

Cryosurgery as an adjuvant treatment in sporotrichosis: a three-case report

Criocirurgia como tratamento adjuvante na esporotricose: relato de três casos

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ABSTRACT

Sporotrichosis is a disease caused by the dimorphic fungus *Sporothrix* spp. The number of cases has been increasing, notably in the city of Rio de Janeiro, Brazil, where it is now considered a public health problem. The recommended treatment employs antifungals, however in case of persistence of the lesions or when there is contraindication, cryosurgery is an option, since the fungus is sensitive to extreme temperatures. The authors report 3 cases of sporotrichosis treated for longer than 6 months with itraconazole and/or potassium iodide, all yielding incomplete response and where cryosurgery was successfully used as an adjuvant treatment.

Keywords: sporotrichosis; opportunistic infections; cryosurgery

RESUMO

*A esporotricose é doença causada pelo fungo dimorfo *Sporothrix* spp., e o número de casos vem aumentando, principalmente na cidade do Rio de Janeiro, onde hoje é considerada um problema de saúde pública. O tratamento recomendado é com antifúngicos, mas em caso de persistência das lesões ou quando houver contraindicação, a criocirurgia é opção, pois o fungo é sensível a temperaturas extremas. São relatados três casos de esporotricose tratados com itraconazol e/ou iodeto de potássio durante mais de seis meses com resposta incompleta, nos quais a criocirurgia foi usada com sucesso como tratamento adjuvante.*

Palavras-chave: esporotricose; infecções oportunistas; criocirurgia

INTRODUCTION

Sporotrichosis is a disease caused by the inoculation of the dimorphic fungus *Sporothrix* spp. on the skin, usually as a result of handling contaminated soil and vegetables.^{1,2} In addition to the rural manifestation, currently it is often urban, with the transmission occurring through infected cats, which is the most important source of contamination in the Brazilian city of Rio de Janeiro.²

Of the clinical forms of sporotrichosis – extracutaneous, localized/fixated, and lymphocutaneous – the latter is the most frequent in humans and emerges with nodules and gums along the lymphatic vessels, progressing to ulceration in the affected body areas.^{1,2} The main tests for diagnosis are the mycological (mainly culture), the histologic and molecular biology.¹

Different drugs have been used in the treatment of sporotrichosis. The choice of the medicament depends on the clinical form, patient's morbidity, side effects and drug

Case report

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interactions. The objective of the present study is to describe 3 cases of sporotrichosis, confirmed by mycological test and treated with itraconazole and / or saturated solution of potassium iodide (KI) for longer than 6 months, in which cryosurgery with liquid nitrogen (LN) was used as an adjuvant treatment.

CASE REPORT

Case 1: A 53-year old male patient residing in the Brazilian city of Rio de Janeiro presented a nodular lesion with 1cm in diameter on the dorsum of the left hand, and a rounded erythematous plaque on the left elbow. After 10.5 months of treatment with 200 mg/day itraconazole, the lesions had little regression (Figures 1A and 1B), with cryosurgery having been indicated. The device used was the Cry-Ac® (Brymill, Ellington, USA), with the intermittent spray technique, tip A, central solid pattern, with a 0.5 cm margin, two cycles of freezing and thawing observing a 4-minute interval between them (Figure 1C). After 2 weeks, the lesion showed healing (Figure 1D). The patient completed 13 months of use of itraconazole and moved to another city, with the follow up having been lost.

Case 2: A 15-year old male patient, student, residing in the Brazilian city of Rio de Janeiro, area of Belford Roxo described the reappearance of nodules with crusts on the third, fourth and fifth fingers and dorsum of the left hand over cicatricial lesions of sporotrichosis (Figure 2A) one month after the completion of treatment with KI, followed by 200 mg/day itraconazole for six months. Itraconazole was reintroduced and 3 sessions of cryosurgery with LN carried out observing intervals of one month, using the Cry-Ac® device, intermittent spray technique, nozzle B, central solid pattern with 2 cycles of freezing and thawing, with 4-minute intervals between the cycles (Figure

2B). Also, the use of itraconazole was recommended for an additional month, making for a total of 10 months. Two months after the procedure, the patient presented scars (Figure 2C). The patient remains free of active lesions of the disease during 3 years of follow-up.

Case 3: Cryosurgery was indicated for a 59-year old female patient, maid by occupation, residing in the Brazilian city of Rio de Janeiro. The indication ensued the use of itraconazole for one year and seven months (100 mg/day for 7 months, and 200 mg/day during the remaining of the period) for the treatment of a resistant ulcerated lesion, without signs of healing (Figure 3A). One session of cryosurgery was carried out with the Nitrospray® device (Criotécnica, Campinas (SP, Brazil), contact probe with 2 cm in diameter, two cycles of freezing and thawing observing a 4-minute interval between the cycles, after total thawing (Figure 3B). The lesion receded (Figure 4A) and after 3 months showed a scar (Figure 4B).

