

CASO CLÍNICO

Dermatitis Flagelada por hongo Shiitake: a propósito de un caso

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RESUMEN

La dermatitis flagelada por hongos Shiitake (*Lentinula edodes*) es una toxicodermia causada por la ingesta de hongos Shiitake crudos o mal cocidos. La reacción cutánea clásica consiste en eritema lineal con presencia de pápulas o papulovesículas, asociado al fenómeno de Koebner con marcado prurito. La fisiopatología es aún estudiada, no obstante, se cree es causado por el Lentinano, un β -glucano termolábil presente en el hongo. Inicialmente reportada en Japón, con aumento de reportes a nivel mundial a medida que el cultivo y consumo del hongo Shiitake incrementa.

REPORTE DE CASO

Paciente masculino de 45 años de edad, natural de la ciudad de Bogotá, Colombia. Sin antecedentes de importancia para el caso. Realiza consulta telefónica por cuadro de 8 horas de evolución consistente en aparición de lesiones en espalda, papulares, eritematosas de patrón lineal, intensamente pruriginosas. Envía fotos por medio telefónico (Figuras 1 y 2).

El prurito de las lesiones presenta mejoría leve al colocar compresas frías sobre las mismas. Familiar médico le formula antihistamínico (Loratadina) sin mejoría alguna del cuadro y aparición rápida de nuevas lesiones, por lo que decide consultar telefónicamente a dermatología.

Se interroga al paciente y no reporta historia previa de medicamentos, contacto con personas enfermas, no sintomatología adicional.

Por las características de las lesiones se indaga sobre ingesta de alimentos en los últimos días donde se da a conocer el consumo de comida oriental con base en hongos Shiitake el mismo día del inicio del cuadro.



Figura 1. Lesiones lineares eritematosas conformadas por pápulas agrupadas en el dorso



Figura 2. Acercamiento de las lesiones con mejor evidencia de pápulas eritematosas.

Dado el cuadro clínico y antecedente positivo de ingesta de hongos Shiitake se da el diagnóstico de dermatitis flagelada por hongos Shiitake y comienza tratamiento.

INTRODUCCIÓN

La dermatitis flagelada por hongos Shiitake fue descrita por primera vez en 1977 por Nakamura,¹ es una reacción cutánea intensamente pruriginosa con un patrón lineal de pápulas, papulovesículas y algunos casos descritos con aparición de pústulas² que se presenta posterior al consumo de hongos Shiitake crudos o mal cocidos. Igualmente se ha reportado la aparición de lesiones al manipular los hongos directamente, lo cual genera una dermatitis de contacto al hongo. Este hongo ha sido ampliamente utilizado en la medicina tradicional China desde los tiempos de la dinastía Ming (1368-1644) como tratamiento para dolor articular,

fatiga e incluso el envejecimiento.³ Hoy en día se ha investigado el potencial del hongo Shiitake como tratamiento anticancerígeno por las propiedades antitumorales del β -glucano de la *Lentinula edodes*⁴ así como sus propiedades antihipertensivas, efectos inmunomoduladores, reducción de colesterol, fuente de vitamina D, entre otras.⁵⁻⁷ De importancia actual y mundial, se ha estado investigando recientemente su posible efecto protector en pacientes COVID-19 dada su capacidad inmunomoduladora y citoprotectora a nivel pulmonar.⁸ El aumento del cultivo y consumo de este hongo en las diferentes cocinas mundiales a incrementado el interés y el número de casos reportados en la literatura de la dermatitis flagelada por hongo Shiitake.

