

Dematiaceous fungal keratitis

Clinical isolates and management

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Dematiaceous fungi are darkly pigmented, filamentary moulds and are common in the environment as plant saprophytes and pathogens.

Incidental reports of corneal ulcers that have been caused by species of this group have appeared in the literature, but the relative importance of this species as potential corneal pathogens has not been appreciated.

As a group, second to *Fusarium solani* and other moniliaceous fungi, we find that dematiaceous fungi comprise the next most common cause of fungal ulcers in south Florida.

The successful treatment of *Fusarium solani* keratitis with Natamycin (Pimaricin) has been reported by Jones, Forster, and Rebell (1972), and we have examined the management of other non-*Fusarium solani* moniliaceous fungal ulcers. The purpose of this communication is to report our study of 16 isolates of dematiaceous fungal keratitis, their features, and management including nine cases that were treated with Natamycin, and to stress their relative clinical importance.

Material and methods

PATIENTS

We have studied 16 cases of keratitis caused by dematiaceous fungi. Ten cases were referred to the Bascom Palmer Eye Institute; three were examined before 1969 and reported by Jones, Sexton, and Rebell (1969), and seven were included in the 53 isolates seen during the last 4½ years. Three cases were examined in Augusta, Georgia, by one of us (LAW) and the isolates were identified and studied at the Bascom Palmer Eye Institute. Three additional isolates from Florida were sent to us; two of the patients received Natamycin, and a third was treated with topical Amphotericin B and was examined by us on completion of treatment.

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CLINICAL-LABORATORY DIAGNOSIS

All the patients had scrapings performed; microscopical examination by KOH preparation, Gram or Giemsa stains; and positive cultures on at least one medium including Sabouraud's agar, blood agar at 26°C and 37°C, and liquid brain-heart infusion (BHI). In one case keratoplasty fragments were cultured on Sabouraud's agar, and histopathology performed by Gomori's methenamine silver nitrate technique (GMS), periodic acid-Schiff (PAS) reaction, and haematoxylin-eosin stain (H and E).

Isolates were identified and speciated by sporulation from the original or lyophilized cultures. Ten of the 16 isolates were confirmed taxonomically by Dr M. B. Ellis, at the Commonwealth Mycological Institute, and the others by Ellis's manual (1971) and Von Arx (1970).

MANAGEMENT

Nine patients were treated topically with Natamycin (Pimaricin) 5 per cent suspension. Two received only Gentamicin topically. One was treated with topical Amphotericin B. A patient seen before 1969 received topical Amphotericin B, Thiabendazole, and Merthiolate and later required a conjunctival flap operation. Two other patients seen before 1969 received topical Amphotericin B, including Case 3, who also received topical Natamycin ointment and Thiabendazole. A therapeutic keratoplasty was necessary in a patient whose eye perforated before fungal diagnosis.

Results

IDENTIFICATION

Before 1969, three of 38 isolates at the Bascom Palmer Eye Institute were identified as dematiaceous fungi. These included a *Curvularia* sp. (originally identified as *C. lunata*, but not confirmed), a case of *Phialophora verrucosa* reported by Wilson, Sexton, and Ahearn (1966), and a *Lasiodiplodia theobromae*, previously diagnosed and reported as *Macrophoma* sp. by Jones and others (1969) (Table I: Cases 1, 2, and 3).

In 53 cases of fungal keratitis which have been personally examined by the author (RKF) since 1969, seven have been identified as dematiaceous fungi. These include *Curvularia senegalensis* (2); *C. pallascens*, and a non-speciated *Curvularia*; and one each *Drechslera*

halodes, *Alternaria* state of *Pleospora infectoria*, and *Lasioidiplodia theobromae* (Table I: Cases 4–10).

One of us (LAW) diagnosed three dematiaceous fungal ulcers in Augusta, Georgia, including *Alternaria alternata*, *Drechslera* state of *Cochliobolus specifer*, and *Cladosporium oxysporum* (Table I: Cases 11–13). Three other Florida isolates included two *Curvularia senegalensis* and a case of *Curvularia verruculosa* which was examined by us after treatment (Table I: Cases 14–16), see Figs 1 to 5.