DISCUSSION

Sporotrichosis is a subcutaneous mycosis with universal distribution and increasing number of cases. ¹ Since 1997, the State of Rio de Janeiro is going through an zoonotic epidemic / endemic with more than 5,000 human cases having been di-

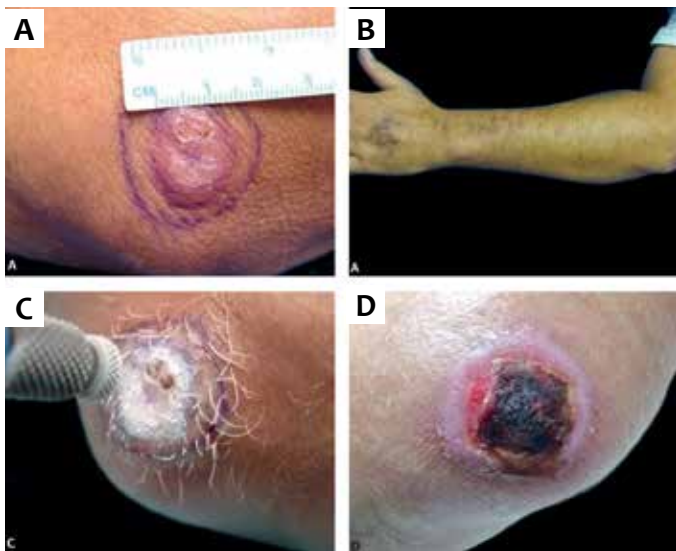


FIGURE 1: **A:** Erythematous plaque of 1.5 cm in diameter with a central crust, located on the left elbow. **B:** Presence of lymphatic cord from the dorsum of the left hand up until the lesion in the left elbow. **C:** Cryosurgery with the device Cry-Ac® / Brymill -USA, spraying technique, tip A. **D:** Ulcerated crusted lesion 2 weeks after cryosurgery



FIGURE 2: **A:** Nodules with crusts on the third, fourth and fifth fingers and dorsum of the left hand, over cicatricial lesions of sporotrichosis. **B:** Exulcerated lesions and erythematous plaque on left hand 15 days after cryosurgery. **C:** Cicatricial lesions two months after cryosurgery



FIGURE 3: **A:** Ulcer with clean and erythematous background, and 2.5cm in diameter, on the back of the right hand **B:** Cryosurgery with the device Nitrospray® (Criotécnica, Campinas (SP), Brazil), contact probe, two cycles of freezing and thawing, 4mm margin



FIGURE 4: **A:** Healing ulcerated lesion with granulation tissue two months after cryosurgery. **B:** Scar three months after cryosurgery

agnosed at the National Institute of Infectious Diseases Evandro Chagas, a REFERENCES center in the city.² Reporting the disease is compulsory.

Itraconazole is the treatment of choice for sporotrichosis, however other substances can also be used: saturated KI solution, terbinafine, fluconazole, ketoconazole and amphotericin B.^{1,3} The average duration of treatment is 3 months, and the criterion for cure is clinical, corresponding to the healing of the lesions and the disappearance of erythema and crusts.³ *Sporothrix spp.* is sensitive to temperature, both to excessive heat and cold. As a result, cryosurgery with LN can be used as an adjuvant to traditional treatment.

Cryosurgery is effective in the treatment of various benign, pre-malignant and malignant cutaneous diseases. It can be used as an isolated treatment or as an adjuvant to conventional or medicated surgical treatments, as in fungal infectious diseases.^{4,6} This form of treatment is based on the selective destruction of cells or tissues through freezing, which depends on the minimum temperature reached during cryogenic injury. In order to obtain a severe injury, the freezing process is maintained for a longer period, reaching -20°C to -30°C , resulting in necrosis. The cryosurgery application techniques depend on the lesion's type, shape, size and location, as well as on the cryosurgeon's experience.^{4,6} The following techniques can be used in sporotrichosis: intermittent spraying with central solid pattern and tips A or B (Cry-Ac®) and tips 8, 9 and 10 (Nitrospray®); confined spraying using open cones for deepening the freezing process without causing lateral damage to the round lesions; and the solid contact technique, which uses previously frozen solid tips (probes) of varying diameters, in flat areas and ulcerated lesions. The lateral margin ranges from 3mm to 4mm, and the freezing

time varies depending on the size of the lesion. Two cycles of freezing and thawing (in the minimum duration ratio of 1:3) are recommended, with a 4-minute interval between the cycles, and sessions every 30 days or with healed lesions.

Ferreira *et al.* described 9 patients with lymphocutaneous and localized sporotrichosis treated with LN (two cycles of 15 seconds and an average of 2.2 sessions at monthly intervals) after having undergone prior treatment with KI, itraconazole (isolated or combined with terbinafine) (Table 1).⁷ Moraes *et al.* cited a case of resistance to the use of KI and itraconazole that experienced regression of signs of the disease activity and good development of healing after cryosurgery (Table 1).⁴ Bargman also reported 3 cases of the fixed form that experienced cure (Table 1).⁸ The present article describes 3 patients who had active sporotrichosis lesions for over 6 months after previous treatment with KI and / or itraconazole, experiencing therapeutic success after undergoing cryosurgery (Table 1).

