

SUBCUTANEOUS PHAEOHYPHOMYCOSIS CAUSED BY *Phoma cava*. REPORT OF A CASE AND REVIEW OF THE LITERATURE

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SUMMARY

We report a case of subcutaneous phaeohyphomycosis observed in a male patient presenting pulmonary sarcoidosis and submitted to corticosteroid treatment. He presented nodular erythematous-violaceous skin lesions in the dorsum of the right hand. Histopathological examination of the biopsied lesion revealed dematiaceous hyphae and yeast-like cells, with a granulomatous tissual reaction. The isolated fungus was identified as *Phoma cava*. A review of the literature on fungal infection caused by different *Phoma* species, is presented. The patient healed after therapy with amphotericin B, followed by itraconazole.

KEYWORDS: Phaeohyphomycosis; *Phoma cava*; Subcutaneous mycosis.

INTRODUCTION

The fungi of the genus *Phoma* (Saccardo, 1812)* [= *Peyronella* Guidanich ex Guidanichi, 1946] are part of a complex of species designated *Pleurophoma* by Hönel (1914). Are primarily soil inhabiting fungi, living on plant debris, but they are also phytopathogens and, eventually, pathogenic for man and animals.

A genus similar to *Phoma* is *Pyrenochaeta*, created by Notaris in 1894 which also has dark pycnidia with papillae and with a single ostiole, but with septate setae, usually concentrated around the ostiole. The conidia are hyaline, frequently guttulate, unicellular, cylindrical or elliptic. The species of *Pyrenochaeta* considered thus far in the fungal taxonomy are: *Pyrenochaeta romeroi* Borelli, 1951, isolated in Venezuela from a black grain foot eumycetoma (this species was named in honor of Prof. Jesus Romero by Dante Borelli), *Pyrenochaeta mackinnonii* Borelli, 1976, also isolated in Venezuela from a black grain eumycetoma of the foot by Dante Borelli, and *Pyrenochaeta unguis-hominis*

* Pier Andrea Saccardo (1845-1920) was a Professor of Botany in Padua (Italy), and one of the most active mycologist of this time who left his name indelibly linked to this specialty. He was the author of the famous opus *Sylloge fungorum hucusque cognitorum* (1882-1925), among others.

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Punithalingam et English, 1975, isolated from a case of onychomycosis. According to Romero & Mackenzie (1989), there is a marked resemblance between *Pyrenochaeta romeroi* and *Madurella grisea*. In a case of subcutaneous phaeohyphomycosis recorded by YOUNG et al. (1973)¹⁷, the fungus isolated and identified as *Phoma* strongly resembled *Pyrenochaeta romeroi*.

Human lesion caused by species of the genus *Phoma* may be superficial or deep, attacking the skin, cornea, subcutaneous cell tissue, and lungs. In the last case, mycelial filaments and dematiaceous round cells are detected inside the inflammatory process, similar to those observed in other cases of phaeohyphomycosis. There are no cases of eumycetoma caused by *Phoma*, in contrast to what occurs with the genus *Pyrenochaeta*. Lesions in other animals have been reported. GORDON et al. (1975)⁷ isolated *P. cava* from skin lesions of a white-tailed deer (*Odoileus virginianus*). Lesions of the skin of the ears caused by *P. glomerata* (*Peyronellaeae glomerata* DAWSON & LEPPER, 1970⁴) have been reported in goats (*Capra hircus*) and sheep. This is the reason why GORDON et al. (1975)⁷ refer to *Phoma* as a pathogen fungus.

Phoma or related fungi belonging to the *Pleurophoma* complex are frequent agents of lesions in different plants, mainly attacking potatoes. Insects may also be parasitized by fungi of the genus *Phoma*. Of interest to human and veterinary pathology is the fact that several antifungal drugs act *in vitro* on *Phoma* "strains". ROSEN et al. (1996)¹⁴, studying the minimum inhibitory concentration (MIC, µg/ml) of some fungistatic agents on a *Phoma* (*Pleurophoma*) strain isolated from a skin lesion, obtained the following results: itraconazole – ≤ 0.0018; ketoconazole – 0.2; fluconazole – 5.0; griseofulvin – 0.5. BAKER et al. (1987)¹ in a study of a *Phoma minutela* "strain" isolated from a case of subcutaneous phaeohyphomycosis, ob-

tained MIC values of 0.625 µg/ml for amphotericin B and 0.06 µg/ml for 5-FC. GORDON et al. (1975)⁷, in a study on *Phoma cava* isolated from a skin lesion of a deer, referred to an article by GALLO & GALLO (1961) in which the authors recorded the sensitivity of this species to nistatin and griseofulvin, without citing the results obtained for the MIC of these agents.

