Thymopentin in Chronic *Trichophyton rubrum* Infection

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**Introduction**

Cellular immunity is of great importance in host defense against fungal diseases, and chronic mycotic infections are considered to occur mainly in patients with T cell dysfunction. This holds true not only for chronic mucocutaneous candidiasis but for chronic dermatophytic infections as well, particularly with regard to *Trichophyton rubrum* [1]. Both in natural and experimental infections with *T. rubrum* it has been shown that the local inflammatory response in the infected area appears simultaneously with delayed-type hypersensitivity reactions, as can be demonstrated by skin testing [2]. In chronic *T. rubrum* infections T cell dysfunction associated with negative delayed skin reaction tests to various antigens has occasionally been reported [3]. In such cases inflammatory response to dermatophytic infections is usually very mild. Because of the potential of thymopentin to restore immune responses in compromised hosts [4, 5], we decided to try this immunomodulating compound in 2 cases of chronic *T. rubrum* infection in whom traditional antifungal treatment had either failed or been impossible due to side effects. Prior to thymopentin therapy both patients had negative or very mild responses to a battery of intradermal delayed-type tests. They showed also only mild inflammatory reactions.

**Case Histories**

*Case 1*

A 48-year-old male had suffered from chronic *T. rubrum* infection of the soles for 12 years. He was not atopic, and there was no evidence of any concomitant skin or systemic disease. Griseofulvin treatment had to be discontinued twice due to gastrointestinal complications, and topical treatment with keratolytics, with Whitfield’s ointment and imidazole drugs – often in combination – had produced only limited effects (fig. 1).

Thymopentin treatment was started with 50 mg s.c., three times weekly and during the first 3 weeks combined with imidazole cream. After this period of time the patient experienced a clear-cut amelioration of erythema and hyperkeratosis and, therefore, he stopped the topical treatment. He continued on thy-
Fig. 1. Chronic plantar T. rubrum infection for 12 years in a 48-years-old male with erythema and dry, rhagadiform hyperkeratosis before thymopentin treatment.

Fig. 2. The same area after 6 weeks thymopentin treatment in almost complete remission with limited slight dry hyperkeratosis but without erythema.

Thymopentin alone for further 3 weeks; at the end of totally 6 weeks of treatment he was substantially improved but not completely healed (fig. 2). After cessation of therapy he improved further, and 6 weeks later an almost complete remission was observed, with only a slight erythema remaining. The first relapse did not occur until 4 months later. Ten months after thymopentin was discontinued his skin condition again looked like the pretreatment state. At this point thymopentin therapy was introduced again, using the same dose regimen as previously for another 6-week period. A quite similar response occurred again, i.e., a subtotal remission (approximately 75%) was noted after 6 weeks of treatment, whereas the lesions were completely healed after having been off therapy for 6 weeks. The remission lasted for about 7 months; during this time he only used emollients topically. After this period of time his condition gradually worsened again and eventually reached the pretreatment state. Even in periods of complete clinical healing the fungi were still present on the skin, as verified by both direct microscopy and cultures.

Case 2
A 55-year-old female had suffered from tinea corporis for about 20 years. The disease presented itself as plaques of various size, characterized by scaling and infiltration, accompanied by slight erythema of the trunk, arms and legs. Two years treatment with griseofulvin had yielded clear-cut regression of clinical signs, but no complete remission of the lesions was achieved; eventually this therapy had to be stopped due to liver toxicity of the drug. Topical treatments with Whitfield’s ointment and imidazole cream were of limited value. Thymopentin treatment was now initiated, using the same dose regimen as outlined above, this time, however, in combination with Whitfield’s ointment. Within 3 weeks an almost complete remission was achieved, and 3 weeks later the lesions were healed. At this point thymopentin was withdrawn, but still the beneficial effect lasted for further 6 weeks before the first relapse was observed.

The patient was started on thymopentin therapy again (same dose regimen), but this time combined with imidazole cream topically. Again the same response pattern as described above was observed; subtotal clearing of the lesions after 3 weeks and complete healing after 6 weeks were achieved. The clinical remission lasted for 7 months, then the skin lesions gradually reappeared. Also in this patient the dermatophytes persisted on the skin, in spite of the excellent clinical responses.

Discussion
Our preliminary observations in 2 patients suffering from chronic T. rubrum infection clearly indicate that thymopentin may