CLINICAL-LABORATORY DIAGNOSIS

The characteristic features of fungal ulcers in a group of 53 cases have been described, and this series of dematiaceous fungal ulcers was not significantly different (Table 1). Ages ranged from 7 to 64 years; 10 of 16 had sustained definite foreign body trauma; and 7 of 16 had already been treated, two with antibiotics alone, and five with antibiotics and steroids.

The severity varied, some of the ulcers were super-

ficial and mild (Fig. 6), but others were deep (Fig. 7). One needed keratoplasty because of perforation, (Case 6).

Microscopical examination of scrapings or corneal fragments was positive for fungal elements in ten cases on one or more preparations using KOH, Gram, Giemsa, or histopathological stains. These included five positive KOH preparations, four positive Giemsa stains, and one positive Gram stain. Corneal fragments were positive histopathologically in Case 6.

Sixteen positive isolates grew on one or more media including 14 on Sabouraud's, two on blood agar at 26°C, four on blood agar at 37°C, and five on BHI liquid broth.

MEDICAL AND SURGICAL MANAGEMENT

Seven of 16 cases retained a visual acuity of 20/40 or better; four were 20/50 to 20/70; three 'healed' with no final vision determined; and two resulted in 20/400 acuity (Table II).

Nine of 16 cases were treated with Natamycin,

Table I Dematiaceous fungal keratitis

Case	Isolate	Trauma*	Earlier treatment		Management**	Visual acuity	
			Antibiotics	Steroids		Initial	Final
1	<i>Curvularia</i> sp.	+	NI	o	Amphotericin B	NI	20/70
2	<i>Phialophora verrucosa</i>	+	+	+	Amphotericin B Other, Conj. flap	20/30	20/400
3	<i>Lasioidiplodia theobromae</i>	+	o	o	Amphotericin B Other, Pimaricin oint	NI	20/30+
4	<i>Curvularia</i> sp.	+	o	o	Natamycin	20/40	20/20
5	<i>Alternaria</i> state of <i>Pleospora infectoria</i>	o	o	o	Natamycin	CF 1.5 m	20/70
6	<i>Curvularia senegalensis</i>	+	+	+	TPK	HM	20/40+
7	<i>Curvularia pallescens</i>	NI	o	o	Gentamicin	20/200	20/50
8	<i>Lasioidiplodia theobromae</i>	+	+	o	Natamycin	20/25+	20/25+
9	<i>Drechslera halodes</i>	o	o	o	Gentamicin	20/15	'Healed'
10	<i>Curvularia senegalensis</i>	o	o	o	Natamycin	20/70	'Healed'
11	<i>Alternaria alternata</i>	+	+	+	Natamycin	20/400	20/400***
12	<i>Drechslera</i> -state of <i>Cochliobolus specifer</i>	+	+	o	Natamycin	20/400	20/40+2
13	<i>Cladosporium oxysporum</i>	Post-keratoplasty	+	+	Amphotericin B, Natamycin	20/400	20/40+2
14	<i>Curvularia senegalensis</i>	NI	o	o	Natamycin	20/20	20/20
15	<i>Curvularia senegalensis</i>	+	o	o	Natamycin and Steroids	20/30	'Healed'
16	<i>Curvularia verruculosa</i>	+	+	+	Amphotericin B	NI	20/60

