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Case Report

An unusually severe case of shiitake mushroom dermatitis with features of drug reaction with eosinophilia and systemic symptoms

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Abstract

Shiitake mushroom dermatitis is a well-documented phenomenon in the literature seen after consuming raw or undercooked shiitake mushrooms (*Lentinus edodes*). However, systemic features resembling a drug reaction with eosinophilia and systemic symptoms (DRESS) are rare. We report a case of severe shiitake mushroom dermatitis with atypical systemic features resembling DRESS. A 51-year-old man presented with acute unilateral periorbital oedema and flagellate erythema with no obvious drug precipitants and was initially managed as allergic contact dermatitis in the emergency department. Further inquiry revealed a history of raw shiitake mushroom ingestion 48 h before the onset of symptoms, which led to a working diagnosis of shiitake mushroom dermatitis. Skin biopsies showed mixed spongiotic and interface inflammatory reactions with a perivascular lymphocytic infiltrate and marked eosinophilia supportive of shiitake mushroom dermatitis. Rheumatological causes of flagellate erythema and periorbital oedema were excluded from clinical and laboratory findings. The patient initially presented with apyrexia and mild eosinophilia but then developed pyrexia, hypereosinophilia, neutrophilia and transaminitis. He subsequently developed bilateral periorbital oedema with his flagellate erythema, both of which were resolved with topical and oral corticosteroids. However, there was a new widespread morbilliform eruption with dorsal oedema of his hands. A diagnosis of DRESS-like shiitake mushroom dermatitis was considered. The patient required a long course of oral prednisolone to achieve clinical and biochemical resolution of his symptoms. Our case underscores the importance of prompt recognition and management of shiitake dermatitis, especially when it presents with DRESS-like features.

What is already known about this topic?

- Shiitake mushroom dermatitis is a toxic dermal reaction that can occur 24 to 72 hours after consuming raw or undercooked shiitake mushrooms.
- It is characterized by widespread pruritic flagellate erythema.
- Shiitake mushroom dermatitis is a benign, self-limiting disease often managed conservatively.

What does this study add?

- Reports an unusually severe shiitake mushroom dermatitis ingestion with DRESS-like features, reported only once in the literature.
- Highlights that shiitake mushroom dermatitis may not always be a benign, self-limiting disease.
- Suggests that cases of shiitake dermatitis be monitored for features suggestive of a DRESS-like presentation and that corticosteroid therapy may be required for management.

Shiitake mushroom (*Lentinus edodes*) is a popular, edible mushroom used in East Asian cuisine and Eastern medicine, believed to have nutraceutical, antineoplastic and immunomodulatory properties.[1] Although widely consumed without issues, a toxic dermal reaction known as shiitake mushroom dermatitis has been described. Lentinan, a thermolabile polysaccharide found in raw or undercooked shiitake mushrooms, has been implicated as the causative agent in shiitake mushroom dermatitis.[1–3] Following ingestion of raw or undercooked shiitake mushrooms, shiitake mushroom

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dermatitis is characterized by a delayed onset (up to 72 h) of pruritus and flagellate erythema postingestion.[1–5]

Here, we present an unusually severe shiitake mushroom dermatitis with a unique clinical trajectory. The patient first presented with flagellate dermatitis, followed by progressive periorbital oedema and dorsal oedema of the hands, with signs and symptoms suggesting drug reaction with eosinophilia and systemic symptoms (DRESS).

Case report

A haemodynamically stable, apyrexial 51-year-old man presented to the emergency department with a 24-h history of acute, pruritic flagellate erythema to his trunk with right-sided periorbital swelling. The patient denied any new medications, preceding illness, unusual exposures or recent travel. There were no systemic complaints aside from pruritus and right periorbital oedema obscuring his vision. No proximal myopathy or other stigma of dermatomyositis was detected on examination, such as myalgia, shawl sign or Gottron papules. The patient was on regular olanzapine and risperidone for the last 3 years, with no new medications commenced in the previous 8 weeks. His drug history did not include any medications associated with drug-induced dermatomyositis, such as statins or anticonvulsants.

