Enferm Infecc Microbiol Clin. 2012;30(3):163–166

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Cartas científicas

Endophthalmitis caused by *Phialophora verrucosa*: A case report and literature review of *Phialophora* ocular infections

Endoftalmitis causada por Phialophora verrucosa: *descripción de un caso y revisión de la literatura sobre infecciones oculares por* Phialophora

Dear Editor,

We present a case of endophthalmitis caused by *Phialophora verrucosa* and review the available literature on *Phialophora* ocular infections.

A 66-year-old man with hypertension, type II diabetes mellitus and bilateral chronic glaucoma consulted the Ophthalmology Department about his red right eye. The patient did not report any previous eye surgery or recent ocular trauma. Episcleritis was diagnosed and he was started on topical corticosteroids and antibiotics. Six months later, he complained about loss of vision, and ophthalmic examination showed a fine brown material in the anterior chamber. Material aspirate and aqueous tumor were sent to the Microbiology and Pathology laboratories. Histological examination showed septate hyphae and fungal spores. After a week on Sabouraud dextrose agar, the material from both samples became black, embedded in the medium, and increased its size. On potato dextrose agar, the colony was initially white and turned to black with a black reverse. Microscopically, hyphae were septate, brown and branched, phialides were flask shaped with a cup-like collarette and ellipsoidal conidia accumulated at the apice of the phialide. All characteristics corresponded to the *Phialophora* genus. The strain was sent to a reference laboratory where it was identified as *P. verrucosa* by morphological criteria and PCR and sequencing using ITS1 and ITS4 primers, and antifungal susceptibility testing was made according to EUCAST methodology. A MIC less than or equal to 0.5 mg/L was obtained for amphotericin B, itraconazole, voriconazole, posaconazole and caspofungin. The patient was started on oral voriconazole (200 mg every 12 h), amphotericin B eye drops (every 6 h) and topical corticosteroid, with no improvement. Vitrectomy and intravitreal amphotericin B injection (5 μg) were performed twice and new samples were taken. Finally, the patient underwent enucleation of the eye due to recurrent pain and blindness. Currently, he is asymptomatic.

There are seven reported cases of ocular infections caused by *Phialophora* species[1–8] (Table 1). Data were not available for one patient. All the remaining patients were men, with a mean age of 52.3 years. The most frequent risk factors were trauma, occurred between days and months before the first ophthalmologic consultation, and treatment with topical corticosteroids. In our case, the patient reported a trauma with a piece of wood thirty five years before, with recurrent episodes of hyperemia during the last few years. As regards the clinical presentation of the infection, six patients had keratitis, and two had endophthalmitis. All patients were initially treated with topical and/or oral antifungals, most of them unsuccessfully. Surgery was required in six patients, keratoplasty in four and vitrectomy in two, followed by intraocular and/or intravenous antifungal therapy in four of them. More than one antifungal agent was used in five cases, and amphotericin B was the most commonly prescribed drug. Due to clinical progression of the infection, the eye was enucleated in three cases. The outcome of the rest of patients was good.

Fungal infections of the eye are mainly caused by *Candida*, *Fusarium* and *Aspergillus* species. Genus *Phialophora*, a dematiaceous fungus, is a rare agent of ocular infection; in fact, we have only found seven reported cases. Ocular trauma was the most common predisposing factor. In our patient, due to the long time passed since the trauma, we cannot assume it as the origin of the infection. More than half of the patients received corticosteroids that could facilitate the fungal infection and its progress. To reach the diagnosis of ocular fungal infections, a collection of appropriate specimens is mandatory: in keratitis, superficial scrapings or a corneal biopsy, and in endophthalmitis, aqueous and vitreous aspirates. A direct microscopic examination offers a rapid presumptive diagnosis and culture is essential to identify the fungus involved, and to determine the susceptibility profile of the strain. Since dematiaceous fungi are commonly found in the environment, their clinical significance needs to be assessed. In our case, histological examination and repeated cultures from several intraocular samples obtained at different times confirmed that *P. verrucosa* was the causative agent. Despite the lack of interpretative MIC breakpoints and limited correlation between MIC and treatment outcome, antifungal susceptibility testing is recommended, especially when the fungus is infrequently isolated. *Phialophora* is usually susceptible to amphotericin, itraconazole and voriconazole.[9] In the management of aspergillus keratitis, the prompt initiation of antifungal therapy and surgery in refractory patients is recommended, and vitrectomy followed by intravitreal amphotericin B or intravitreal or systemic voriconazole in aspergillus endophthalmitis.[10] Currently, there are no therapeutic recommendations for ocular infections caused by fungi other than *Aspergillus*.

In summary, although *Phialophora* is rarely involved in eye infections, its role as a potential pathogen should be kept in mind when it is isolated from ocular samples. Given the availability of antifungals, susceptibility testing of the strain is important to select the optimal therapy.

Table 1
Ocular infections caused by *Phialophora* spp. including the present case.