* + = positive, o = negative, NI = not indicated

** TPK—therapeutic penetrating keratoplasty

*** Cornea clinically better than 20/400

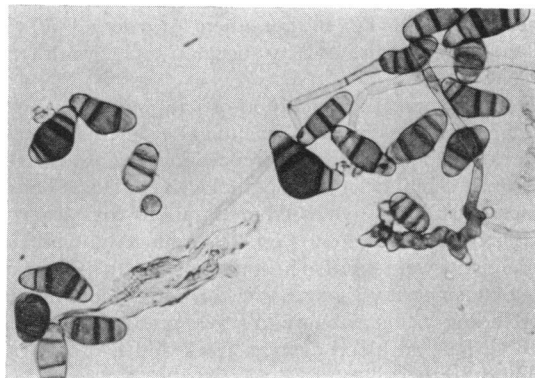


FIG. 1 *Conidia of Curvularia senegalensis* (Case 15). $\times 430$

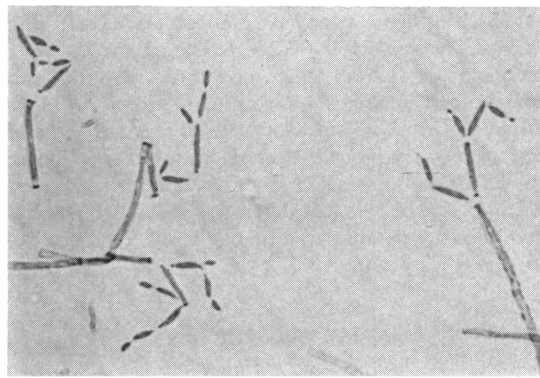


FIG. 4 *Conidia of Cladosporium oxysporium* (Case 13). $\times 430$

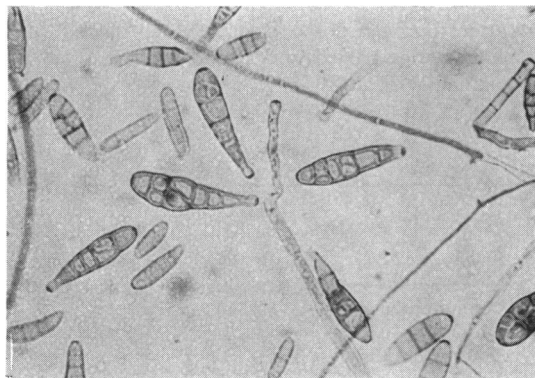


FIG. 2 *Conidia of Alternaria—state of Pleospora infectoria* (Case 5). $\times 430$

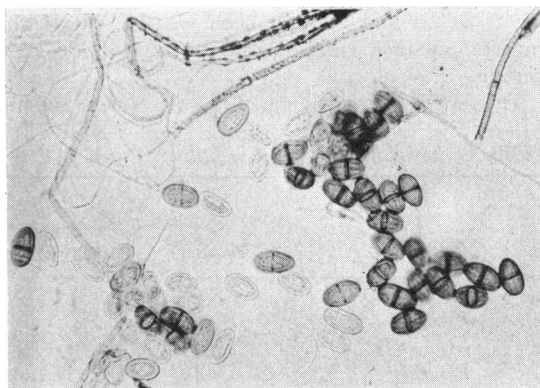


FIG. 5 *Pycnoconidia of Lasiodiplodia theobromae* (Case 8). $\times 250$

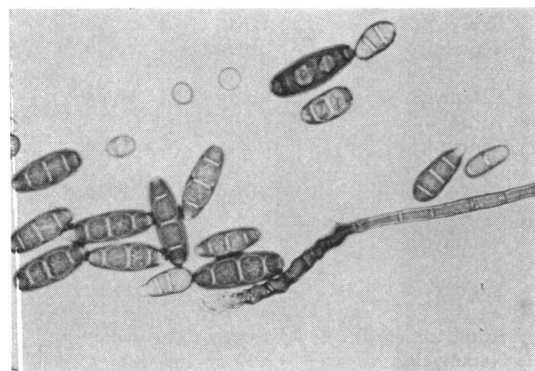


FIG. 3 *Conidia of Drechslera—state of Cochliobulus specifer* (Case 12). $\times 430$

her home, and was treated with a multitude of medications including topical steroid-antibiotics before referral with a perforated cornea, 2½ months after injury. She did not receive Natamycin, but she had culture and histology positive corneal fragments, and after keratoplasty the visual acuity was 20/40+ (Case 6).