Contrast computed tomography of the patient's face revealed marked thickening of the right eyelid associated with extensive regional subcutaneous oedema and subgaleal fluid extending over the scalp bilaterally. Ophthalmological consultation did not identify intraocular pathology. He had mild eosinophilia of 0.68×10^9 cells L^{-1} (reference range $<0.5 \times 10^9$ cells L^{-1}) and raised C-reactive protein (CRP) of 14.0 mg L^{-1} (reference range <5.0 mg L^{-1}) at presentation, with normal thyroid function tests, normal ferritin levels, negative antinuclear antibody and a negative myositis antibody panel.

The patient was admitted to the acute medical unit with a working diagnosis of allergic contact dermatitis of uncertain aetiology. He commenced prednisolone, loratadine and hydrocortisone eye ointment.

During a dermatology consultation on day 3 of the patient's admission, he was noted to have bilateral periorbital oedema and widespread truncal and axillary flagellate erythema without lymphadenopathy (Figure 1). He continued to display normal vital parameters. Upon further inquiry, the patient disclosed consuming raw shiitake mushrooms 2 days before his presentation.

Therefore, a new diagnosis of shiitake dermatitis was made, and the patient was commenced on three times daily topical corticosteroids (methylprednisolone 0.1% fatty ointment and betamethasone dipropionate 0.05% ointment) to his face and body under wet wraps, respectively. Skin biopsies of the flagellate erythema performed before initiation of corticosteroid therapy revealed a mixed spongiotic and interface inflammatory reaction with a perivascular lymphocytic infiltrate and marked eosinophilia, in keeping with published histological features seen in shiitake dermatitis[2,6] (Figure 2). Direct immunofluorescence was nondiagnostic. Other causes of flagellate erythema, such as adult-onset Still disease and bleomycin, were excluded from the patient's laboratory findings and drug history.[5,6]

On day 7, the patient's periorbital oedema resolved, but he developed bilateral oedema in his hands and lower

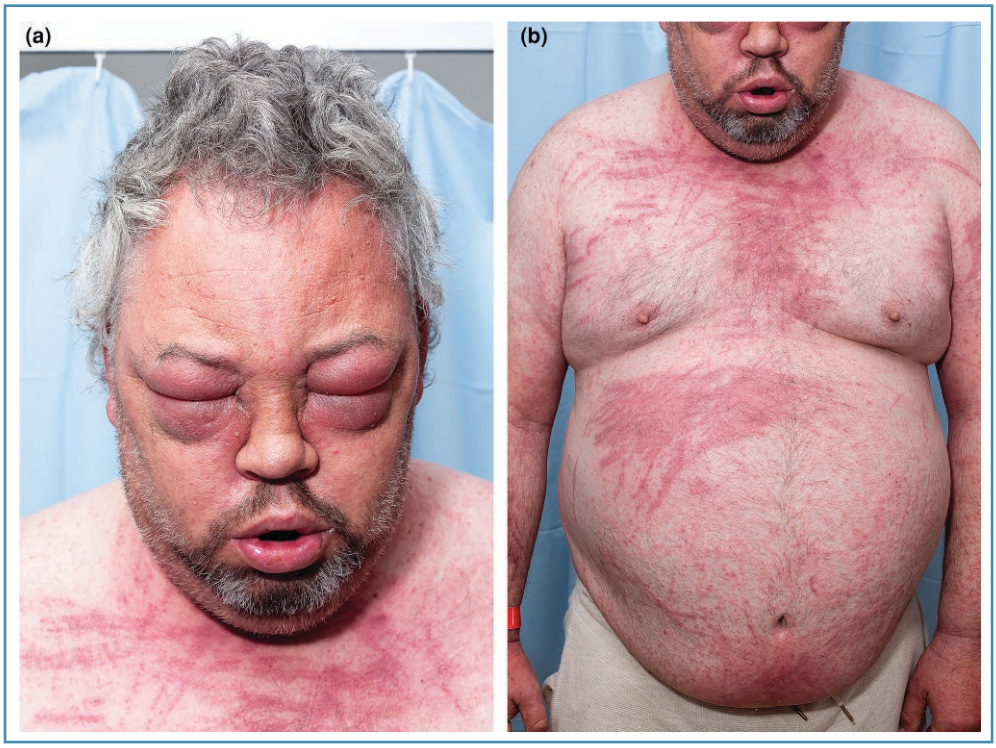

Figure 1 (a) Facial oedema with bilateral periorbital oedema. (b) Extensive flagellate dermatitis involving the patient's chest, abdomen, bilateral arms and axillae.