CASE REPORT

E.C., a 63 year-old white male, from Barretos (SP), presenting with dyspnea and a palpable cervical lymph node was examined at the Dermatology Clinic of the Faculty of Medical Sciences, Santa Casa de São Paulo. A biopsy of the lymph node was performed and the diagnosis of sarcoidosis was achieved. The patient was submitted to corticoid therapy. One month later nodular and slightly erythematous-violaceous lesions appeared. On physical examination nodules measuring 1 to 1.5 cm in diameter were palpable in infiltrated skin on the dorsum of the right hand and on the sternal region (Fig. 1). A chest X-ray revealed a diffuse interstitial infiltrate. Bacilloscopy and PPD were negative. Pulmonary scintigraphy was normal. A chest tomography revealed hilar and mediastinal lymphadenomegalies. An uncharacteristic pneumopathy was detected. A lung fragment obtained by transbronchial lung biopsy did not revealed bacilli and fungi. Sections of a biopsy of the skin revealed the epidermis thickened by acanthosis and elongated cristae. The dermis showed a small area of necrosis surrounded by an inflammatory reaction consisting of mononuclear cells and tending to form a granulomatous arrangement. PAS stain revealed hyphal fragments and yeast-like cells isolated or in small chains (Fig. 2). A search for acid fast bacilli was negative. In culture grew up a dematiaceous fungus, initially identified as *Phoma* sp. Corticoid therapy was gradually discontinued and amphotericin B was administered in a cumulative dose of 610 mg. The patient was kept maintained on itraconazole 400 mg/day. Skin lesions healed.



Fig. 1 - Slightly erythematous-violaceous nodular lesions located on the dorsum of the right hand.

