

## Ocular infections caused by *Scedosporium apiospermum*: A case series

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The aim of our retrospective study is to report a case series of ocular infections caused by a rare fungus, *Scedosporium apiospermum*, in a South Indian population. Thirteen cases of culture-positive *S. apiospermum* infections diagnosed between January 2011 and March 2016 were included in this study. The parameters evaluated were predisposing factors, treatment and final clinical outcome. The most common mode of presentation was keratitis (84.6%) followed by sclerokeratitis (15.3%). The predisposing factors involved were unspecified foreign body injury (30.7%), organic matter injury (15.3%), uncontrolled diabetes (7.6%), and recent manual small-incision cataract surgery (7.6%). Five cases (38.46%) had no predisposing factor. Of the 11 keratitis cases, nine (69.2%) responded well to combination medical therapy while one case (7.6%) required therapeutic keratoplasty. One case was lost to follow-up. Both cases which presented with sclerokeratitis showed no response to medico-surgical treatment progressing to panophthalmitis and evisceration.

**Key words:** Keratitis, *Scedosporium apiospermum*, sclerokeratitis

Keratomycosis is commonly seen in posttraumatic cases, particularly in a rural environment. Over 60 different species of fungi have been reported to cause mycotic keratitis, *Fusarium*, and *Aspergillus* being the most common.<sup>[1]</sup> *Scedosporium apiospermum*, previously known as *Monosporium apiospermum*, is a ubiquitous dematiaceous filamentous fungus. It can be recovered from soil, decaying matter, and polluted water.<sup>[2]</sup> The histopathological morphology of this species is similar to *Fusarium* spp. and *Aspergillus* spp. Infections caused by *S. apiospermum* species infections can be found in immunocompetent as well as in immunocompromised individuals.<sup>[2]</sup> *Pseudallescheria boydii*, also known as *Petriellidium boydii*, is the sexual form of this fungus.<sup>[3]</sup> Here, we report a

series of cases of ocular infections caused by this rare fungus, *S. apiospermum*, in a South Indian population.

### Methods

Retrospective, observational study of medical records of patients diagnosed with culture-positive *S. apiospermum*-induced keratitis, scleritis, and endophthalmitis was done in the Cornea Services of Aravind Eye Hospital, Puducherry, Tamil Nadu, after obtaining the required permission from the institutional review board. Thirteen such cases diagnosed between January 2011 and March 2016 which were treated medically or surgically were included in this study. The main parameters evaluated in this study were predisposing factors, treatment modality used and outcome of various treatment modalities. Time to healing was noted as the duration from initiation of treatment at our hospital to the follow-up visit when antifungal medications were stopped upon complete scarring of infiltrate. The statistical analysis was done using SPSS software, version 20 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

### Results

The total number of culture-positive fungal keratitis during the study period was 1621, out of which those caused by *Scedosporium* were 13 (0.8%). The mean age of presentation was 54.3 years (range 30–85 years). Out of the total 13 patients, seven (53.8%) were male and six (46.15%) were female. Four (30.7%) patients had been using some ocular medications before presenting to our hospital. The average time to presentation from the onset of symptoms was 7.15 days (range 2–20 days). The different modes of presentation were keratitis 11 cases (84.6%) which was most common, followed by two cases of sclerokeratitis (15.3%). The mean size of infiltrate (longest diameter of infiltrate multiplied by its longest perpendicular diameter) was 20 mm<sup>2</sup>. Four cases (30.7%) showed hypopyon at presentation. Furthermore, one case following recent manual small-incision cataract surgery (MSICS), performed elsewhere, showed sclerocorneal wound infiltrate with superior corneal ring infiltrate. Case-wise details of every patient are elaborated in Table 1.

Out of the 11 keratitis cases, nine (69.2%) responded well to medical therapy with topical natamycin along with an azole (fluconazole in seven and voriconazole in two cases) while one case required therapeutic keratoplasty for progressive keratitis with perforation. Average time to healing in the nine keratitis cases that showed healing was 44.44 days (range 26–71 days). Both cases which presented with sclerokeratitis showed no response to medico-surgical treatment progressing to panophthalmitis and evisceration. One of these two sclerokeratitis cases [case no. 2 in Table 1] grew *Scedosporium*

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in the initial corneal scraping culture and *Aspergillus fumigatus* in the final evisceration specimen, indicating a mixed fungal infection. One case was lost to follow-up.