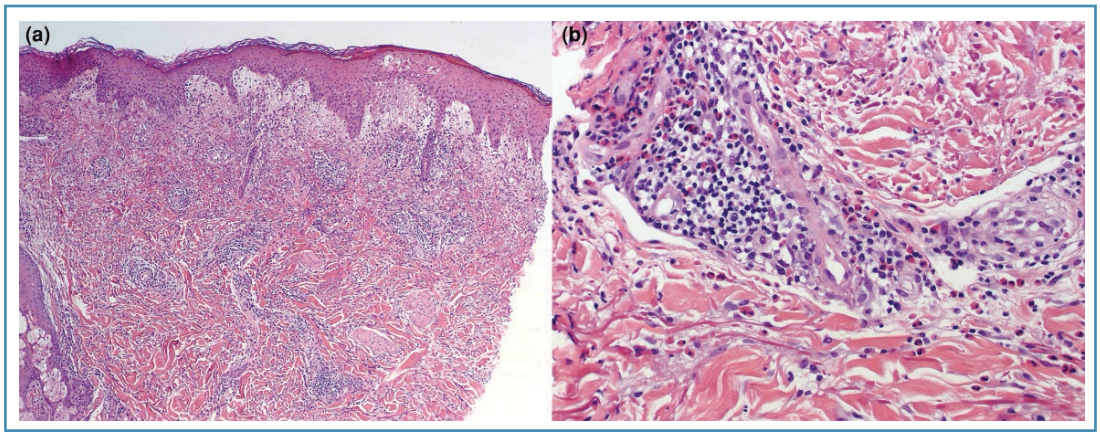

Figure 2 Histology of the punch biopsies obtained from the patient's forearm (a) at superficial ×40 magnification and (b) ×200 magnification of the perivascular structures. At ×40 magnification, focal parakeratosis overlying the epidermis, with mild spongiosis and acanthosis, is seen with prominent papillary dermal oedema. At ×200 magnification, a moderate superficial and deep dermal perivascular inflammatory infiltrate comprising lymphocytes, histiocytes and numerous eosinophils is present.

limbs. The patient's initial flagellate erythema evolved into confluent truncal erythema with vesicular eruption on his upper limbs (Figure 3) without mucosal involvement. The patient remained systemically well save for intermittent pyrexia measuring up to 38.5 °C that resolved with paracetamol.

Daily phlebotomy was not possible due to the patient's needle phobia, which posed a challenge in monitoring his condition. Laboratory investigations on day 12 showed new hypereosinophilia of 4.88×10^9 cells L^{-1}, neutrophilia of 12.85×10^9 cells L^{-1} (reference range $2.00–7.50 \times 10^9$ cells L^{-1}), transaminitis with an alanine aminotransferase of 72 (reference range <40 U L^{-1}), γ-glutamyl transferase 128 U L^{-1} (reference range <60 U L^{-1}) and elevated C-reactive protein of 12 mg L^{-1} (reference range <5 mg L^{-1}). Urinalysis revealed proteinuria with a mildly elevated protein : creatinine ratio of 17 (reference range <13) with negative bacterial cultures. Blood cultures and a nasopharyngeal respiratory viral panel were also negative.

Serological tests for HIV, hepatitis B and C, cytomegalovirus, Epstein–Barr virus, *Strongyloides*, *Treponema* and *Mycoplasma pneumoniae* were negative. Indirect fluorescent antibody IgG antibodies against human herpesvirus 6

