

Topical Antifungal Therapy Combined with Nail Abrasion for the Treatment of Dermatophytoma: Single-Center Results — A Secondary Publication

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Abstract: *Objective:* Recently, topical antifungal agents have become available for the treatment of dermatophytoma. However, there are few reports of topical onychomycotic agents in combination with debridement of dermatophytoma. *Methods:* Twelve patients with dermatophytoma diagnosed and treated between April 2017 and March 2020 at the Department of Dermatology, Kansai Rosai Hospital were selected, including two patients with lesions on both toe nails and 14 nails. At the initial visit, the affected nail plate was removed and topical treatment was administered. The observation was terminated when the lesions were completely healed within 1 year. If the patients were not completely healed, the initial efficacy was determined at the date of the first visit closest to 1 year after the start of treatment. The second efficacy evaluation was conducted at the last visit or when the concomitant drug was changed. *Results:* Three patients dropped out of the study before the time of the initial efficacy evaluation. In the second efficacy evaluation, eight nails were completely healed, one nail was significantly healed, and one nail was effective. *Conclusions:* Dermatophytoma can be treated with topical onychomycotic agents in combination with surgical debridement to improve efficacy.

Keywords: Onychomycosis; Dermatophytoma; Nail abrasion; Topical antifungal drugs

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1. Introduction

Dermatophytomas are characterized by the melting of the nail plate and the formation of a cavity in which keratin, mycelium, and fungi are clustered. Clinically, the lesions are white to yellowish brown, linear or mottled, including wedge-shaped lesions ^[1]. The disease is resistant to treatment, with debridement as the basic treatment. The reason for resistance to treatment is thought to be that the fungus forms cavities that do not allow sufficient concentrations of drugs to reach the fungus ^[1], that the fungal colonies form biofilms, and that the spore-forming elements are dormant ^[2]. Although the treatment of tinea onychomycosis has advanced with the availability of new antifungal agents, patients may still experience refractory dermatophytoma even with these drugs. Debridement is recommended as adjunctive therapy for dermatophytoma ^[3], but there are few studies on the effectiveness of combined treatment with cutting in multiple cases using topical onychomycosis treatments.

2. Methods

2.1. Subjects

Twelve patients (8 males, 4 females, mean age 73 years) diagnosed with dermatophytoma who visited the Department of Dermatology, Kansai Rosai Hospital, between April 2017 and March 2020 underwent cutting treatment, and a total of 14 nails were cut. The diagnosis was confirmed by cutting the nail surface, observing the formation of a cavity in the nail surface, and confirming the presence of a fungal colony containing spore-shaped elements (**Figure 1**) by direct KOH microscopy of the internal keratinocyte.

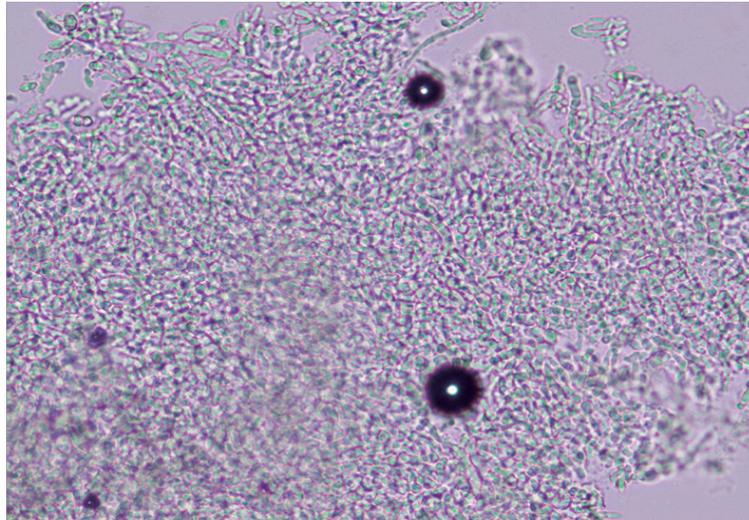


Figure 1. Direct specimen of dermatophytoma ($\times 200$) showing clumps of target nail No. 1: Short, thick mycelial and sporophytic fungal elements are clumped together

2.2. Usage of onychomycosis treatment

Topical therapy:

- (1) 10% efinaconazole topical nail solution once a day
- (2) 5% luliconazole topical nail solution once a day

2.3. Cutting of the affected nail bed

At the initial visit, the affected nail plate was removed as much as possible using a grinder (Urawa Industries G3, b-2, b-3), and the lesion was opened. Cutting was also performed during the course of the treatment when it was considered necessary.