HALLAZGOS CLÍNICOS

La presentación clásica de este cuadro consta de lesiones urticariformes, lineares, eritematosas e intensamente pruriginosas 24 a 48 horas posterior al consumo de hongo Shiitake, asociado al fenómeno de Koebner. Se han reportado lesiones menos frecuentes como petequias, pústulas e hiper pigmentación con la exposición al sol.⁹ En algunos casos se han descrito síntomas y signos sistémicos tales como fiebre, diarrea, parestesias en manos, compromiso de mucosas y conjuntivitis.^{7,10} La mayoría de lesiones se presentan en el tronco y extremidades no obstante hay reportes de aparición de lesiones en rostro y cuero cabelludo.¹¹

ETIOLOGÍA

El mecanismo de toxicidad del hongo en la piel no es completamente entendido hasta el momento. Una hipótesis es que trata de un mecanismo de toxicidad por el polisacárido lentinano, propio del hongo Shiitake. Este es un β -glucano termolábil que es inactivado al ser expuesto a temperaturas elevadas (alrededor de 150°C) condición que explicaría que la dermatitis flagelada por este hongo es únicamente presentada posterior al consumo crudo o mal cocido, en cantidades excesivas.¹² Una segunda hipótesis propone una reacción de hipersensibilidad mediada por linfocitos Th1, en pacientes genéticamente predispuestos por

presentar alelos HLA específicos, que les genere mayor riesgo de presentar la toxicodermia con ingesta de cantidades de lentinano. Hasta el momento no hay conocimiento de alelos específicos que generen esta reacción de hipersensibilidad.⁷

DIAGNÓSTICO

El diagnóstico es clínico y basado en antecedentes de consumo del hongo. No es imprescindible la realización de un estudio de coloración en biopsia. De ser realizada, la patología es inespecífica. Muestra espongiosis e infiltrado linfocítico perivascular en la dermis superficial con presencia ocasional de infiltrado eosinófilo o neutrofilico.^{7,13} Los estudios de laboratorio no se muestran alterados o son inespecíficos y no son una ayuda diagnóstica en este caso.

Dentro de los diagnósticos diferenciales a tener en cuenta, importante la dermatitis flagelada por bleomicina (Figura 3) con una incidencia de hasta 22%.¹⁴ Igualmente se han reportado casos de dermatitis flageladas en pacientes VIH positivo o como reacción cutánea a otros agentes antineoplásicos como el trastuzumab y la combinación Tegafur/Gimeracil/Oteracil designados para el tratamiento de cáncer gástrico, de seno, esofágico, entre otros.^{15,16}



Figura 3. Dermatitis flagelada por bleomicina en extremidad superior.

TRATAMIENTO

El tratamiento se enfoca en el manejo sintomático, ya que en la gran mayoría de los casos esta toxicodermia es autolimitada. El manejo se basa en corticoesteroides tópicos y antihistamínicos aunque en ocasiones se puede considerar el uso de corticoesteroides sistémicos en casos de pacientes con síntomas severos.⁷

PRONÓSTICO

La dermatitis por hongos Shiitake resuelve por completo dentro de un rango de 6-8 semanas, a nuestro conocimiento no hay presencia de secuelas tales como hiperpigmentación o cicatrización. Dentro de los primeros días y semanas se debe tener precaución con la exposición al sol ya que en estos momentos se puede generar hiperpigmentación transitoria por complejos inflamatorios.

BIBLIOGRAFÍA

1. Nakamura T. Shiitake { *Lentinus edodes*) dermatitis. 1992;65-70.
2. Hamer SE, Kulkarni K, Cohen SN. Shiitake dermatitis with oral ulceration and pustules. *Clin Exp Dermatol*. 2015;40(3):332-3.
3. Money NP. Are mushrooms medicinal? *Fungal Biol [Internet]*. 2016;120(4):449-53. Available from: <http://dx.doi.org/10.1016/j.funbio.2016.01.006>
4. Xu H, Zou S, Xu X, Zhang L. Anti-Tumor effect of β -glucan from *Lentinus edodes* and the underlying mechanism. *Sci Rep [Internet]*. 2016;6(February):1-13. Available from: <http://dx.doi.org/10.1038/srep28802>
5. Yang HJ, Kim MJ, Kwon DY, Kim DS, Zhang T, Ha C, et al. Combination of aronia, red ginseng, shiitake mushroom and nattokinase potentiated insulin secretion and reduced insulin resistance with improving gut microbiome dysbiosis in insulin deficient type 2 diabetic rats. *Nutrients*. 2018;10(7).
6. Cardwell G, Bornman JF, James AP, Black LJ. A review of mushrooms as a potential source of dietary vitamin D. *Nutrients*. 2018;10(10):1-11.
7. Nguyen AH, Gonzaga MI, Lim VM, Adler MJ, Mitkov M V., Cappel MA. Clinical features of shiitake dermatitis: a systematic review. *Int J Dermatol*. 2017;56(6):610-6.