## Discussion

Being a rare filamentary fungus to affect the eye, reports of *Scedosporium*<sup>[4-6]</sup> ocular infections in literature are usually solitary and uncommon. The literature has attributed the low incidence of *Scedosporium* keratitis to difficulty in distinguishing *Scedosporium* from *Aspergillus*, *Fusarium*, and other hyaline hyphomycetes due to common histopathological and clinical features. However, sporulation in culture followed by staining with lactophenol cotton blue, a stain commonly used to identify fungi, helps in identifying *scedosporium*<sup>[1]</sup> [Fig. 1]. Even the large National Eye Institute supported studies, MUTT I<sup>[7]</sup> and MUTT II<sup>[8]</sup> that enrolled 563 patients in all had only one case of proven *Scedosporium* keratitis (personal communication with the authors). Only two cases series of *Scedosporium* ocular infections have been reported till date, one from Australia and another from southern India. The Australian study<sup>[9]</sup> has reported scleritis due to *Scedosporium* as the most common presenting feature, with six of nine patients with history of previous pterygium surgery. Most of our patients, on the other hand, had keratitis as the common presenting feature and even the two patients who had a scleritis component did not give any history of previous pterygium surgery. One of them had undergone a

recent MSICS and was on topical steroids when she developed the sclerokeratitis, while the other patient developed *Scedosporium* sclerokeratitis in a previously scarred, nonseeing eye with an anterior staphyloma.

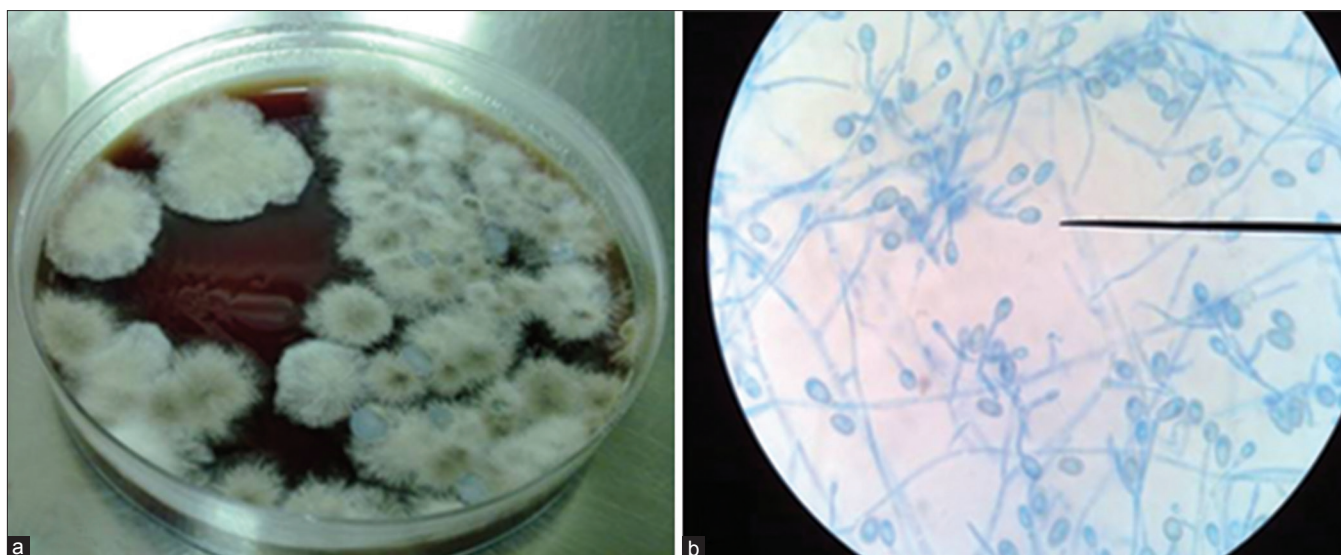
Of special interest was the case that developed infection of the superior sclerocorneal wound along with the adjacent superior cornea, 2 weeks post-MSICS. Though culture from the initial corneal scraping revealed *S. apiospermum*, the final evisceration specimen grew *A. fumigatus*, indicating a mixed fungal infection. The concomitant use of topical steroids, delay in referral, involvement of the sclera, and a mixed fungal infection, all could have contributed to the downhill course of disease in this patient who progressed to endophthalmitis and panophthalmitis, finally necessitating evisceration. To the best of our knowledge, this is the first reported case of proven *Scedosporium* wound infection in the early postoperative period following cataract surgery.

