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Subcutaneous phaeohyphomycotic abscess caused by *Pleurophomopsis lignicola*

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A 41-year-old man with a past medical history of diabetes mellitus type II, AIDS (diagnosed 2 years earlier; CD4 count <10), peripheral neuropathy, and pulmonary tuberculosis of 2 years duration was admitted to the hospital with abnormal liver function tests. There was a chronic hepatitis/cholestasis that had worsened while the patient was undergoing directly observed tuberculosis therapy. On admission, the patient complained of a painful swelling on his right arm. In the posterior aspect of the arm, there was a 3–4-cm subcutaneous mass that was fluctuant, mobile and tender. Incision of the mass released yellowish pus mixed with blood. Direct examination of the pus in KOH mounts and Gram-stained smears revealed subhyaline, septate, branched hyphae. When the pus was cultured on Sabouraud dextrose agar containing chloramphenicol, several velvety, olivaceous grey colonies grew after 7 days at 25°C. When grown on oatmeal agar, the fungus produced subglobose, rostrate pycnidia with phialidic conidiogenous cells, and 1-celled cylindrical conidia. It was identified as *Pleurophomopsis lignicola* Petrak. This report describes the third known case of subcutaneous infection caused by *P. lignicola* in an immunocompromized patient.

Keywords amphotericin B, immunocompromized patient with AIDS, *Pleurophomopsis lignicola*, subcutaneous phaeohyphomycosis, surgical intervention, treatment – early diagnosis

Introduction

Coelomycetous fungi are being reported in increasing numbers as causing opportunistic infections especially in immunocompromized patients [1]. Such infections are frequently acquired through traumatic implantation. At present, 25 species belonging to 12 coelomycete genera are known to cause opportunistic infections [2]. We describe a coelomycetous fungus, *Pleurophomopsis lignicola* Petrak, that caused a subcutaneous, painful swelling in the posterior aspect of the right arm of a 41-year-old male patient with diabetes mellitus type II and AIDS.

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Case report

A 41-year-old man from Senegal was admitted to the hospital with abnormal liver function tests. Past history included diabetes mellitus type II, AIDS (diagnosed 2 years earlier; CD4 count <10), peripheral neuropathy and pulmonary tuberculosis diagnosed 2 years earlier. There was a chronic hepatitis/ cholestasis that had worsened while the patient was undergoing directly observed tuberculosis therapy.

On admission, the patient was comfortable except that he complained of a painful swelling on his right arm. He had noted it 2 years earlier. In the posterior aspect of the right upper arm, there was a 3–4-cm diameter subcutaneous mass that was fluctuant, mobile and tender. Incision of the mass revealed yellowish pus mixed with blood. Direct examination of the pus in KOH mounts and smears stained by the Gram stain

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revealed subhyaline, septate, branched hyphae (Fig. 1). Cultures for bacteria were negative. Examination of stained preparations were negative for acid-fast bacilli including cultures for *Mycobacterium tuberculosis.* Culture of the pus on Sabouraud dextrose agar with chloramphenicol (Difco Laboratories, Detroit, MI, USA) yielded several velvety, olivaceous grey fungal colonies.

Over the following 2 weeks, the wound healed without recurrence of the mass. The patient had elevated transaminases and alkaline phosphatase. He underwent a liver biopsy that revealed chronic hepatitis and cholestasis without evidence of bacterial, viral, mycobacterial or fungal infection. He was discharged approximately 3 weeks after admission to complete his therapy for tuberculosis.

Mycological studies

A microscopic examination of the colonies showed that they consisted of septate, branched, pale brown hyphae without sporulation. Subcultures were made on several nutritionally low media such as cornmeal, lactrimel, oatmeal salts, pablum cereal, and V8 juice agars to induce sporulation. Subcultures on the above media were incubated at 25°C and subjected to 12 h daylight followed by 12 h darkness in order to induce sporulation. None of the cultures showed sporulation at the end of 4 weeks. A subculture was sent to the Commonwealth Agricultural Bureau International (CABI) (Bioscience, Egham, Surrey, UK), where it was studied by one of us (E.P.).

