

## REVIEW

# Emerging fungal infections: focus on *Saksenaea Erythrospora*

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## Keywords

Fungi • Emerging infections • Review

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## summary

**Introduction.** In recent times, improved diagnostic techniques have revealed an alarming number of cases of mucormycosis in immunocompetent individuals. The *Saksenaea* species, is a rare cause of mucormycosis, and is often associated with skin and subcutaneous infection due to trauma in both immunocompromised and immunocompetent subjects. The purpose of this study was therefore, through a review of the literature, to investigate the problem of infections caused by *Saksenaea Erythrospora*, evaluating the clinical manifestations of the infection, the triggering factors, the therapies and patients' outcomes, implementing and updating what already reported in literature.

**Methods.** A research of peer-reviewed literature in the electronic databases MEDLINE (PubMed) and Scopus was conducted in the period June 2020-January 2021 using the key word "*Saksenaea erythrospora*". Studies in Italian, English, French, Spanish focused on cases of *Saksenaea erythrospora* were included, without time restrictions. Studies that provided ambiguous or insufficient data were excluded.

**Results.** Bibliographic research yielded 23 publications; 7 were included in the review. The studies were published between 2011 and 2015 and involved a total of 11 patients of average age 37.9 years (SD 17.23) hospitalized in several hospitals in: USA, India, Argentina, Colombia, Thailand. 6 patients were women, 5 men. All patients had an almost normal immune status. The causes of the infection were: injections, traumas, surgery. Two patients, despite surgical and medical therapy, died.

**Conclusions.** Our review partially updated what already published, because only one new study was found. Serious necrotizing infections from *Saksenaea erythrospora* have been observed in recent years and a early identification and timely management are essential to reduce morbidity and mortality. A greater awareness and education about the risks deriving from carrying out surgical procedures abroad, especially in precarious hygiene situations, could be additional effective weapons to reduce the incidence of these infections.

## Introduction

Immunotherapies have revolutionized the treatment of cancers and autoimmune diseases and invasive fungal infections have become major complications of some of these new immunomodulators. The emergence of mucormycosis, a fungal infection caused by *Mucorales*, has been attracting the spotlight in recent years [1].

The significant increase in cases, high mortality rates (even up to 90%) in widespread infections, and the lack of effective antifungal treatments raised the alarm for this emerging disease. In the past, it was considered a rare and limited infection in immunocompromised patients suffering from AIDS, diabetes, organ transplants or other conditions associated with immunosuppression. In fact, in patients undergoing allogeneic bone marrow transplantation, the prevalence of mucormycosis could be up to 2-3%. However, iatrogenic outbreaks have also been described in the context of medications or use of contaminated medical instruments [2].

Soft tissue infections usually occur in patients with altered skin barriers, either as a result of traumatic

impact with the soil, maceration of the skin caused by a wet surface or in nosocomial environments by direct access through intravenous catheters or subcutaneous injections. Contaminated surgical dressings have also been implicated in skin mucormycosis. In one case, skin mucormycosis occurred due to a contaminated tape used to secure an endotracheal tube in a ventilated patient [2]. However, the current improvement in diagnostic techniques has revealed an alarming number of cases of mucormycosis in immunocompetent individuals.

The *Saksenaea* species is a rare cause of mucormycosis, and is often associated with skin and subcutaneous infection as the result of trauma in both immunocompromised and immunocompetent subjects [3].

In order to deepen this argument we conducted a brief review of the literature with a focus on *Saksenaea Erythrospora*, a species identified only in recent years, evaluating the clinical manifestations of the infection, the triggering factors, the therapies and patients' outcomes, with the aim of implementing and updating what reported in 2019 by Putthirangsiwong et al. [4] and Chander et al. in 2017 [5].

**Tab. I.** Main characteristics of the studies included in our review (LAMB = liposomal formulation of amphotericin B, MRI = magnetic resonance imaging, CT = computerized tomography, \*= all cases are included in a unique article).