The other case series by Rathi *et al.*,<sup>[10]</sup> also from South India, showed healing with natamycin monotherapy in five of eight cases while natamycin along with voriconazole was used in two of eight cases. At our hospital, we administer natamycin monotherapy to mild ulcers (<2 mm in largest diameter, involving the anterior stromal third only and noncentral, none of the ulcers in our series fit these criteria).<sup>[11]</sup> Since polyenes and azoles act at two different levels of ergosterol biosynthesis pathway, we prefer to take advantage of this possible

**Table 1: Clinical features and outcome**

Num ber	Previous medica tions	Days to first presen tation	Predis posing factors	BCVA presen tation (Snellen)	Smear	Treat ment	Clinical presen tation	Infiltrate		Time to healing (days)	BCVA final (Snellen)	Final outcome
								Size (mm <sup>2</sup> )	Depth of stroma			
1	V + G	3	Unspecified FB fall	2/60	+	N + V	K	8	Anterior 1/3	58	6/18	Healed
2	G + P	14	MSICS	HM	+	A + F	S	15	Full	NA	NA	Evisceration
3	Nil	3	NIL	6/60	+	N + F	K	9	Full	26	6/12	Healed
4	Nil	5	Unspecified FB fall	1/60	+	N + F	K	15	Full	NA	NA	Lost to follow-up
5	Nil	5	Nil	CF	+	N + V	K	20	Anterior 2/3	39	6/36	Healed
6	Nil	3	Sugarcane leaf	3/60	+	N + F	K	16	Anterior 1/3	35	5/60	Healed
7	Nil	10	DM	CF	+	N + F	K	20	Full	34	1/60	Healed
8	Nil	20	Nil	HM	+	N + F	K	20	Full	71	HM	Healed
9	Nil	2	Wooden stick injury	HM	-	N + F	K	32	Full	51	1/60	Healed
10	Nil	10	Unspecified FB fall	6/36	+	N + F	K	9	Anterior 2/3	44	6/9	Healed
11	C	4	Nil	5/60	+	N + F	K	6	Anterior 1/3	42	6/12	Healed
12	Nil	7	Unspecified FB fall	PL	-	N + F + V	K	60	Full	NA	PL, PR accurate	TPK
13	Nil	7	Nil	? PL	+	N + F + V + K	S	42	Full	NA	NA	Evisceration

FB: Foreign body, MSICS: Manual small-incision cataract surgery, DM: Diabetes mellitus, N: Natamycin 5% eye drops, F: Fluconazole 0.3% eye drops, V: Voriconazole 1% eye drops, A: Amphotericin B 0.15% eye drops, G: Gatifloxacin eye drops, C: Ciprofloxacin eye drops, P: Prednisolone eye drops, K: Ketoconazole oral tablets, NA: Not applicable, K: Keratitis, S: Sclerokeratitis, PR: Projection of rays, HM: Hand movements, CF: Counting finger, TPK: Therapeutic penetrating keratoplasty, BCVA: Best-corrected visual acuity, PL: Perception of light, +: Perception is present, -: Perception is absent, ?PL: Perception of light is doubtful



**Figure 1:** (a) Chocolate agar showing dirty white cottony colonies on inoculation of corneal scraping material. Growth was seen after 3 days of incubation at 25°C. (b) Lactophenol cotton blue staining showing septate hyphae, ovoid conidia (as shown by the microscope pointer) with truncated bases suggestive of *Scedosporium apiospermum* as visualized using a binocular compound microscope with high power and  $\times 45$

synergistic effect in treating moderate and severe ulcers, as in our series. Hence, we instituted a topical combination therapy of 5% natamycin, a polyene (shown to be very effective against filamentous fungi)<sup>[7]</sup> as the primary drug and an azole, either 0.3% fluconazole or the relatively newer 1% voriconazole.<sup>[12]</sup> All three drugs are commercially available and hence are easy to dispense and use. The effectiveness of topical fluconazole has been debated in literature with some studies showing poor susceptibility of filamentous fungi to fluconazole *in vitro*<sup>[13]</sup> and in the clinical scenario,<sup>[14]</sup> while other authors have claimed clinical benefit even with fluconazole monotherapy in filamentary fungal keratitis.<sup>[15]</sup> We found that in our series, natamycin and fluconazole combination therapy succeeded in seven of 10 cases. Of the remaining three, one was lost to follow-up, one progressed to therapeutic keratoplasty, and one had scleral involvement and progressed to evisceration.

Time to healing in our series may appear quite prolonged since it was a retrospective analysis, and we have taken the visit at which topical antifungals were stopped completely. We usually stop antifungals after 10–14 days of complete scarring as visualized on slit lamp.

## Conclusion

Most *Scedosporium* infections of the cornea alone responded well to commercially available antifungals with natamycin as the primary drug. Cases which involved the sclera showed grave prognosis eventually leading to panophthalmitis and evisceration.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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