Two patients were treated with only topical Gentamicin 3 mg/ml; one attained 20/50 vision, and

including five of the seven with 20/40 or better visual acuity.

Only one patient required therapeutic keratoplasty. A 46-year-old woman sustained a mild injury from a splinter of old wood while redecorating the inside of

Table II *Visual results in 16 cases of dematiaceous fungal keratitis*

Final visual acuity	Therapy		Total
	Natamycin	Other	
20/40 or better	5	2	7
20/50–20/70	1	3	4
'Healed'	2	1	3
20/400	1	1	2
Total cases	9	7	16

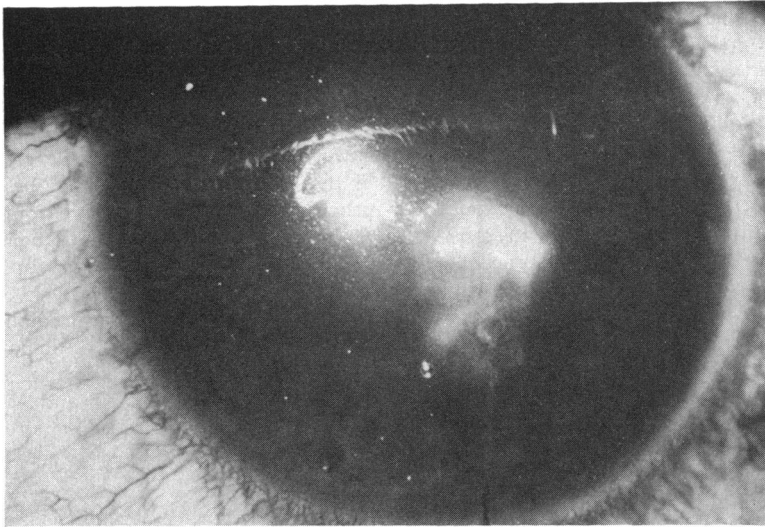


FIG. 6 *Dematiaceous fungal ulcer due to Curvularia species* (Case 4)

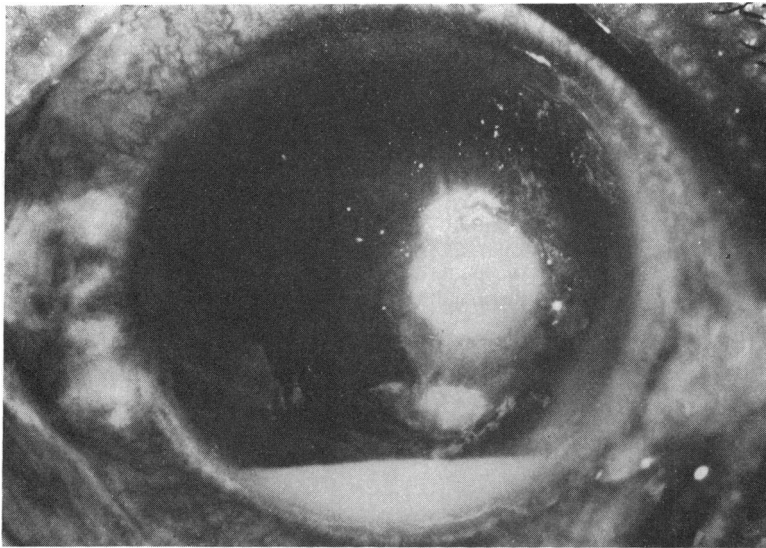


FIG. 7 *Dematiaceous fungal ulcer due to a Drechslera species* (Case 12).

the other 'healed' without returning for a final test of visual acuity. In both cases scrapings were negative on microscopical examination, and after 36 hours, when the cultures were positive for *Curvularia pallescens* and *Drechslera halodes*, the ulcers had improved, and therefore, Gentamicin was continued without instituting Natamycin (Cases 7 and 9).