#	Author, year	Gender	Age (years)	Country	Clinical presentation	Immune status	Cause of Infection	Undergone Procedures	Laboratory Diagnosis	Pharmacological Treatment	Outcome
1	Hospenthal, 2011	M	26	USA	Proptosis of the left eye	Normal	Combat Trauma	CT + enucleation of the left eyes	Incubation on potato flake agar (PFA), subculturing on Czapek Dox agar and multilocus molecular study	Not reported	Death
2	Reloso, 2014	M	55	Argentina	Abscess on the thigh	Normal	Sailing accident with deep skin and soft tissue injuries, with muscular avulsion	MRI + debridement	Microscopic examination using Giemsa stains. Culture on malt extract agar, potato dextrose agar and agar block with sterile distilled water and salt water (0.85% NaCl) + PCR	LAMB + hyperbaric oxygen therapy + posaconazole + interferon gamma	Resolution
3	Tendolkar, 2015	F	44	India	Right-sided orbital cellulitis	Normal	History of recurrent sinusitis. No history of trauma, nasal blockage, epistaxis or dental caries	CT + MRI + Endoscopic endonasal debridement + right orbital exenteration	Incubation on Sabouraud dextrose agar; then a slide culture on water agar + PCR	Amphotericin B	Resolution
4	Rodríguez, 2016	F	29	Colombia	Fever and chills, pain and erythema in the surgical wound. Then skin necrosis.	Normal	Breast Augmentation Surgery	Radical right mastectomy and surgical debridement	Incubation on Potato dextrose agar, malt extract agar, Sabouraud glucose agar + PCR	Amphotericin B + caspofungin	Resolution
5	Chander, 2017*	F	31	India	Large ulcerative lesion on left gluteal region	Normal	Injection	Extensive surgical debridement	Incubation on Czapek Dox agar and molecular sequencing	LAMB	Resolution
5	Chander, 2017*	M	37	India	Necrotizing area on left shoulder	Normal	Unknown	Extensive surgical debridement	Incubation on Czapek Dox agar and molecular sequencing	LAMB	Resolution
5	Chander, 2017*	F	40	India	Large necrotic area on right gluteal region	Normal	Injection	Extensive surgical debridement	Incubation on Czapek Dox agar and molecular sequencing	LAMB	Resolution
5	Chander, 2017*	M	60	India	Large necrotic area on right gluteal region	Normal	Injection	Extensive surgical debridement	Incubation on Czapek Dox agar and molecular sequencing	LAMB	Death
5	Chander, 2017*	F	55	India	Large necrotic area on right gluteal region	Normal	Injection	Extensive surgical debridement	Incubation on Czapek Dox agar and molecular sequencing	LAMB	Resolution
6	Putthirangsiwong, 2019	M	16 months	Thailand	Progressive painful mass at the right medial canthus and upper cheek	Normal	Unknown	MRI + Anterior orbitotomy with biopsy + multiple surgical debridements	Incubation in Sabouraud dextrose agar and DNA extraction, amplification and sequencing analysis	LAMB + itraconazole repeated because of a recurrent right lower eyelid swelling and redness	Resolution
7	Mukherjee, 2018	F	2	India	Rapidly progressive swelling in the medial canthal region of her right eyes	Normal	Unknown. No history of trauma, nasal blockage, epistaxis or weight loss	MRI + incisional biopsy	Histopathological examination + PCR	Amphotericin B + posaconazole	Resolution

## Methods

The narrative review was conducted in June 2020-January 2021 in the electronic databases MEDLINE (PubMed) and Scopus using the keyword “*Saksenaea erythrospora*”. We considered eligible articles that met the following inclusion criteria:

- language: Italian, English, French, Spanish;
- publishing time: no time restrictions;
- available information: gender and age of the case (due to *Saksenaea erythrospora*), clinical presentation, undergone diagnostic and therapeutic procedures, pharmacological treatment, outcomes.

Studies that provided ambiguous or insufficient data were excluded.

## Results

Bibliographic research yielded 23 publications. After the analysis of the titles and abstracts, 13 studies were excluded: 9 as duplicates, 2 as reviews, 3 because they reported data not in line with the present study. The full text of the 9 remaining articles was analyzed: 2 articles were excluded because they focused on elements not in line with the study. The overall analysis was therefore conducted on 7 studies [4-10] (Tab. I).

