensitivity to infecting microorganisms and/or their metabolic products have a well-established immunologic basis, and the microbid is a proved clinical phenomenon in dermatologic allergy. Thus, the familiar allergic "id" reaction seen in patients with cutaneous fungus infections is an accepted clinical entity. Extensive data pertaining to the subject, including the experimental basis for the development of this concept, the immunologic factors involved, and detailed descriptions of clinical types, can be found in comprehensive reviews by Sulzberger,^{1, 2} Peck,³ and Lewis and Hopper.⁴

The etiologic nature of a trichophytid or cutaneous sensitization arising out of either present or past infection with a fungus of the genus *Trichophyton* may be demonstrated by the intracutaneous test with an appropriate trichophytin extract. Here the usual positive reaction is that of the forty-eight-hour delayed, inflammatory, tuberculin-like reaction and only occasionally is an immediate wheal type urticarial response noted. During recent experience with a patient in whom a primary fungus infection was associated with an immediate wheal response and a negative forty-eight-hour delayed reaction to the trichophytin test, other unusual clinical features were noted. It was felt that these observations should be reported for the following reasons: (1) the unusual type and nature of the associated "id" reaction, suggesting a fixed tissue response; (2) recording observations on this clinical manifestation of trichophytin sensitivity might contribute some evidence to the significance of the urticarial immediate skin test, a still unestablished point,^{1, 5} and (3) to record the therapeutic response to the administration of hydrocortisone, since in a review of the literature there cannot be found any previous reports of the effect of adrenal corticosteroids in this clinical state.

CASE REPORT

The patient, a 59-year-old white housewife with a ten-year history of recurrent dermatitis involving (1) the inguinal-vulval-perianal areas and (2) the buttocks, thighs, and flexor surfaces of the elbows and knees, was first seen in June, 1954. The present episode was typical of previous occurrences in regard to the location, appearance, and sequence of

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involved sites. In at least ten known previous episodes the crural area was initially involved and lesions repeatedly appeared on the same sites of the extremities and buttocks after the crural area had been secondarily inflamed by topical medications which either were too irritating or contained ammoniated mercury or benzocaine to which she had contact sensitivity, as later proved by patch tests. During this present episode, however, the secondary areas of fixed cutaneous involvement occurred spontaneously two weeks after the onset of the crural dermatitis which had been treated only with potassium permanganate 1:10,000 wet compresses and zinc undecylenate-undecylenic acid powder, which were tolerated well locally and to which negative patch tests were later demonstrated. The history, including a complete systemic review, was otherwise negative; there was no past history of any atopic diseases, allergic manifestations, drug reactions, childhood eczema, urticaria, or other skin diseases.

When first seen, the crural dermatitis was characterized by large confluent and smaller discrete plaques which were erythematous and lichenified, with sharply demarcated borders and relative healing in the central portions with increased infiltration and scaling at the peripheral portions. The flexor surfaces of the elbows, forearms, and knees, the entire buttocks, and the upper two-thirds of the lateral aspects of both thighs were involved with totally different lesions, which were diffusely and intensely erythematous with a moderate degree of nonpitting edema. The remainder of the complete physical examination was within normal limits.

Laboratory Studies.—A complete blood count and sedimentation rate revealed normal findings, and a urinalysis was negative. Scrapings of the cutaneous lesions of the inguinal and vulval areas on direct examination revealed the typical branched hyphae of pathogenic fungi, which culture on Sabouraud's dextrose agar proved to be *Trichophyton gypsum*. Fungi could not be demonstrated in the lesions of the knees, buttocks, or thighs.

Intracutaneous tests to trichophytin extract on uninvolved portions of the skin showed (1) a 3+ immediate wheal occurring within fifteen minutes and (2) a negative reaction after twenty-four and forty-eight hours. Similar tests were obtained on the previously involved skin sites at a later date after healing had occurred. Passive transfer studies with the patient's serum, according to the Prausnitz-Küstner technique, elicited a 1 to 2+ equivocal reaction on testing recipient sites with the trichophytin extract.