At CABI Bioscience, subcultures of the isolate were grown on oat agar and subjected to a regime of 12 h near-UV irradiation (black light) and 12 h darkness between 22 and 25°C to stimulate sporulation. Four-week-old colonies were initially greyish but later turned sienna to umber brown to black with abundant aerial mycelium. The reverse of the colony became dark brown to black. The mycelium consisted of branched, septate, smooth to finely verruculose, yellowish brown hyphae 1.5–2-μm wide (Figs. 5–7). As the colony aged, simple chains of chlamydospores or swollen cells in chains on hyphae were occasionally seen. The conidiomata were scattered; unilocular pycnidia of variable morphology with flexuous hyphae and circular ostioles were partially immersed in the agar medium amongst hyphae. Pycnidia that were subglobose were 130–350-μm wide with the floor of the pycnidial cavity nearly smooth or slightly uneven or distinctly convoluted (Figs. 2 and 3). Pycnidia that were rostrate were generally bulbous at the base, 150–250-μm wide, with a prominent elongated neck 250–500-μm long and with lateral flexuous hyphae (Fig. 4). The pycnidial wall was stromatic, 30–45-μm wide, and consisted of an outer region, a middle region and an inner region composed of many cell layers. The outer region was 12–15 μm thick, dark brown and consisted of two to four layers of thick-walled cells; the middle region was 16–20 μm wide, light brown but gradually becoming hyaline towards the inner side and consisted of three to five layers of thick-walled (sclerenchymatous) cells. The innermost region was 10–15 μm wide, hyaline and composed of three to five thick-walled cell layers with

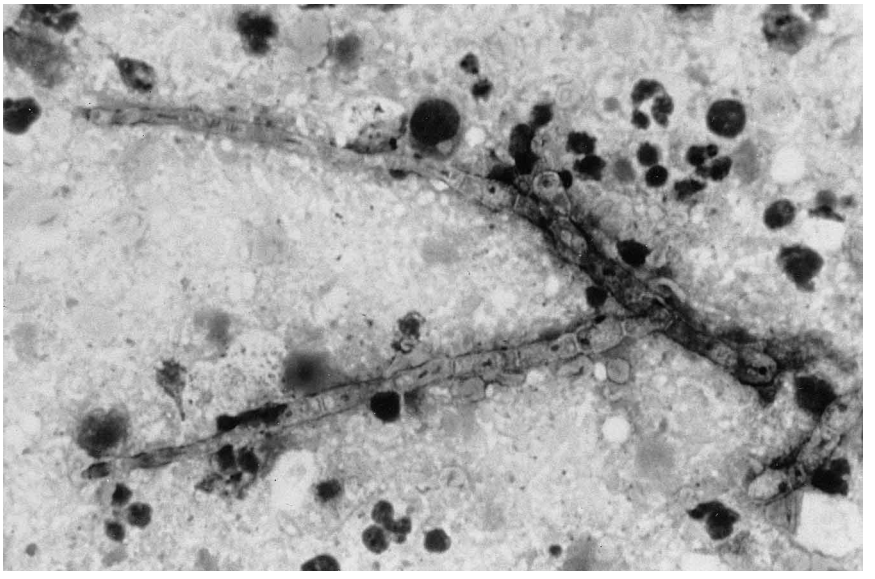

Fig. 1 Gram-stained smear of subcutaneous arm lesion pus showing septate, branched hyphae of *Pleurophomopsis lignicola*, magnification × 560.

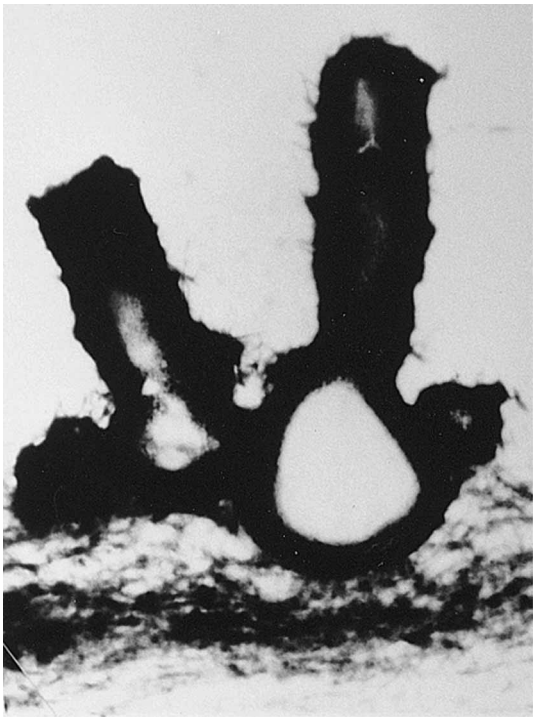

Fig. 2 Vertical sections of rostrate and subglobose pycnidia of *Pleurophomopsis lignicola*; magnification: × 170.

