Rhinosinusitis caused by *Saksenaea erythrospora* in an immunocompetent patient in India: a first report

Uma Tendolkar,1 Anne van Diepeningen,2 Anagha Joshi,3 Jeroen Koomen,2 Renuka Bradoo,3 Sujata Baveja1 and Shailesh Agrawal3

**Correspondence**

Uma Tendolkar
umatendolkar@gmail.com

1Department of Microbiology, Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai 400 022, India

2CBS-KNAW Fungal Biodiversity Centre, Institute of the Royal Netherlands Academy of Arts and Sciences (KNAW), Uppsalalaan 8, 3584 CT, Utrecht, The Netherlands

3Department of Ear, Nose & Throat Surgery, Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai, 400 022, India

**Introduction:** *Saksenaea erythrospora* is a recently described species that has been reported in two human cases of cutaneous infection. The present case is, to the best of our knowledge, the first with invasive infection of the sinuses by this fungus and the first report of its isolation from India.

**Case presentation:** A 44-year-old woman was diagnosed with a pre-septal cellulitis and pansinusitis. She was non-diabetic and did not have any other co-morbidity. The patient underwent emergency endoscopic endonasal debridement for right pansinusitis with right orbital nerve decompression and left-sided functional endoscopic sinus surgery. A right orbital exenteration was performed to prevent further spread of the infection. Debrided material from the orbit grew *S. erythrospora*, the identity of which was confirmed by molecular techniques. The infection spread subcutaneously to the cheek and neck. The patient was treated with intravenous amphotericin B, to which she responded favourably.

**Conclusion:** *S. erythrospora* can cause rhinosinusitis and appears to have a propensity for subcutaneous spread. The fungus is present in the environment in India. Treatment with amphotericin B was successful in our case.

**Keywords:** amphotericin B; fungal rhinosinusitis; mucormycosis; *Saksenaea; Saksenaea erythrospora*; sinusitis.

**Case report**

A 44-year-old female, a resident of Mumbai, India, was admitted with a history of right-sided orbital cellulitis, which was sudden in onset and painful, and with complete loss of vision for 3 days. The patient also had swelling of the right cheek for 3 days. The symptoms began with a right earache radiating to the cheek 7 days prior to admission, followed by complete loss of vision, and was associated with fever with chills. The patient also complained of a dull aching type of headache. The patient had a history of recurrent sinusitis over several years. There was no history of trauma, nor a history of nasal blockage, epistaxis or dental caries. The patient had not travelled out of Mumbai over the past year. The patient also did not have any other co-morbid condition such as diabetes mellitus, tuberculosis, hypertension, human immunodeficiency virus infection or any other obvious immunocompromising condition.
nor was there any history of long-term steroid or broad-spectrum antibiotic intake.

On examination, the patient was conscious and oriented. She had proptosis, chemosis and ptosis in the right eye. The eye movements were restricted and the pupil was dilated with no perception of light. She had a right-sided facial palsy with deviation of the tongue, drooling of saliva and a poor gag reflex (Fig. 1a). On anterior rhinoscopy, there was nasal discharge with polyps and no crust- ing or blackening of the mucosa. The ear and throat examination showed no abnormality.

**Investigations**

Computerized tomography of the paranasal sinuses was carried out on the patient and the results were suggestive of deformations in the orbit with bilateral maxillary, frontal and ethmoidal sinusitis. Magnetic resonance imaging showed orbital cellulitis with optic neuritis (Fig. 1d). Debrided orbital tissue was collected for fungal culture. On a potassium hydroxide mount, abundant broad, sparsely septate fungal hyphae were seen, which were also seen with a simplified Gomori’s methenamine silver stain (Tendolkar & Gogate, 1997). Woolly fungal growth was seen within 2 days on Sabouraud dextrose agar incubated at 28 °C as well as 37 °C, later filling the tube with a characteristic abrupt cessation of growth resulting in a very flat matted surface. A slide culture on potato dextrose agar failed to produce any conidia so a slide culture was set up on water agar (Ellis & Ajello, 1982) with the block being placed submerged in the water. After 3 weeks of incubation at 26 °C, sporulation was seen on the coverslip. The long sporangiophores, flask-shaped sporangia and ellipsoid, biconcave sporangiospores were suggestive of *Saksenaea erythrospora* (Fig. 2b, c). In contrast, the sporangiospores of *S. vasiformis* are cylindrical and those of *S. oblongispora* are oblong. These morphological differences have been found to correlate with molecular studies (Alvarez et al., 2010). On other nutrient-rich media, such as malt extract agar, oatmeal agar and potato dextrose agar, no sporulation was observed in this particular strain.