Clinical efficacy was determined by taking photographs at the time of examination and quantifying the entire nail surface area and the area of the opacity using ImageJ, and using the following efficacy criteria.

2.4. Clinical efficacy criteria

- (1) Ineffective: Change in the area ratio of the nail plate (opacity area of the nail plate/area of the nail plate) decreased or increased by less than 30%.
- (2) Effective: Decrease of more than 30% and less than 60% in the area ratio of nail plate opacity.
- (3) Markedly effective: Change in the area ratio of nail plate opacity is greater than 60% and less than 60% opacity disappearance.
- (4) Healed: The nail plate opacity area disappeared and no fungal elements were observed by direct microscopic examination.

The efficacy was evaluated on the date of the visit closest to 1 year after the start of treatment and on the

date of the last visit or change of concomitant medication. If the patient was cured, the duration of the cure was also noted.

3. Results

Three patients dropped out of the study before the time of the initial efficacy evaluation. Among the ten nails, seven were completely healed and three were inoperable at the time of the initial efficacy evaluation. The results of concomitant drug treatment showed that efinaconazole cured five nails, luliconazole cured two nails and failed to cure three nails, and the second efficacy evaluation showed that eight nails were completely cured, one nail was markedly effective, and one nail was effective (**Table 1** and **Figure 2**). Photographs of representative cases are shown in **Figure 3**.

Table 1. All target nail progress

No.	Age and sex	Claw	Cultivation result	Antifungal	Evaluation of the initial clinical efficacy (period)	Progress (period)
1	77 years old male	Left big toe	T. interdigitale	EFCZ	Healed (11 months)	
2	70 years old male	Left big toe	T. interdigitale	EFCZ	Healed (5 months)	
3	52 years old female*	Left big toe	T. interdigitale	EFCZ	Hospital visits discontinued (0 months)	
4	52 years old female*	Right big toe	T. interdigitale	EFCZ	Hospital visits discontinued (0 months)	
5	71 years old female	Right big toe	Negative	EFCZ	Healed (11 months)	
6	76 years old male	Right big toe	Unassessed	EFCZ	Healed (5 months)	
7	72 years old female	Right big toe	Contamination	EFCZ	58% decrease in hospital visit discontinuation (3 months)	
8	70 years old female	Right big toe	Negative	EFCZ	Healed (8 months)	
9	89 years old male	Left big toe	T. interdigitale	LLCZ	Hospital visits discontinued (0 months)	
10	71 years old male	Right big toe	Unassessed	LLCZ	Ineffective (13 months)	Healed (22 months)
11	72 years old male**	Left big toe	Unassessed	LLCZ	Healed (6 months)	
12	72 years old male**	Right big toe	Unassessed	LLCZ	Ineffective (13 months)	Markedly effective (41 months)
13	81years old male	Right big toe	Unassessed	LLCZ	Healed (10 months)	
14	70 years old male	Right big toe	Unassessed	LLCZ	Ineffective (13 months)	Effective (32 months) then healed with EFCZ (36 months)