Species (case)	Year of publication (Reference)	Fungal identification procedure	Type of ocular infection	Age/sex	Risk factors	Ocular symptoms and signs	Antifungal therapy	Surgery	Outcome
P. verrucosa (1)	1966 (1,2)	Morphological identification	Keratitis	47/M	Trauma. Topical steroids	Discomfort, hyperemia, photophobia	AMB (TOP), TBZ (TOP)	Keratoplasty twice	Cured
P. verrucosa (2) (+*C. cladosporioides*)	1976 (3)	Morphological identification	Keratitis	56/M	Trauma. Topical steroids	Persistent ocular inflammation, loss of vision. Hypopyon	NTM (TOP)	Keratoplasty twice	Cured
P. bubakii (3)	1983 (4)	Morphological identification	Keratitis	34/M	Trauma	Hypopyon	FCT (TOP)	None	Cured
Phialophora sp. (4)	1995 (5)	NDA	Keratitis	34/M	Contact lenses use. Topical steroids	Discomfort, pain, photophobia, loss of vision	NTM (TOP), AMB (TOP + EV)	Keratoplasty	Cured
P. verrucosa (5) (*C. tropicalis*, *P. acnes*)	2008 (6)	NDA	Keratitis	79/M	Trauma	Pain, loss of vision	AMB (TOP), KTZ (PO), VCZ (TOP, PO, IO), ITZ (PO)	Keratoplasty twice	Enucleation
Phialophora sp. (6)	2010 (7)	Morphological identification	Keratitis	NDA	NDA	NDA	NDA	NDA	NDA
P. verrucosa (7)	2010 (8)	Morphological identification. Sequencing	Endophthalmitis	50/M	Trauma	Loss of vision	AMB (IO), FC (IO, TOP), NTM (TOP)	Vitrectomy	Enucleation
P. verrucosa (8)	Present report	Morphological identification. Sequencing	Endophthalmitis	66/M	Topical steroids	Pain, hyperemia, loss of vision	VCZ (PO), AMB (TOP, IO)	Vitrectomy twice	Enucleation

AMB: amphotericin B; EV: endovenous; FC: fluconazole; FCT: flucytosine; IO: intraocular; ITZ: itraconazole; KTZ: ketoconazole; NDA: no data available; NTM: natamycin; PO: by mouth; TOP: topical; TBZ: thiabendazole; VCZ: voriconazole.

Acknowledgments

We thank Dr. Calixto Arias for his assistance in editing the manuscript. We also thank the Servicio de Micología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, for the identification of the species and antifungal susceptibility of the strain.

References

1. Wilson LA, Sexton RR, Ahearn D. Keratochromomycosis. Arch Ophthal. 1966;76:811–6.
2. Jones DB, Sexton R, Rebell G. Mycotic keratitis in South Florida: a review of thirty-nine cases. Trans Ophthalmol Soc UK. 1969;89:781–97.
3. Polack FM, Siverio C, Bresky RH. Corneal chromomycosis. Double infection by *Phialophora verrucosa* (Medlar) and *Cladosporium cladosporiodes* (Frescenius). Ann Ophthalmol. 1976;2:139–44.
4. Eiferman RA, Snyder JW, Barbee JV. Corneal chromomycosis. Am J Ophthalmol. 1983;95:255–6.
5. Hirst LW, Stallard K, Whitby M, Perrin R. Phialophora corneal ulcer. Aust N Z J Ophthalmol. 1995;25:223–5.
6. Banitt M, Berenbom A, Shah M, Buxton D, Milman T. A Case of polymicrobial keratitis violating an intact lens capsule. Cornea. 2008;27:1057–61.
7. Vanzzini Zago V, Manzano-Gayosso P, Hernández-Hernández F, Méndez-Tovar LJ, Gómez-Leal A, López-Martinez R. Mycotic keratitis in an eye care hospital in México city [Queratomicosis en un centro de atención oftalmológica en la Ciudad de México]. Rev Iberoam Micol. 2010;27:57–61.
8. Sun S, Yuan G, Zhao G, Chen H, Yu B. Endophthalmitis caused by *Phialophora verrucosa* and Streptococcus intermedius: a case report. Med Mycol. 2010;48:1108–11.
9. Hoog GS, Guarro J, Gené J, Figueras MJ. Hyphomycetes: explanatory chapters, and keys to the genera. In: Atlas of clinical fungi. 2nd ed. The Netherlands and Spain: Centraalbureau voor Schimmelcultures and Universitat Rovira i Virgili; 2000. p. 879.
10. Walsh T, Anaissie EJ, Denning DW, Herbrecht R, Kontoyiannis DP, Marr KA, et al. Treatment of aspergillosis: clinical practice guidelines of the infectious diseases Society of America. Clin Infect Dis. 2008;46:327–60.