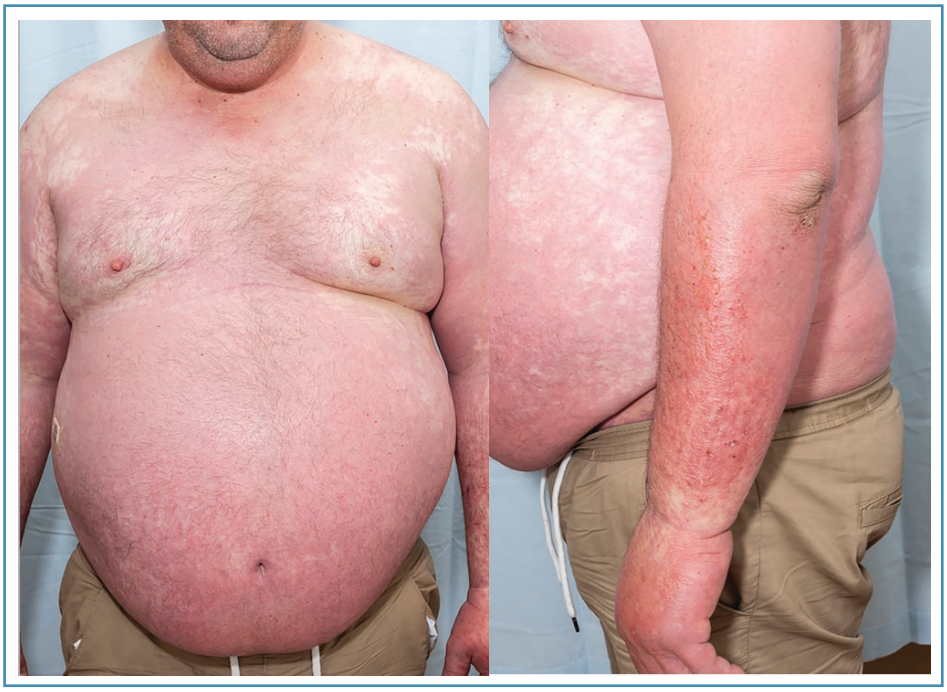

Figure 3 Morphological change of the patient's flagellate erythema to diffuse, confluent erythematous patches involving his trunk and upper and lower limbs with secondary purpura and vesicular eruption on the forearms on day 7 resembling a morbilliform eruption of DRESS. Note the dorsal oedema of the patient's right hand.

(HHV6) were positive, but a HHV6 polymerase chain reaction was negative. Based on the above investigations, the patient was suspected of having probable DRESS, with a RegiSCAR score of 5 (Table S1; see Supporting Information).[7,8]

A final diagnosis of shiitake mushroom dermatitis with systemic features resembling DRESS was made. At this juncture, his oral prednisolone was increased to 50 mg. The patient continued high-dose oral steroids and topical corticosteroid wet wraps until his hand oedema subsided and the generalized confluent erythematous rash improved. He was discharged with a tapering dose of prednisolone on day 13 and instructed to avoid consuming shiitake mushrooms henceforth.

At a 1-month outpatient dermatology clinic follow-up, the patient had normal haematological parameters but was found to have ongoing urticarial-like dermatitis on his bilateral forearms, which necessitated a prolonged course of topical corticosteroids for more than a month.

Discussion

The pathophysiology of shiitake dermatitis is unclear but theorized to involve a type IV hypersensitivity reaction.[4] Based on systematic reviews, supporting features of shiitake dermatitis include an acute onset (40–72 h) of pruritic linear dermatitis following mushroom ingestion, and parakeratosis, epidermal spongiosis and lymphocytic, eosinophilic perivascular infiltrates on histopathology.[3,9] Eight other published cases of shiitake dermatitis in which rash morphology was described and histopathology was performed support this (Table 1).

DRESS is defined as a severe cutaneous adverse reaction from drug hypersensitivity and is also considered to represent a type IV reaction.[13] Common agents implicated in DRESS are allopurinol, sulfonamides, antiepileptics and antibiotics such as vancomycin, minocycline and β-lactams.[14] No singular universal diagnostic criteria are used to diagnose DRESS, although

Table 1 Main clinical and histological features of reported cases of shiitake dermatitis