Because of the severity and extent of the secondarily occurring erythematous-edematous sterile skin lesions believed to have arisen on a hypersensitive trichophytid etiology basis, the patient was given a therapeutic trial with hydrocortisone. A course of this oral therapy was started with divided doses totaling 80 mg. daily on the first day and gradually diminishing by 10 mg. daily until a dose 40 mg. had been reached by the fifth day. This had resulted in a dramatic clearing of the lesions on the buttocks, thighs, forearms, and flexor aspects of the elbows and knees by the fourth day of treatment. The crural dermatitis was unaffected by the orally administered hydrocortisone and gradually subsided and cleared after two weeks of treatment with wet compresses of potassium permanganate 1:12,000 solution and topical applications of a 1 per cent aqueous gentian violet solution. On prophylactic applications of proprionate-caprylate powder to the crural area, there have been no recurrences of lesions during the past year and one-half. However, during that period the patient used ointments containing benzocaine and dibucaine applied to the anal area for external hemorrhoids, as prescribed by a physician who was not aware of her contact sensitivity to these local anesthetic agents. When seen following this, she exhibited an erythematous papulovesicular eruption typical of contact dermatitis of the buttocks and perianal area but had no secondarily occurring erythematous-edematous lesions of the extremities, as were observed in association with the previously occurring crural mycotic infection.

COMMENT

Although the clinical pattern and appearance of this erythematous-edematous cutaneous involvement, repetitiously associated with recurrent tinea cruris,

possessed several characteristics not typical of the classical dermatophytid, the diagnostic impression of a possible "id" reaction was nevertheless considered justified by satisfying the following criteria.³

1. The causative fungus organism was demonstrated by direct microscopic observation of skin scrapings and culture from a focus resembling a typical manifestation of cutaneous fungus infection.
2. The organism cultured from the primary lesion was of a pathogenic species, *Trichophyton gypseum*.
3. The intracutaneous test with trichophytin revealed a positive reaction at the test site.
4. The associated "id" cutaneous lesion developed subsequent to the primary infection.
5. Fungi could not be demonstrated by direct microscopic observation of scrapings from the lesions of the dermatophytid, and positive cultures were not obtained.
6. The associated secondary ("id") lesions, after subsiding, did not recur when the primary focus of infection had been eradicated.

Only the requirement for a positive blood culture of the infecting pathogenic fungus was not met and, in this regard, it has been felt that this is too drastic a dictum.⁴

Reasons for the clinical type and appearance of these secondary erythematous-edematous lesions associated with a primary cutaneous mycotic infection are not apparent. Similarity to the erysipelas-like "ids" reported by Sulzberger, Rostenberg, and Goetze⁶ is suggested, but the signs of systemic toxicity and an inflammatory type of cellulitis or lymphangitis noted in their patients was not characteristic of this instance. Possibly this may bear a clinical relationship to the infrequently reported urticarial⁷⁻⁹ or erythrodermic¹⁰ "id," but a further analogy is impossible without a knowledge of the basic immunologic mechanisms involved. The clinical appearance of these lesions is compatible with the type of suspected underlying sensitivity as evidenced by the immediate trichophytin wheal test, for it is not surprising that an urticarial wheal-flare type test response would have as its clinical counterpart a similar pathologic picture in the form of tissue edema and erythema upon exposure to the same antigen, in larger doses, naturally elaborated during the course of active infection.

The factors—physiologic, anatomic, pathologic, or immunologic—that may have been operative in determining the localization of these secondary lesions are likewise not apparent. Lymphatic or venous drainage of trichophytin from its natural source of origin, as in those patients reported by Sulzberger, Rostenberg, and Goetze,⁶ could not explain the limited localization of the "id" response to the thighs, buttocks, forearms, and flexor surfaces of the knees and elbows in this primary crural infection. In this instance, as in the cases of other patients with cutaneous fungus infections, the secondary "id" lesions are often precipitated by irritation of the primary mycotic focus. Superimposed allergic

contact dermatitis was not a factor in this episode and it is noteworthy that these secondary sites did not become involved when the patient experienced a severe contact dermatitis on the same perianal-inguinal-vulval areas due to sensitivity to local anesthetic drugs when applied to these sites at a time when the skin was normal. The clinical picture of limited localization, definite association and time relationship between the primary and secondary lesions, and the pattern of long-standing repetitious response in this manner would suggest some type of fixed tissue sensitization, such as occurs in fixed drug eruptions.