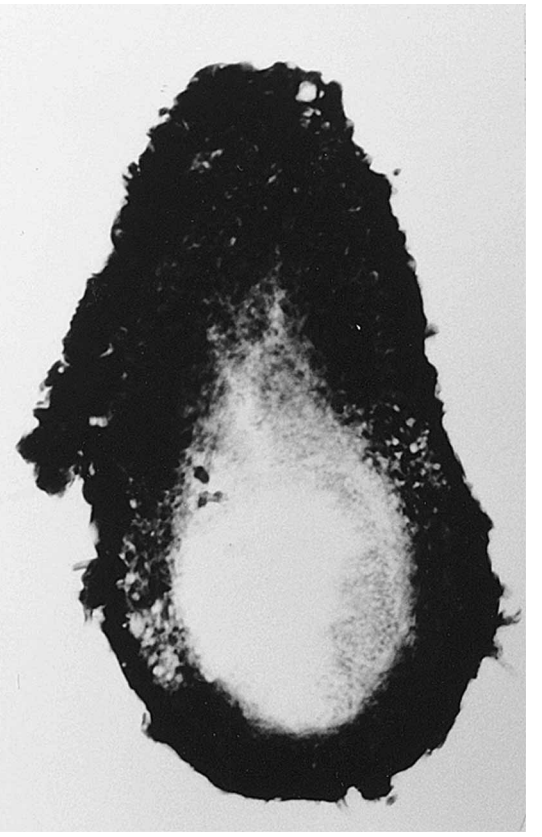

Fig. 3 Vertical sections of rostrate and subglobose pycnidia of *Pleurophomopsis lignicola*; magnification: × 380.

conidiophores arising from cells lining the pycnidial cavity. The conidiophores formed within pycnidia were closely packed, branched at the base, hyaline, smooth, cylindrical, and septate (Figs. 8, 11). The conidiogenous cells were phialidic, and determinate and were integrated or discrete with gradually tapered apices, 5–8 × 1–2 μm, hyaline and cylindrical, with conidia developing from their apices. Conidia were hyaline, smooth-walled, aseptate, straight, and cylindrical to oblong with obtuse ends, and measured 2–3 × 1–1.5 μm with the majority being 2.5 × 1–1.25 μm (Figs. 8–11).

The isolate (CDC B-5716, Centers for Disease Control and Prevention, USA = IMI 372964, CABI Biosciences, UK) agreed with the isotype (Petrak's exsiccatum no. 1689) of *P. lignicola* Petrak, originally recorded from rotting wood in Europe, in all essential morphological details.

Discussion

In the last 5 years, *P. lignicola* has been reported several times from opportunistic infections. In the first recorded case, it was the causal agent of a subcutaneous cyst on the left leg of a patient from France who had been treated with corticosteroids for asthma [3]. The second infection was reported from Italy in a kidney transplant recipient who developed a soft tissue abscess and a subcutaneous tibio-fibular fistula on his left leg [4]. In the US, *P. lignicola* was reported to cause allergic, non-invasive, maxillary sinusitis in an immunocompetent man after he had cut down a rotted maple tree [5]. The patient acquired the infection probably from exposure to the fungus on the rotten tree that he cut down. However, no attempt was made to isolate *P. lignicola* from the tree.

Coelomycetous fungi are presently known to cause a variety of human mycoses including onychomycosis, cutaneous and subcutaneous phaeohyphomycosis, keratitis, endophthalmitis, sinusitis, osteomyelitis, fungemia, and eumycotic black grain mycetomas [2]. The majority of systemic infections occur in immunocompromized patients and are frequently acquired through traumatic implantation [1]. The genus *Pleurophomopsis* includes seven species, of which only *P. lignicola* is known to cause infections in humans. *P. lignicola* can be distinguished from typical *Phoma* species by production of numerous predominantly septate, branched

Fig. 4 Vertical sections of rostrate and subglobose pycnidia of *Pleurophomopsis lignicola*; magnification: × 380.

Fig. 5 *Pleurophomopsis lignicola* Smooth-walled hyphae; magnification × 1520.

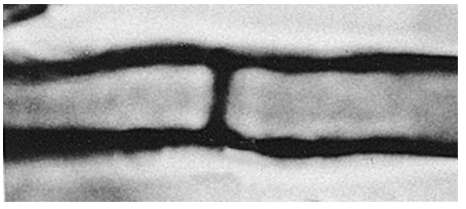

Fig. 6 Thick-walled hyphae; magnification × 3600.

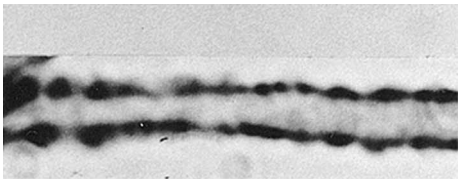

Fig. 7 Roughened or verruculose hyphae; magnification × 3800.