M. Isolina Campos-Herrero[a,*], Luis Tandón[b], Iballa Horcajada[a], Francisco Medina-Rivero[b]

[a] *Servicio de Microbiología, Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain*
[b] *Servicio de Oftalmología, Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain*

* Corresponding author.
E-mail address: mcamnavl@gobiernodecanarias.org (M.I. Campos-Herrero).

doi:10.1016/j.eimc.2011.10.012

Jugo gástrico versus esputo inducido para el diagnóstico de tuberculosis pulmonar en niños

Gastric juice versus induced sputum for the diagnosis of pulmonary tuberculosis in children

En la tuberculosis (TB) pulmonar infantil, la confirmación microbiológica se consigue en un 30-40% de los casos[1] respecto al 80-85% de la población adulta[2], y generalmente se debe recurrir a técnicas molestas como el aspirado de jugo gástrico (JG). Estas dificultades se deben a que la TB en los niños es típicamente paucibacilar[3,4] y a la dificultad para obtener muestras, ya que no pueden expectorar eficazmente[4]. Por ello se ha introducido el esputo inducido (EI) como alternativa.

El objetivo del estudio fue comparar si las muestras de EI obtienen mejores resultados que las de JG en niños con TB.

Para ello se revisaron las historias clínicas de todos los pacientes ingresados con sospecha de TB en el Servicio de Pediatría del Hospital Universitario Príncipe de Asturias de Alcalá de Henares entre 2002 y 2010. Fueron excluidos aquellos con inmunodeficiencia, en los que se aislaron micobacterias no tuberculosas y los que habían recibido tratamiento antituberculínico previo. Ingresaron 12 horas antes de la recogida de muestras y durante 3 días. El aspirado gástrico se realiza al despertar, mientras el niño permanece tumbado en la cama. La inducción del esputo se realiza 2-3 horas después, manteniendo el ayuno, monitorización con pulsioxímetro y pre-tratamiento con 200 mcg de salbutamol. Se nebulizan 5 ml de ClNa 5% con O_2 a presión y un flujo de 5 litros por minuto durante 15 minutos y se aspiran las secreciones de nasofaringe tras percusión torácica. Las muestras son procesadas en las 2 horas siguientes o, en caso de que esto no fuera posible, se guardan en nevera entre 5 °C y 8 °C. El análisis estadístico fue realizado con el programa SPSS 17.0 con el test de McNemar para el contraste entre variables cualitativas pareadas.

Como resultado de esta revisión, se obtuvo un total de veintiséis pacientes diagnosticados de enfermedad tuberculosa. Nueve (34,6%) eran varones con una mediana de edad de 67 meses (rango 6-173 meses). Todos tenían prueba de tuberculina positiva (mayor a 5 mm de induración) y 21 (80,7%) de ellos presentaban alteraciones radiológicas; siendo la alteración más frecuente las adenopatías hiliares. En 8 pacientes (30,8%) se aisló *M. tuberculosis* en muestras de JG y de ellos, en 2 (7,7%), también en las muestras de EI. Con un total de 22 (14,5%) muestras positivas, solo 3 (4%), pertenecían al EI (tabla 1). La tinción de auramina detectó bacilos ácido-alcohol resistente en solo 1 de los pacientes (1,3% del total de muestras). Existen diferencias estadísticamente significativas entre los resultados obtenidos a partir de todas las muestras de JG respecto a las de EI (24,7 respecto a un 4%, p = 0,03. Odds ratio 1,33 [IC 95% 0,89–1,98]) aunque no se confirma esta diferencia al realizar las mismas comparaciones entre la primera toma de muestra realizada por cada método (26,9 respecto a un 7,7%, p = 0,06. Odds ratio 1,4 [IC 95% 0,87–2,2]) ni entre la segunda (19,2 respecto a un 4%, p = 0,12. Odds ratio 1,25 [IC 95% 0,80–1,93]).

Tabla 1
Resultado del total de muestras analizadas de esputo inducido y jugo gástrico

	N.° muestras recogidas	Cultivos positivos (porcentaje)	Porcentaje respecto del total de muestras
ESPUTO INDUCIDO			
1.ª muestra	26	2 (7,7%)	2,6%
2.ª muestra	25	1 (4%)	1,3%
3.ª muestra	24	0 (0%)	0%
Total	75	3 (4%)	4%
JUGO GÁSTRICO			
1.ª muestra	26	7 (26,9%)	9,1%
2.ª muestra	26	5 (19,2%)	6,5%
3.ª muestra	25	7 (28%)	9,1%
Total	77	19 (24,7%)	24,7%
TOTAL	152	22 (14,5%)	14,5%

El diagnóstico de TB en pediatría se basa en criterios poco objetivos[1,3–5]. Los estudios sobre qué método de recogida de muestras es mejor se vienen realizando en los últimos 20 años sin una gran evidencia[6–9]. Este trabajo revela que en nuestra población, la rentabilidad diagnóstica del JG supera la del EI en más de un 20%. Esta diferencia respecto a la literatura puede deberse a la variabil-