8. Murphy EJ, Masterson C, Rezoagli E, Toole DO, Major I, Stack GD, et al. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website. Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. β -Glucan extracts from the same edible shiitake mushroom *Lentinus edodes* produce differential in-vitro immunomodulatory and pulmonary cytoprotective effects —Implications for coronavirus disease (COVID-19) immunotherapies. 2020;(January).
9. Ribeiro CS, Sodré CT, Ramos-E-Silva M. Flagellate dermatitis by Shiitake mushroom. *Case Rep Dermatol.* 2019;11(2):220–5.
10. Netchiporouk E, Pehr K, Ben-Shoshan M, Billick RC, Sasseville D, Singer M. Pustular flagellate dermatitis after consumption of shiitake mushrooms. *JAAD Case Reports [Internet].* 2015;1(3):117–9. Available from: <http://dx.doi.org/10.1016/j.jdc.2015.02.010>
11. Mendonça FMI, Márquez-García A, Méndez-Abad C, Rodríguez-Pichardo A, Perea-Cejudo M, Ríos Martín JJ, et al. Flagellate dermatitis and flagellate erythema: report of 4 cases. *Int J Dermatol.* 2017;56(4):461–3.
12. Boels D, Landreau A, Bruneau C, Garnier R, Pulce C, Labadie M, et al. Shiitake dermatitis recorded by French Poison Control Centers—new case series with clinical observations. *Clin Toxicol.* 2014;52(6):625–8.
13. Stephany MP, Chung S, Handler MZ, Handler NS, Handler GA, Schwartz RA. Shiitake Mushroom Dermatitis: A Review. *Am J Clin Dermatol.* 2016;17(5):485–9.
14. Erkek ET, Karaali CN. Bleomycin-Induced Flagellate Dermatitis. *Turkish J Haematol Off J Turkish Soc Haematol.* 2019;36(2):137–8.
15. Cohen PR. Trastuzumab-Associated Flagellate Erythema: Report in a Woman with Metastatic Breast Cancer and Review of Antineoplastic Therapy-Induced Flagellate Dermatoses. *Dermatol Ther (Heidelb).* 2015;5(4):253–64.
16. Goto H, Sugita K, Yanagihara S, Yamamoto O. Shiitake Dermatitis-like Eruption Due to Tegafur / Gimeracil / Oteracil Combination Usage. 2017;179–81.

CASE REPORT

Shiitake mushroom Flagellate Dermatitis: Case report

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ABSTRACT

Shiitake mushroom flagellate (*Lentinula edodes*) dermatitis is a cutaneous reaction caused by ingestion of raw or undercooked Shiitake mushrooms. Classic cutaneous symptoms consist of linear erythema with the presence of papules or papulovesicles, associated with the Koebner phenomenon and marked itching. Pathophysiology is currently under study. However, it is believed to be caused by Lentinan, a heat-labile β -glucan that is present in the fungus. It was initially reported in Japan. Nonetheless, cases escalated worldwide as cultivation and consumption of the Shiitake mushroom became more popular.

CASE REPORT

A 45-year-old male patient from the city of Bogota, Colombia presented with a case with no relevant medical history. The patient made a telephone consultation regarding a consistent eight-hour evolution case manifesting papular, erythematous, heavily pruriginous, linear lesions on the back. Pictures are sent through telephone (Figures 1 and 2).

Itching of lesions slightly improves after application of cold compresses. A physician in the family prescribes antihistaminic drug (Loratadine), which shows no improvement. Furthermore, there is a rapid reappearance of lesions, for which the patient decides to have a dermatology phone consultation.

The patient is inquired, and he reports no medical history regarding medicine intake, contact with the ill and additional symptoms.

The features of the lesions suggest an inquiry about food ingestion during the last few days, which reveals intake of oriental food based on Shiitake mushrooms on the same day the clinical picture initiated.