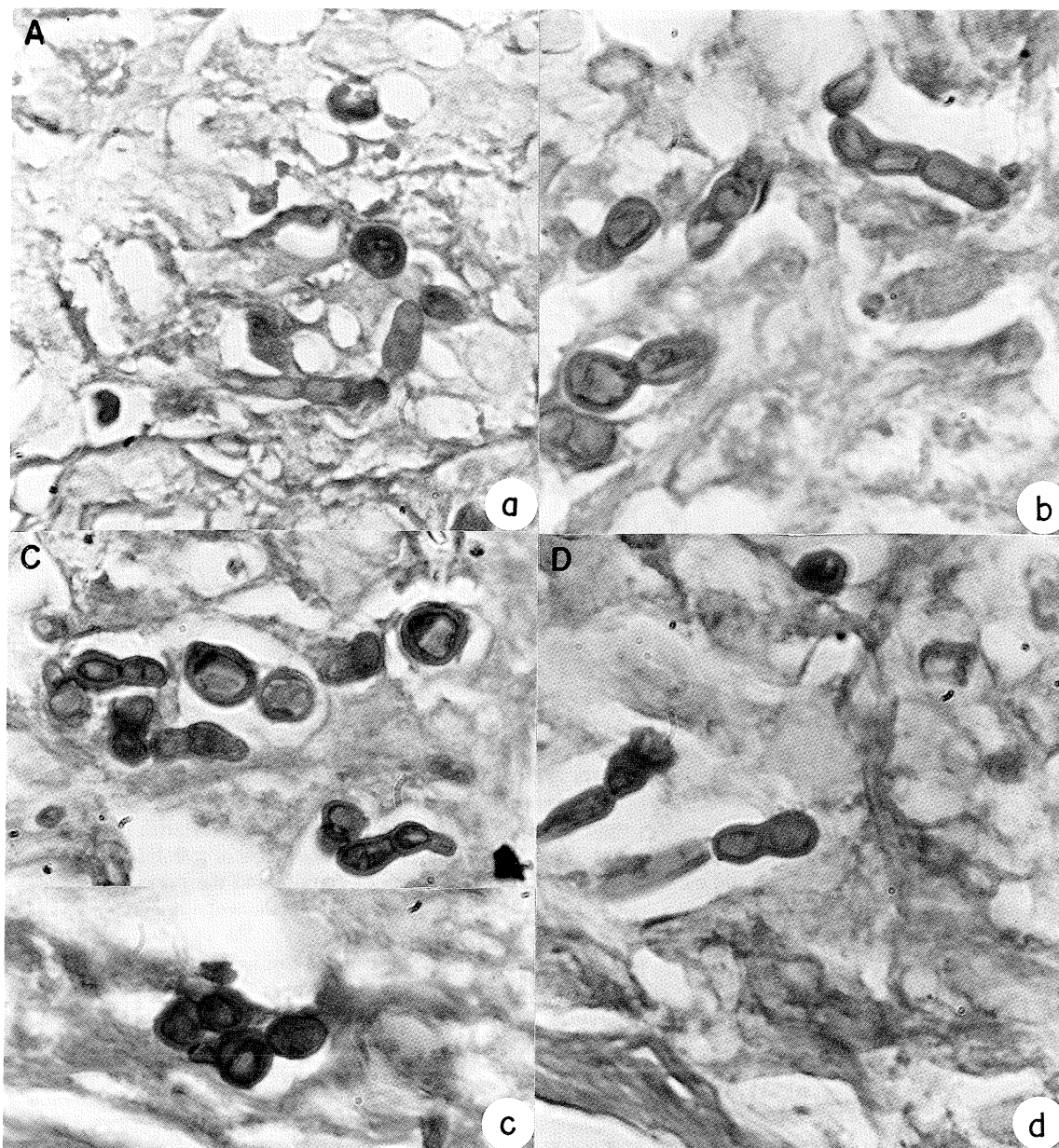


Fig. 2 - *Phoma cava*. Histological section stained with PAS. Note septate hyphae and yeast-like cells isolated, clustered or arranged in small chains. a, c) 400 X; b, d) 500 X.

MYCOLOGIC STUDY

The isolated fungus was identified as *Phoma cava* on the basis of the following characteristics: a fast growing colony, ash grey-olive in color, and becoming black. Sparse and reverse brown mycelium (Fig. 3). Pycnidia were observed after 30 days on Sabouraud-agar and potato-agar at room temperature. They were globose to subglobose, brown, ostiolate, releasing large amounts of conidia. Pycnoconidia were straight and slightly curved, light brown in color and occasionally guttulate. Setae and chlamydoconidia were absent (Fig. 4).

DISCUSSION

Cases of phaeohyphomycosis caused by dematiaceous fungi of the genus *Phoma* have been rarely reported in the literature. YOUNG et al. (1973)¹⁷ observed a case of subcutaneous cystic lesion located in the posterior region of Achilles tendon in a black male submitted to renal transplantation. The histopathological picture of this lesion was closely similar to that detected in cystic lesions provoked by *Exophiala jeanselmei* or *Phialophora richardsiae*. No grain formation was observed upon histopathological examination. Dematiaceous hyphae and yeast-like

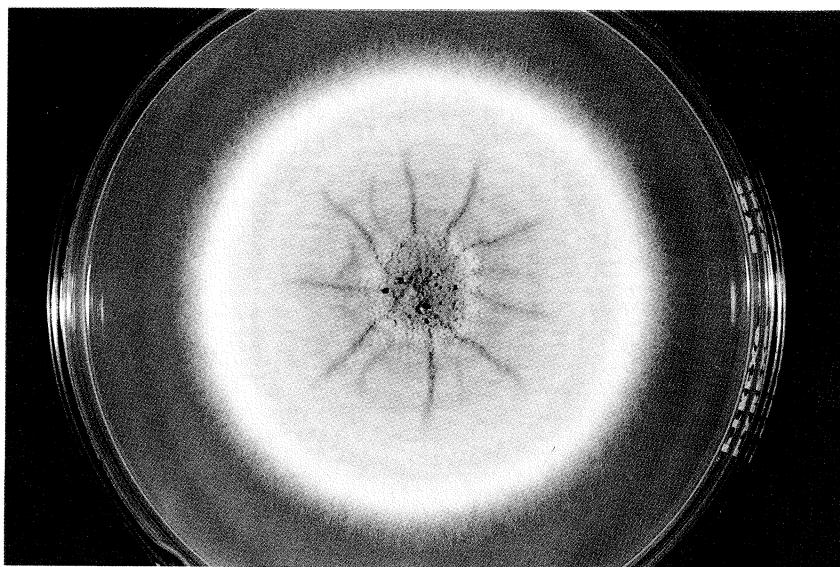


Fig. 3 – *Phoma cava*. Colony on Sabouraud-agar after 7 days of growth at room temperature.

cells were present and ostiolate pycnidia were detected in culture. Table 1 list the lesions caused by fungi of the genus *Phoma* on the skin or in other locations, according to ROSEN et al. (1996)¹⁴, modified.