The studies were published between 2011 and 2015 and involved a total of 11 patients of average age 37.9 years (SD 17.23) hospitalized in several hospitals in: USA, India, Argentina, Colombia, Thailand. Six (54.5%) patients were female, 5 (45.5%) male. All patients had an immune status that could be considered normal.

In 4 cases the trigger factor was an injection [5], in 1 case a combat trauma [6], in 1 an accident injury [8], in 1 case cosmetic surgery undergone in another country [9], in 4 cases the trigger was not identified.

In most cases (90.9%) the treatment was based on amphotericin B in various formulations; in 4 (36.3%), at least one other antifungal (posaconazole, caspofungin, itraconazole) was also associated. Surgical debridement was necessary in 100% of cases: in 3 cases also extensive demolition operations were necessary (eye removal or breast removal) [4, 6, 9].

Healing occurred in 9 patients. Two patients, instead, died (one had developed the infection after a combat trauma; the other a necrotizing infection after an injection) [5, 6].

## Discussion

Our review tried to update what already reported by Putthirangsiwong et al. in 2019 [4] and Chander et al. in 2017 [5], but was limited by the exiguous number of new studies (only one) that we found. This is the major limit of the study. However, we collected the information contained in the previously published studies and organized them in order to have a more complete a unique overview of this topic. Another limit is represented by authors' choice to focus only on

*Saksenaea Erythrospora*, excluding the other species of *Saksenaea*.

Results confirmed that most *S. erythrospora* infections occur in immunocompetent subjects. The ability of the *Mucorales* to invade the arteries is responsible for thrombosis and the gradual generation of large necrotic areas: this promotes the progression and invasion of deep tissues [8].

As Pelroth et al. recommended, for the eradication of mucormycosis (including *Saksenaea Erythrospora* infections) four factors are fundamental: rapidity of diagnosis, correction of predisposing factors (if possible), adequate surgical debridement of the infected tissue and appropriate antifungal therapy.

Early diagnosis is important because small focal lesions can often be surgically removed before they progress. Unfortunately, there are no serological or PCR-based tests for a rapid diagnosis. In many cases, unfortunately, cases of mucormycosis are diagnosed post mortem [2].

The use of molecular methods based on PCR amplification and sequencing should be used in cases of atypical unresolved skin and soft tissue infections [11].

The most of cases has been associated with traumas; some with injections (that could be considered as slight traumas): correcting or controlling predisposing conditions is essential to improve the treatment outcome.

Mucormycosis is often rapidly progressive and antifungal therapy alone is often inadequate to control the infection. In addition, the angioinvasion, thrombosis and distinctive tissue necrosis of this disease result in poor penetration of anti-infectious agents into the infection site. Therefore, even if the causative organism is susceptible to the antifungal agent in vitro, the antifungal may be ineffective in vivo. Surgical debridement of infected and necrotic tissue must be done urgently [2].

The case described in 2016 by Rodriguez et al. is certainly interesting [9]: it is the first case of mucormycosis following breast augmentation performed in a context of “medical tourism”.

Although many of the institutions involved in medical tourism work very well and are organized with high quality standards, many procedures can be unconventionally performed or performed in institutions that do not meet the appropriate infection control standards. Therefore, patients should be informed of the risks associated with the medical tourism procedures, including the risk of infection; moreover, doctors must be vigilant and must know the local epidemiological characteristics of the places where medical tourism procedures have been performed [12, 13].

## Conclusions

Concluding, invasive fungal infections are increasingly frequent nosocomial problems [14, 15] and episodes of infections from new and rare species of fungi have been increasingly frequent. The analysis of these phenomena is a unique opportunity to learn how to quickly identify the cases, implement adequate control measures (even

when published data are lacking) and strengthen community awareness of this new risk.

Especially during severe necrotizing *Saksenaea erythrospora* infections, early identification and timely management are essential to reduce morbidity and mortality in these patients.

A greater awareness and education about the risks deriving from carrying out surgical procedures abroad, especially in precarious hygiene situations, could be further effective strategies for the reduction of these infections [16].

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## Conflict of interest statement

The authors declare no conflict of interest.

## Authors' contributions

GT had the idea of the study, collected data and wrote the article. NN helped to conceptualize the ideas and to write the article.

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