Case/age (years)/sex	Time from shiitake mushroom ingestion to flagellate erythema (h)	Clinical signs and symptoms	Histological features from skin biopsy	Reference
1/64/male	24	Pruritic erythematous papules configured in a flagellate pattern on the back and abdomen	Spongiotic dermatitis with acanthosis, dermal oedema, and mixed cellular inflammatory infiltrate comprising eosinophils, scattered mast cells, lymphocytes and histiocytes	Albuscheit *et al.* 2020[4]
2/55/female	24–72	Vesicles overlying erythema over face, dorsum of hands and forearms, evolving within 24 h to confluent flagellate erythema on the torso	Focal parakeratosis overlying mildly spongiotic epidermis and dense mixed superficial perivascular dermatitis with eosinophils	Adler and Larsen 2012[5]
3/54/female	24–72	Burning, pruritic, linear vesicles on the back, crossing multiple dermatomes	Focal parakeratosis overlying mildly spongiotic epidermis and dense mixed superficial perivascular dermatitis with eosinophils	Adler and Larsen 2012[5]
4/52/male	24–72	Nonpruritic morbilliform eruption in a flagellate configuration on the torso	Focal parakeratosis overlying mildly spongiotic epidermis and dense mixed superficial perivascular dermatitis with eosinophils	Adler and Larsen 2012[5]
5/35/male	36	Flagellate erythema on trunk, buttocks, legs and arms	Mild epidermal spongiosis with focal parakeratosis, lymphocytic exocytosis and Langerhans cell aggregation	Ching *et al.* 2019[6]
6/70/male	48	Pruritic erythematous papules and papulovesicular eruption in a flagellate configuration involving neck, trunk and extremities	Spongiosis, marked papillary dermal oedema and dermal lymphocytic and eosinophilic perivascular inflammatory infiltrate	Ma and Liu 2022[10]
7/31/male	24	Pruritic erythematous-violaceous streaks in a flagellate pattern over limbs, with confluence of rash on chest and scalp; discrete pustules on the trunk and intertriginous areas	Follicular sterile pustules with mild mixed perivascular infiltrate	Netchiporouk *et al.* 2015[11]
8/42/male	36	Generalized pruritic flagellate erythema initially on the axillae and groin with a cluster of oral ulcers	Epidermal spongiosis, papillary dermal oedema and heavy dermal neutrophilic infiltrate	Hamer *et al.* 2015[12]
9/51/male	48	Bilateral periorbital oedema, pruritic flagellate erythema involving the anterior and posterior trunk, axillae, and abdomen	Focal parakeratosis overlying the epidermis, with mild spongiosis and acanthosis. Prominent papillary dermal oedema with superficial and deep dermal perivascular inflammatory infiltrate comprising lymphocytes, histiocytes and numerous eosinophils	Ng *et al.* (our case)

the RegiSCAR criteria is a validated tool used to support the diagnosis of DRESS.[14] For example, high-grade pyrexia, eosinophilia, lymphadenopathy and visceral involvement are supportive features used in RegiSCAR. DRESS treatment is two-pronged: ceasing the offending drug and initiating topical and systemic corticosteroids.[13,14]

While eosinophilia, erythema, photodistributed oedema and, rarely, fever and malaise have been associated with shiitake mushroom dermatitis, the combination of the above meeting DRESS criteria is exceedingly rare.[15,16]

Only one other case of DRESS secondary to shiitake mushroom ingestion has been published.[17] This was a French case in 2011 describing a patient with 'DRESS-like syndrome' with shiitake flagellate dermatitis, hypereosinophilia, pyrexia, raised inflammatory markers, and facial and acral oedema following shiitake mushroom ingestion.[17]

In contrast, our patient experienced an unusual morphological change in his rash. He initially presented with flagellate dermatitis and periorbital oedema, which then developed into confluent erythema with secondary vesiculation and purpura, resembling a morbilliform eruption of DRESS.

We elucidate an unusual, severe case of shiitake mushroom dermatitis with features of DRESS, initially presenting as flagellate dermatitis and facial oedema with marked periorbital involvement, which progressed to peripheral oedema, fever and visceral involvement with morbilliform eruption. A meticulous food and drug history should be taken in all patients presenting with flagellate erythema to ascertain the aetiology of the rash. In cases where a diagnosis of shiitake mushroom dermatitis has been made, care must be taken to continue monitoring the patient's clinical improvement and vital and haematological parameters for signs of deterioration.

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Conflicts of interest

The authors declare no conflicts of interest.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethics statement

The Royal Perth Hospital's Human Research Ethics Committee (HREC) waived ethical approval for this study, as the review of patients to report as a case study or case series is considered anecdotal and can proceed without HREC review.

Patient consent

Written informed consent was obtained to publish patient information, including clinical photographs, in this article.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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