The systematic of fungi assigned to the genus *Phoma* has not been fully established. MCGINNIS (1980)¹¹ accepts as valid the species *P. hibernica* and *P. glomerata*. HOOG & GUARRO (1995)⁹ consider the following species of *Phoma* to be pathogenic for man and other animals: *P. cava*, *P. cruris-hominis*, *P. eupyrena* (type species created in 1812 by Saccardo), *P. glomerata*, *P. herbarum* (= *P. hibernica* according to Grimis, O'Connor et Cummins, 1932), *P. minutella*, *P. minutispora*, *P. oculo-hominis* and *P. sorghina*.

These fungi belonging to the subdivision *Deuteromycotina*, *Coelomycetes* class, which comprises two order: *Sphaeropsidales*, which form pycnidia, structures constituted by asexual fruiting bodies containing conidia born on short phialides or directly from the cells of the peridium, and *Melanconiales*, which produce saucer-shaped acervules (also called conidiomas or sporocarps) in whose basal portion (hymenium) are found conidiophores arranged in rows giving origin to conidia. This order is of great interest in Phytopathology. In the genus *Phoma*, created by Saccardo in 1812, the pycnidia are ostiolate, black or ash grey in color and measure 40 to 200 µm. They contain elongated or curved, and eventually guttulate pycnoconidia. The ostiole cannot always be identified in the pycnidium since it may be obliterated by compact paraphyses. Aerial mycelium may or not be present. Chlamydoconidia are detected in *Phoma eupyrena* and *Phoma glomerata*. Some of them of moriform, aspect and intercalary the mycelial filaments, catenu-

late or not. The pycnidia may or not be submersed in the medium. They are rounded or piriform and some of them are flasks like shape with a usually short "neck" on Sabouraud-agar. *Phoma* colonies (teleomorph *Pleospora*) grow slowly at room temperature and are gray to black in color. To characterize the various species of *Phoma*, the structure and shape of pycnidia as also are the morphology and size of conidia and the presence and arrangement of chlamydoconidia, is fundamental importance.

Phoma minutella was isolated from subcutaneous lesions on the left foot (dorsal region) of a farmer from the Dominican Republic who had myasthenia gravis and who was being treated with corticoids. In observations of Indian patients reported by RAI (1989)¹³, skin lesions were superficial, with on particular dermatologic characteristics and were provoked by *Phoma minutispora* (SHUKLA et al., 1984)¹⁵ and by *Phoma sorghina*. Corneal lesions were observed in a case reported by PUNITHALINGAM (1979)¹².

Phoma cava was isolated by GORDON et al. (1975)⁷ from superficial skin lesions located above the ear of a child. The same species was also isolated from a dermatitis observed in a deer.

RESUMO

Feo-hifomicose subcutânea causada por *Phoma cava*. Relato de caso e revisão da literatura

O presente trabalho registra um caso de feo-hifomicose subcutânea em paciente do sexo masculino com o diagnóstico de sarcoidose pulmonar, submetido à terapêutica por corticosteróides quando apresentou no dorso da mão direita lesões cutâneas nodulares, eritemato-violáceas, de aspecto

infiltrado, exigindo biópsia para o diagnóstico. O exame histopatológico revelou processo granulomatoso, com a presença de hifas e células arredondadas demécias. Cultivo positivo para fungo identificado com *Phoma cava*. Os Autores fizeram revisão da literatura sobre as infecções fúngicas provocadas por diversas espécies de *Phoma*, mostrando a raridade desta observação. A evolução foi favorável com a administração da anfotericina B (via venosa) seguida do itraconazol (via oral).