Figure 1. Linear erythematous lesions conformed by grouped papules on the back.



Figure 2. Approximation of lesions showing improved evidence of erythematous papules.

Diagnosis of Shiitake mushroom flagellate dermatitis is confirmed due to the observed clinical picture and positive history regarding Shiitake ingestion. Consequently, treatment commences.

INTRODUCTION

Shiitake mushroom flagellate dermatitis was initially described by Nakamura in 1977¹ as a severely pruriginous cutaneous reaction of linear pattern conformed by papules, papulovesicles and, in some cases, pustules.² The condition manifests as a result of raw or under-cooked Shiitake mushroom consumption. Moreover, there are reports of lesions caused by direct manipulation of the mushroom, generating contact dermatitis. This mushroom has been widely employed in Chinese traditional medicine since the ruling of the Ming dynasty (1368–1644) to treat joint

pain, fatigue and even old age.³ There is current research of the Shiitake mushroom as a potential anticancer treatment considering the antitumor properties of *Lentinula edodes*' β -glucan,⁴ as well as its antihypertensive properties, immunomodulating effects, cholesterol reduction, vitamin D source, among others.^{5–7} The potential protective effect (pulmonary immunomodulating and cytoprotective capacity) of this world-renowned mushroom for COVID-19 patients is currently under research. The augmentation of Shiitake cultivation and consumption throughout global cuisine has increased the interest and case reports in the literature regarding Shiitake mushroom flagellate dermatitis.

CLINICAL FINDINGS

The clinical picture's classic presentation presents with urticarial, linear, erythematous and severely pruriginous lesions, surging 24 to 48 hours after Shiitake mushroom consumption, associated to the Koebner phenomenon. There are reports of less frequent lesions, such as petechiae, pustules and hyperpigmentation due to sun exposure.⁹ Some cases have reported symptoms and systemic signs of fever, diarrhea, hand paresthesias, mucosal involvement and conjunctivitis.^{7,10} Most lesions manifest in the torso and limbs. Nevertheless, reports of lesions in the face and scalp have been described.¹¹

ETIOLOGY

At the moment, Shiitake's cutaneous toxicity mechanism still poses questions. A hypothesis states the toxicity mechanism exists because of the mushroom's lentinan polysaccharide. This thermolabile β -glucan becomes inactivated after high temperature exposure (around 150°C). Such condition explains why one would present with flagellate dermatitis after excessive raw or under-cooked consumption of this mushroom.¹² A second hypothesis proposes the toxicity is set in motion due to a hypersensitivity reaction mediated by Th1 lymphocytes in genetically predisposed patients which present specific HLA alleles and

are at a greater risk of suffering from toxicoderm by lentinan ingestion. There is no current knowledge about which alleles generate such hypersensitivity reaction.⁷

DIAGNOSIS

Diagnosis is clinical and based on Shiitake mushroom consumption history. Staining examination of biopsy is not essential. If performed, the pathology is inconclusive. It reveals spongiosis and perivascular lymphocytic infiltrate at the superficial dermis with occasional presence of eosinophil or neutrophil infiltrate.^{7,13} Laboratory tests do not show any alteration. Furthermore, they are unspecific, which does not contribute to the diagnosis of the case.

Among differential diagnoses, bleomycin flagellate dermatitis (Figure 3) is to be considered with an incidence of up to 22%.¹⁴ Additionally, there are case reports regarding flagellate dermatitis in HIV-positive patients or as a cutaneous reaction to other antineoplastic agents, such as trastuzumab and the tegafur/gimeracil/oteracil combination prescribed for gastric, breast, esophageal cancer, and others.^{15,16}



Figure 3. Bleomycin flagellate dermatitis in upper limb.

TREATMENT

The focus of treatment lies on symptomatic management, as most cases present with autolimited toxicoderm. This treatment is based on topical corticosteroids and antihistaminics. However, in many occasions, the use of systemic corticosteroids may be considered on patients with severe symptoms.⁷

PROGNOSIS

Shiitake mushroom dermatitis was fully cured after a period of six to eight weeks with no presence of side effects, such as hyperpigmentation or scarring. During the first few days and weeks, sun exposure must be limited as to avoid postinflammatory temporary hyperpigmentation.