For molecular confirmation of the identification, multilocus sequence analysis was performed. DNA was extracted with a cetyltrimethyl ammonium bromide-based extraction method (Möller et al., 1992). For identification to the genus level, the barcoding internally transcribed spacer region, the 28S large ribosomal subunit and partial transcription elongation factor 1α were used, as in a recent study on clinical *Saksenaea* (Alvarez et al., 2010). The PCR fragments were sequenced with an ABI Prism Big Dye™ Terminator v.3.0 Ready Reaction Cycle Sequencing kit (Applied Biosystems) and analysed on an ABI PRISM 3700 Genetic Analyzer (Applied Biosystems). Sequences were BLASTed against GenBank for identification and showed 99–100% nucleotide identity with corresponding sequences of *S. erythrospora* strains. A selection of the strains in the study by Alvarez et al. (2010) was used for phylogenetic analysis to test this relationship further. The phylogenetic trees of each gene separately and a concatenated tree (Fig. 2a) were inferred with MrBayes v.3.2 (Ronquist et al., 2012), using 10⁷ generations in the Markov chain Monte Carlo simulation.
Carlo protocol to estimate the posterior distribution of the model parameters, mixed character states, a gamma distribution of the rates, a burn in fraction of 0.25 and four chains. In all separate and combined gene trees, the studied aetiological agent fitted with posterior probability values >0.95 within the S. erythrospora clade. Hence, the strain has been deposited in the CBS culture collection as S. erythrospora under accession number CBS 138279.

Diagnosis
A diagnosis of a preseptal orbital cellulitis with invasive fungal pansinusitis was made based on the investigations.

Treatment
In view of the relentless progression of the disease, the patient underwent emergency endoscopic endonasal debridement for right pansinusitis with right orbital nerve decompression. The patient also underwent right orbital exenteration to prevent further spread of the infection (Fig. 1c). She was treated with intravenous amphotericin B at a dose of 1 mg kg⁻¹ day⁻¹. While recuperating from surgery, the swelling from her cheek extended to the neck (Fig. 1b), a biopsy of which also showed sparsely septate fungal hyphae, but there was no growth in culture. This finding indicated local subcutaneous spread of the fungus, which was contained by the antifungal therapy. During the course of amphotericin B therapy, the drug was withdrawn intermittently due to increased serum creatinine levels. However, the patient received a cumulative total dose of amphotericin B of 2.4 g. After she had stabilized, she was discharged.

Outcome and follow-up
The patient is asymptomatic at present with no recurrence.

Discussion
The genus Saksenaea was first described from forest soil in India (Saksena, 1953). Most of the human cutaneous infections described so far are due to the more common species S. vasiformis and have resulted from soil contamination of wounds (Ribes et al., 2000), from inhalation of spores into sinuses resulting in rhinosinusitis (Kaufman et al., 1988) or by direct inoculation into facial wounds or sinuses by contaminated water (Gonis & Starr, 1997). The first report of S. erythrospora was by Hospenthal et al. (2011), in a patient with deep facial burns as a result of combat trauma. The fungus was isolated from the rhinofacial area from skin and also from the orbit, indicating direct entry of the fungus into the tissues through the burnt skin. The clinical course was complicated by the development of invasive mucormycosis of the orbit and facial area by S. erythrospora, 14 days after the burns, and the patient finally died. Relloso et al. (2014) reported an infection following soft-tissue contamination with water and soil following a sailing accident. In the present case, the route of infection appeared to be by deposition of infectious propagules in the sinonasal area, as in other sinonasal infections of this organism. Although S. erythrospora does not sporulate on routine culture medium, similar to S. vasiformis, it appears to have pathogenic potential similar to this established pathogen, which causes infection in immunocompromised as well as in immunocompetent subjects. Infection in a newborn calf due to S. erythrospora has also been reported (Lawhon et al., 2012). Saksenaea spp. are considered to be unique amongst zygomycetes due to their flask-shaped sporangia and the gelatin plug on them. Sporulation of Saksenaea spp. can be induced on water agar and Czapec agar (Alvarez et al., 2010). Amphotericin B is commonly used in the treatment of S. vasiformis infections, and posaconazole has been used as an alternative drug (Gomes et al., 2011). The in vitro susceptibility of S. erythrospora to amphotericin B, the echinocandins and voriconazole appears to be low (Alvarez et al., 2010; Gomes et al., 2011), but a good clinical response was obtained with surgical intervention and amphotericin B, supported by a non-immunocompromised status in the present case. The present report also confirms the presence of S. erythrospora in India and its ability to cause invasive rhinosinusitis.

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