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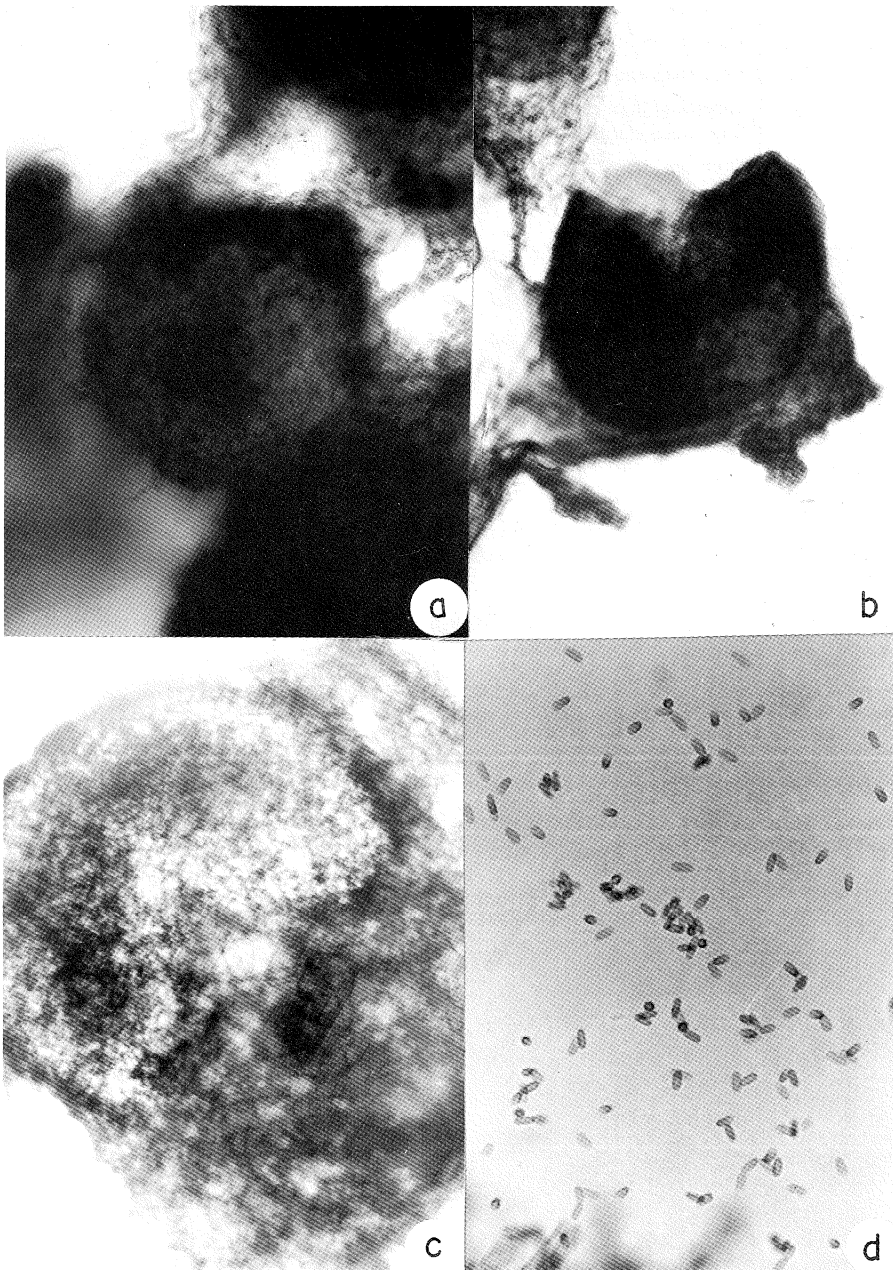


Fig. 4 – *Phoma cava*. Globose brown pycnidia: a, b) 100 X; c) 400 X; d) abundant cylindrical conidia released from the pycnidia (1000 X).

TABLE 1
Skin and other lesions caused by fungi of the genus *Phoma* according to ROSEN et al. (1996), modified.

Author(s)	Isolated fungus	Lesions	Immunodepression
1. JANKE (1956)	<i>Phoma (Peyronellaea) sp.</i>	Pulmonary	–
2. BAKERSPIGEL (1970)	<i>Phoma hibernica</i>	Deep (leg)	Topical steroids
3. YOUNG et al. (1973)	<i>Phoma sp.</i>	Deep (heel)	Azathioprine, prednisone (renal transplant)
4. GORDON et al. (1975)	<i>Phoma cava</i>	Superficial above the ear	–
5. PUNITHALINGAM (1979)	<i>Phoma cruris-hominis</i>	Deep	–
6. BAKERSPIGEL et al. (1981)	<i>Phoma eupyrena</i>	Superficial (perioral lesion)	–
7. SHUKLA et al. (1984)	<i>Phoma minutispora</i> <i>Phoma minutispora</i>	Superficial (face) Superficial (neck)	Typhoid fever Oral steroids
8. BAKER et al. (1987)	<i>Phoma minutella</i>	Deep (foot)	Corticoids. Diabetes
9. STONE et al. (1988)		Deep (forearm)	–
10. DOOLEY et al. (1989)	<i>Pleurophoma pleurospora</i>	Deep (legs and arms)	Cyclosporin, prednisone (heart transplant)
11. RAI (1989)	<i>Phoma sorghina</i> <i>Phoma sorghina</i>	Superficial (face neck and hands) Superficial (face)	– –
12. HIRSH & SCHIFF (1996)	<i>Phoma sp.</i>	Deep (hands)	–
13. ROSEN et al. (1996)	<i>Pleurophoma sp.</i>	Deep (face)	Topical steroids
14. ZAITZ et al. (1997)	<i>Phoma cava</i>	Deep (hand)	Oral corticoids

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