The combination of cryosurgery with itraconazole for the treatment of feline sporotrichosis lends effectiveness and swiftness to the therapy. Souza *et al.* found clinical cure in 84.6% of cats treated with the combination therapy for an average duration of 32 weeks, decreasing the cost and side effects of antifungals.⁹

It is worth noting that the accessories used in cryosurgery, such as probes and open tips, must be sterilized in autoclave or ethylene oxide.

Furthermore, the fact that sporotrichosis is a zoonosis with a larger number of cases caused by infected animals, implies that the disease should be diagnosed and treated early with a view to stop the epidemiological chain.

TABLE 1: Profile of the cases with sporotrichosis treated with cryosurgery

Author,Year	Gender	Age (years)	Clinical form	Medication, Total duration	Number of cryosurgery sessions	Follow-up without recurrence
Bargman, 1995	M	60	fixed	KI, 8 weeks	11	24 Months
	F	12	fixed	Absence of previous treatment	12	24 Months
Morales et al, 2008	F	58	fixed	Absence of previous treatment	4	18 Months
	M	ND	fixed	Itraconazole and KI, NA	1	ND
Ferreira et al, 2010	5 Patients:itraconazole weeks 28.8 *		Lymphocutaneous and fixed	1 patient: KI 12 weeks 3 Patients :itraconazole 21.2weeks *;andterbinafine,16 weeks *	2,2	ND
	7 F	45				ND
	2 M	45				ND
Secchin et al	M	53	lymphocutaneous	Itraconazole,52 weeks	1	ND
	M	15	fixed	KI, 4 weeksand Itraconazole,40 weeks	3	36 Months
	F	59	fixed	Itraconazole,76 weeks	1	3 Months

M: male, F: female, NA: not available, * Mean KI: potassium iodide

CONCLUSION

Indications and outcomes of treating sporotrichosis with cryosurgery still need even better definitions. The scarce literature on the subject and the observation of the three reported cas-

es suggest it is useful in cases of lymphocutaneous or localized / fixed forms of the disease that were not resolved with the use of itraconazole and / or KI for a period exceeding 6 months. ●

DECLARATION OF PARTICIPATION:

Pedro Secchin:

Study design and planning

Giselle Ribeiro Pereira Seabra:

Clinical evaluation of cases and indication of cryosurgery, definition of parameters to be used in the procedure (lesion location, tips, freezing and thawing time control, safety margins), patient follow-up, evaluation and indication of additional sessions

Cleide Eiko Ishida:

Research study design and guidance, preparation and final review of the manuscript

David Rubem Azulay

Participation in research orientation and final text revision

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Participation in research orientation and final text revision

REFERENCES

- Carrasco-Zuber JE, Navarrete-Dechent C, Bonifaz A, Fich F, Vial-Letelier V, Berroeta-Mauriziano D. Cutaneous Involvement in the Deep Mycoses: A Literature Review. Part I-Subcutaneous Mycoses. *Actas Dermosifiliogr*. 2016;107(10):806-15.
- Gutierrez-Galhardo MC, Freitas DFS, Valle ACF, Almeida-Paes R, Oliveira MME, Zancopé-Oliveira RM. Epidemiological Aspects of Sporotrichosis Epidemic in Brazil. *Curr Fungal Infect Rep*. 2015;9(4):238-45.
- Gerência de Doenças Transmitidas por Vetores e Zoonoses. Vigilância da esporotricose: orientações sobre vigilância da esporotricose no estado do Rio de Janeiro. Rio de Janeiro: Gerência de Doenças Transmitidas por Vetores e Zoonoses (GDTVZ); 23 dez. 2014. Informe técnico 005/2014. Secretaria de Estado de Saúde do Rio de Janeiro.
- Morales AM, Velho PENF, Magalhães RF. Criocirurgia com nitrogênio líquido e as dermatoses infecciosas. *An Bras Dermatol*. 2008;83(4):285-98.
- Reis CMS, Ishida CE. Criocirurgia. Outras indicações e Condições Especiais. In: Gadelha AR, Costa IMC, editors. *Cirurgia Dermatológica em Consultório*. 2ª ed. São Paulo: Editora Atheneu; 2009. p. 495-517.
- Ishida CE. Criocirurgia. In: Kadunc B, Palermo E, Addor F, Metsavaht L, Rabello L, Mattos R, et al, editors. *Tratado de Cirurgia Dermatológica, Cosmiatria e Laser da Sociedade Brasileira de Dermatologia*. Rio de Janeiro: Elsevier; 2013. p. 541-557.
- Ferreira CP, Galhardo MC, Valle AC. Cryosurgery as adjuvant therapy in cutaneous sporotrichosis. *Braz J Infect Dis*. 2011;15(2):181-3.
- Bargman H. Successful treatment of cutaneous sporotrichosis with liquid nitrogen: report of three cases. *Mycoses*. 1995;38(7-8):285-7.
- de Souza CP, Lucas R, Ramadina RH, Pires TB. Cryosurgery in association with itraconazole for the treatment of feline sporotrichosis. *J Feline Med Surg*. 2016;18(2):137-43.