The fact that some few persons may exhibit an urticarial intracutaneous reaction to trichophytin has previously been reported by Sulzberger and Kerr,⁸ Marcussen,¹¹ and Lewis and co-workers,¹² and even the occurrence of passive serum transfer reactions has been noted in some instances.^{7, 8, 11, 13} Rajka¹⁴ has observed its occurrence during the course of trichophytin desensitization. When found, however, they are more common in *Trichophyton purpureum* infections than in those due to *Trichophyton gypseum*.¹² The considered significance of the urticarial reaction is not clear^{1, 5} and it has never been determined whether these test responses and findings of reagins are more common in atopic than in nonatopic persons.^{1, 5} Trichophytin does possess antigenic properties capable of inducing anaphylactic sensitization¹³ and true allergic sensitization has been demonstrated by Sulzberger and Wise¹⁵ in a case of asthma and allergic rhinitis. Urticaria has, on rare occasions, been reported in association with this possible etiological factor.⁷⁻⁹

There is no evidence that this patient with a negative delayed response, but showing an immediate wheal-flare reaction to trichophytin, was an atopic person. It is difficult, therefore, to determine whether trichophytin may have been acting as a true allergen in this instance. It is impossible to prove or disprove that this intracutaneous test may have been a false positive reaction, since this occurred with trichophytin extracts of three different sources (used to avoid any limitations of species specificity of the extracts¹³) and these were employed in concentrations found to be nonreactive in the skins of both atopic and normal persons in control studies. Recipients chosen for the passive serum transfer studies were not only trichophytin-negative nonallergic persons, but they also had no evidence of either active or a past history of recent fungus infections, in view of Sulzberger's⁷ studies demonstrating the peculiar resistance of such persons to accept passive sensitization with reagins to trichophytin. Apparently there are three basic types of trichophytin sensitization that may represent clinical manifestations of distinct immunologic phenomena: (1) the classic delayed type which is manifested by the forty-eight-hour inflammatory delayed response to the intracutaneous test and may be mediated, like tuberculin sensitivity which it resembles, through a "cellular factor"; (2) the immediate wheal type intracutaneous response associated with circulating reagins as a manifestation of true atopic sensitization; and (3) the contact eczematous type as demonstrated by positive patch test.¹⁶ It is not clear whether this patient with an erythematous-edematous "id" reaction and positive wheal type intracutaneous test may in some way be related to Group 1 or to Group 2 in which

the serum fraction containing the skin-sensitizing antibody was not capable of being passively transferred or in which the reagin titer was too low to be definitely demonstrated by this technique. It is entirely possible that she may belong to a fourth and distinct category whose tissue sensitization may be mediated through an unrelated and ill-understood mechanism.

In contrast with all previous episodes that occurred during the past ten years, these secondary erythematous-edematous lesions responded much more rapidly and effectively following the oral administration of hydrocortisone than with other forms of therapy employed during previous exacerbations. Although we can find no previous reports on the use of adrenal corticosteroids in the treatment of an eruption of this type to suggest its effect, the response was not too surprising in view of the reports of the anti-inflammatory action of the adrenal cortical steroids, especially in anaphylactoid edema¹⁷ and their well-known beneficial effect in the treatment of acute urticaria and angio-edema due to other allergens. Saunders¹⁸ has reported a dramatic therapeutic response of vesicular dermatophytids to oral cortisone, but I have had no experience with adrenal cortical steroid therapy in this condition. The primary cutaneous crural fungus infection itself was unaffected by the administration of hydrocortisone. This would seem to parallel the effects of adrenal corticosteroids noted in experimentally induced cutaneous fungus infections in laboratory animals, as described by Jadassohn, Mach, and Nardin.¹⁹ However, similar experimental studies by Kligman and associates²⁰ would indicate some adverse effects. This relationship in clinical states requires further evaluation.

SUMMARY

A case report is presented of a 59-year-old white woman with a ten-year history of recurrent episodes of crural fungus infections with secondary erythematous-edematous lesions of the buttocks, thighs, forearms, and flexor surfaces of the elbows and knees. *Trichophyton gypseum* was cultured from the crural lesions, and intracutaneous testing with trichophytin extracts resulted in an immediate positive wheal-flare response and a negative forty-eight-hour delayed type reaction. The presence of circulating reagins to trichophytin could not definitely be proved.

Evidence is presented to suggest that this represents an unusual type of dermatophytid characterized by fixed tissue sensitization.

The secondary erythematous-edematous "id" lesions responded dramatically to orally administered hydrocortisone, while the primary fungus infection was unaffected by the adrenal corticosteroid therapy.

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