Abbreviation: EFCZ, efinaconazole; LLCZ, luliconazole; *,**same patient

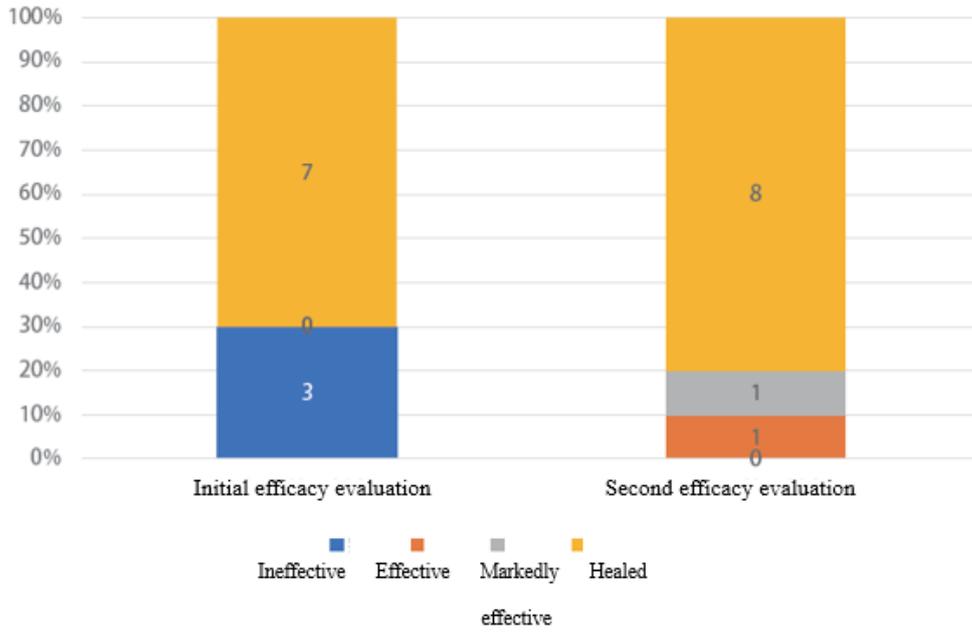


Figure 2. Target nail evaluation of first (approximately 1 year) and second efficacy evaluation (n = 10)



Figure 3. The clinical course of typical cases

4. Discussion

In 1998, Roberts and Evans first described dermatophytoma as a keratinous aggregate with thick walls and abnormal-looking mycelium and sporophytic elements forming clumps ^[1]. Clinically, it is an area of mottled or linear opacity that is clearly demarcated from the surrounding area. We consider that debridement may be necessary for antifungal drugs to be effective because they do not penetrate in sufficient concentrations. Dermatophytoma is a fungal mass that is less in contact with the nail bed than distal marginal subungual onychomycosis, and therefore, the drug does not reach the nail bed sufficiently ^[3]. It is also speculated that the clumps form biofilms and the spore-forming fungal elements are dormant, making them resistant to treatment ^[2]. A study of 199 patients treated with oral terbinafine ^[4] showed that dermatophytoma had a high odds ratio of not being cured (OR 3.453; 95% CI: 1.170–10.197). Thus, dermatophytoma is generally recognized as being difficult to cure, and debridement is recommended prior to treatment ^[5]. The purpose of debridement is to eliminate the causes of dermatophytoma refractoriness. There are few reports on whether the treatment of dermatophytoma is more effective when combined with debridement. In Japan, Ninomiya reported that nine patients with wedge-shaped dermatophytoma were completely cured by the combined use of itraconazole pulse therapy and surgical removal, with the exception of three patients who dropped out of the study ^[6]. In our study, all dermatophytoma lesions had disappeared by the 16th month except for the cases that had dropped out (**Figure 4**). However, there were cases in which other areas remained cloudy or worsened even after the dermatophytoma lesions disappeared, resulting in a low rate of complete healing and a time lag between the disappearance of dermatophytoma lesions and complete healing.