REFERENCES

1. Nakamura T. Shiitake { *Lentinus edodes* } dermatitis. 1992;65–70.
2. Hamer SE, Kulkarni K, Cohen SN. Shiitake dermatitis with oral ulceration and pustules. *Clin Exp Dermatol*. 2015;40(3):332–3.
3. Money NP. Are mushrooms medicinal? *Fungal Biol [Internet]*. 2016;120(4):449–53. Available from: <http://dx.doi.org/10.1016/j.funbio.2016.01.006>
4. Xu H, Zou S, Xu X, Zhang L. Anti-Tumor effect of β -glucan from *Lentinus edodes* and the underlying mechanism. *Sci Rep [Internet]*. 2016;6(February):1–13. Available from: <http://dx.doi.org/10.1038/srep28802>
5. Yang HJ, Kim MJ, Kwon DY, Kim DS, Zhang T, Ha C, et al. Combination of aronia, red ginseng, shiitake mushroom and nattokinase potentiated insulin secretion and reduced insulin resistance with improving gut microbiome dysbiosis in insulin deficient type 2 diabetic rats. *Nutrients*. 2018;10(7).
6. Cardwell G, Bornman JF, James AP, Black LJ. A review of mushrooms as a potential source of dietary vitamin D. *Nutrients*. 2018;10(10):1–11.
7. Nguyen AH, Gonzaga MI, Lim VM, Adler MJ, Mitkov M V., Cappel MA. Clinical features of shiitake dermatitis: a systematic review. *Int J Dermatol*. 2017;56(6):610–6.

8. Murphy EJ, Masterson C, Rezoagli E, Toole DO, Major I, Stack GD, et al. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website. Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content -immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. β -Glucan extracts from the same edible shiitake mushroom *Lentinus edodes* produce differential in-vitro immunomodulatory and pulmonary cytoprotective effects —Implications for coronavirus disease (COVID-19) immunotherapies. 2020;(January).
9. Ribeiro CS, Sodré CT, Ramos-E-Silva M. Flagellate dermatitis by Shiitake mushroom. *Case Rep Dermatol.* 2019;11(2):220–5.
10. Netchiporouk E, Pehr K, Ben-Shoshan M, Billick RC, Sasseville D, Singer M. Pustular flagellate dermatitis after consumption of shiitake mushrooms. *JAAD Case Reports [Internet].* 2015;1(3):117–9. Available from: <http://dx.doi.org/10.1016/j.jdc.2015.02.010>
11. Mendonça FMI, Márquez-García A, Méndez-Abad C, Rodríguez-Pichardo A, Perea-Cejudo M, Ríos Martín JJ, et al. Flagellate dermatitis and flagellate erythema: report of 4 cases. *Int J Dermatol.* 2017;56(4):461–3.
12. Boels D, Landreau A, Bruneau C, Garnier R, Pulce C, Labadie M, et al. Shiitake dermatitis recorded by French Poison Control Centers—new case series with clinical observations. *Clin Toxicol.* 2014;52(6):625–8.
13. Stephany MP, Chung S, Handler MZ, Handler NS, Handler GA, Schwartz RA. Shiitake Mushroom Dermatitis: A Review. *Am J Clin Dermatol.* 2016;17(5):485–9.
14. Erkek ET, Karaali CN. Bleomycin-Induced Flagellate Dermatitis. *Turkish J Haematol Off J Turkish Soc Haematol.* 2019;36(2):137–8.
15. Cohen PR. Trastuzumab-Associated Flagellate Erythema: Report in a Woman with Metastatic Breast Cancer and Review of Antineoplastic Therapy-Induced Flagellate Dermatoses. *Dermatol Ther (Heidelb).* 2015;5(4):253–64.
16. Goto H, Sugita K, Yanagihara S, Yamamoto O. Shiitake Dermatitis-like Eruption Due to Tegafur / Gimeracil / Oteracil Combination Usage. 2017;179–81.