Case 16 was treated with Amphotericin B, 2 mg/ml topically, and achieved a cure and a visual acuity of 20/60.

The three additional cases were seen before 1969. Case 1 attained 20/70 vision with Amphotericin B treatment, and Case 3 attained 20/30+ visual acuity after topical Amphotericin B, Thiabendazole, and Natamycin ointment. A final case due to *Phialophora*

verrucosa (Case 2) reported by Wilson and others (1966) was treated with Amphotericin B (0.3 per cent), thiabendazole (0.3 per cent), thiomersal, and subsequently required a conjunctival flap operation.

Discussion

The term dematiaceous fungi is a convenient designation for the major pigmented fungi implicated in keratitis, including the Dematiaceous Hyphomycetes (Moniliales) and other pigmented isolates such as *Lasiodiplodia theobromae* (Sphaeropsidales).

Case reports of keratitis caused by these fungi are infrequent, and vary in clinical presentation and course. Keratitis caused by *Curvularia* species has been

reported in single cases by Nityananda, Sivasubramaniam, and Ajello (1962, 1964) (2 species), Anderson, Roberts, Gonzalez, and Chick (1959), Anderson and Chick (1963), Georg (1964), Llamozas, Suprani, and De Albornoz (1966), Salceda, Nievera, and Abendaño (1969), and Wind and Polack (1970). *Alternaria* species have been reported by Orlov (1914), and Halde and Okumoto (1966). *Drechslera* and *Helminthosporium* case reports are probably lacking. There are reports of *Phialophora verrucosa* by Wilson and others (1966), of *P. gougerotii* and *Lasiodiplodia theobromae* by Laverde, Vera, Moncada, Restrepo, and Diaz (1972), Laverde, Moncada, Restrepo, and Vera (1973), and Puttanna (1967), and of *Cladosporium (Hormodendrum)* by Suie and Havener (1963), and François and Rysselaera (1972).

Whereas, keratitis due to *Fusarium solani* has been recognized as progressive and destructive, the dematiaceous ulcers are more variable and less predictable. If neglected or augmented by steroids the ulcers may become deep and lead to perforation such as Case 6. On the other hand, debridement alone or treatment with non-antifungal antibiotics may lead to a self-limited infection and healing, such as in Cases 7 and 9.

Dematiaceous fungal keratitis presented in similar age groups to those ulcers due to moniliaceous fungi; were usually preceded by outdoor trauma; and often occurred as primary infections, not necessarily aggravated by topical steroids or antibiotics. Three of the five cases that had already been treated with steroids, however, had the most complicated course (Cases 2, 6, and 11). Case 15, due to *Curvularia senegalensis*, had the same fungus cultured from a piece of garden plant, from which the injurious foreign body came.

This series serves to alert the ophthalmologist to the

relative frequency of keratitis due to pigmented fungi, and it stresses the importance of prompt, careful diagnostic, and therapeutic debridement of the ulcer. If recognized early and not aggravated by steroids, the diagnosis should not be so discouraging as it has been with most fungal keratitis. However, it should be noted that one of the fungi, *Phialophora verrucosa*, is a recognized pathogen causing chromomycosis. Prompt therapy with available antifungals, particularly Natamycin, should be instituted upon culture identification.

Although many variables alter the reproducibility of antifungal sensitivity studies, 12 stains of dematiaceous fungi tested *in vitro* have in general been more sensitive to antifungals such as Natamycin and Amphotericin B than 19 strains of *Fusarium solani* tested.

Summary

Clinical and laboratory features of 16 cases of keratitis that were caused by dematiaceous pigmented fungi are reported. Management, including the treatment of nine cases with Natamycin (Pimaricin), resulted in corneal healing in 14 cases, and therapeutic surgery in two cases.

We should like to acknowledge the help of M.B. Ellis PhD, Principal Mycologist, Commonwealth Mycological Institute, Kew, for identifying many of these fungal isolates.

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