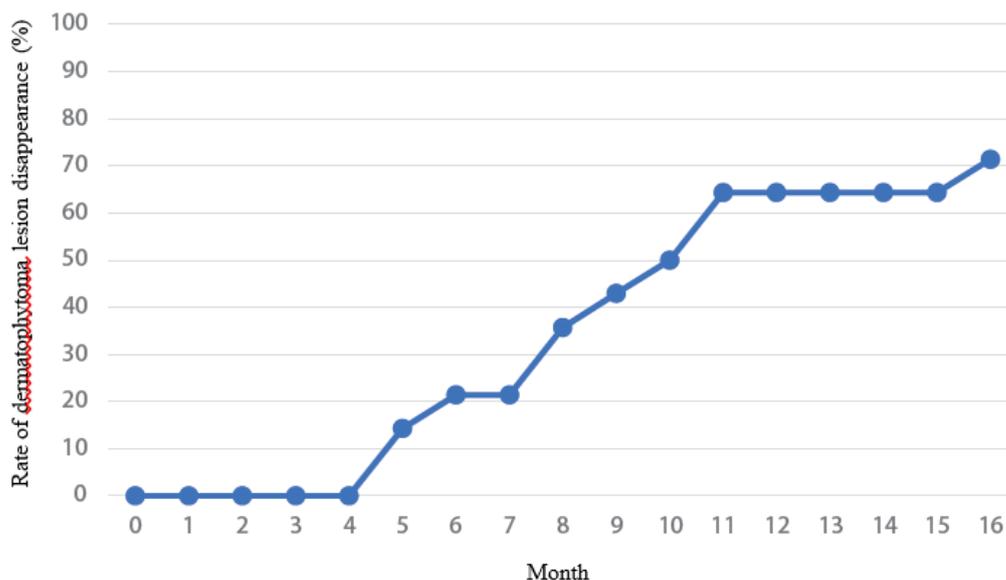


Figure 4. Change over time in the rate of dermatophytoma lesion disappearance (number of nails with dermatophytoma disappearance/total number of nails covered), n = 14

In recent years, new antifungal drugs have been launched one after another to treat onychomycosis. For example, 10% efinaconazole nail liquid for topical use in 2014, 5% luliconazole nail liquid for topical use in 2015, and oral fosravuconazole capsules in 2018 became available in Japan. Casey *et al.* reported the results of patients who used 10% efinaconazole topical solution for onychomycosis, excluding two dropout cases. It was reported that 13 of 19 patients with dermatophytoma (including one patient with two affected nails) were healed at 58 weeks (< 10% nail plate opacity and negative direct microscopy) and all dermatophytoma lesions had resolved ^[7]. Shimoyama *et al.* conducted a single-center, retrospective study of 109 patients with tinea onychomycosis treated with foslavuconazole. 12 of 21 patients with dermatophytoma were completely healed at

the last visit without special treatment (mean duration 34.3 ± 11.1 weeks). This is contrary to the conventional view that medical therapy without treatment for dermatophytoma is ineffective. Fosravuconazole may be effective against dermatophytosis without additional treatment.

The availability of highly effective tinea onychomycosis drugs has reduced the need for therapeutic innovations, but there is still room for innovations in the treatment of difficult-to-treat forms. The present study is a retrospective review of actual treatment and clinical practice in our department. The results showed that 50% (7/14) of the patients were completely cured in about 1 year, and 57.1% (8/14) were completely cured at the second evaluation. This indicates that the combination of cutting and topical onychomycosis treatment for dermatophytoma is as effective as oral fosravuconazole treatment without any special treatment. The efficacy of topical 10% efinaconazole solution without special treatment for longitudinal spikes, which are not completely identical to dermatophytoma but seem to overlap with the linear form of dermatophytoma for the most part, has also been reported^[9]. 82 cases were studied and the spike lesions disappeared in about 80% of the patients at 72 weeks. The complete healing rate ranged from 3–40% at 48 weeks. Although not directly comparable, the complete healing rate was high in the autologous cases at the same time period, and the addition of cutting may increase the efficacy of the procedure.

There were many cases of treatment discontinuation, and one patient with two lesions did not come to the hospital after the initial treatment. We felt that adherence to treatment of tinea onychomycosis is a serious problem. In this study, we showed that the combination of cutting and topical onychomycosis treatment for dermatophytoma was effective in eradicating the lesions and was as effective as oral fosravuconazole therapy. With the availability of new antifungal agents, the effectiveness of adjuvant therapy should be reaffirmed, although the use of such therapy has become less common.

Disclosure statement

The author declares no conflict of interest.

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