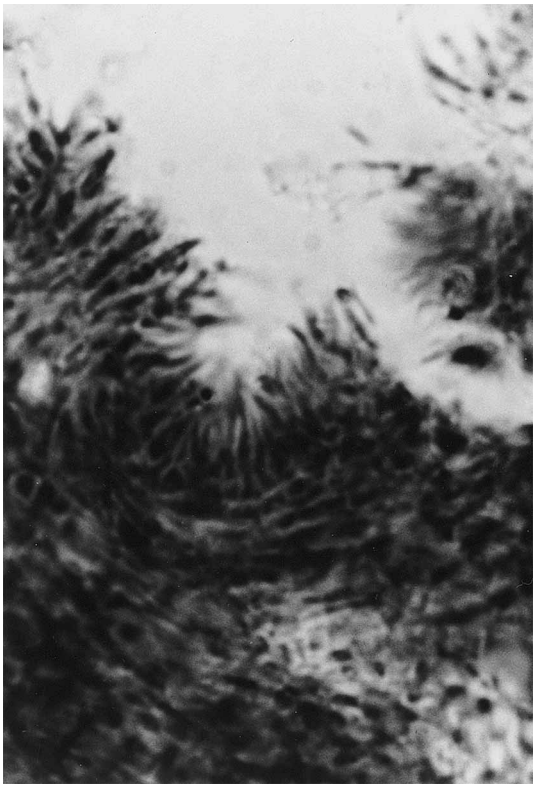

Fig. 8 Part of the inner pycnidial wall showing conidiophores, conidiogenous cells, and immature conidia; magnification × 2200.

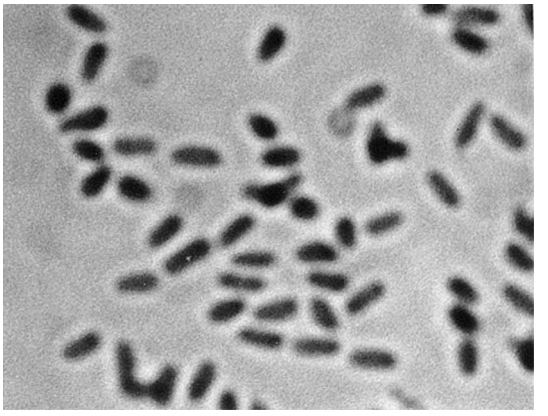

Fig. 9 Smooth-walled, aseptate conidia; magnification × 2200.

conidiophores that bear conidiogenous cells and conidia. It can be differentiated from true *Pyrenochaeta* species by the absence of stiff setae on pycnidia and the presence of one- to two-septate conidiophores bearing conidiogenous cells with terminal loci on one or two branches [6]. *P. lignicola* can also be distinguished from

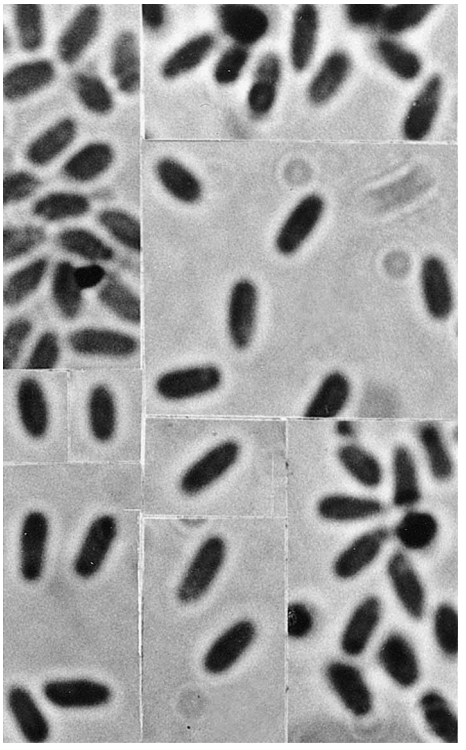

Fig. 10 Smooth-walled, aseptate, cylindrical conidia; magnification × 3800.

Pleurophoma pleurospora (type species of *Pleurophoma*) and *Phialophorophoma litoralis* (type species of *Phialophorophoma*) by comparing the conidiophores and conidiogenous cells. In *P. lignicola*, the conidiophores usually have one or two branches. Conidiogenous cells are cylindrical and form terminal loci on branches whereas in *P. pleurospora*, conidiophores are long and septate and the phialides have apertures that open immediately below the transverse septa. In *P. litoralis*, the conidiogenous cells terminate in a cup-shaped apex or a flared collarette, features that are lacking in *P. lignicola*. In *Phoma cava*, also known as *Pleurophoma cava*, the pycnidial ostioles have periphyses, which are lacking in *P. lignicola.* In *P. lignicola*, the conidia are straight and not curved as in *P. cava*.

The *in-vitro* sensitivity data of several coelomycetous etiologic agents show that the majority of species are susceptible to amphotericin B. Among the triazoles, itraconazole was found to be active against several agents; however, some of the species were resistant [1]. The other triazole tested, fluconazole, also manifested low MIC in tests with several species [1]. However, the outcome of treatment depends on several important factors, such site of infection, host factors, virulence of the causal agent, absorption and metabolism of the antifungal agent used and its mode of action [7]. In the present case, drainage of the lesion allowed healing over a period of 2 weeks without recurrence of the lesion.

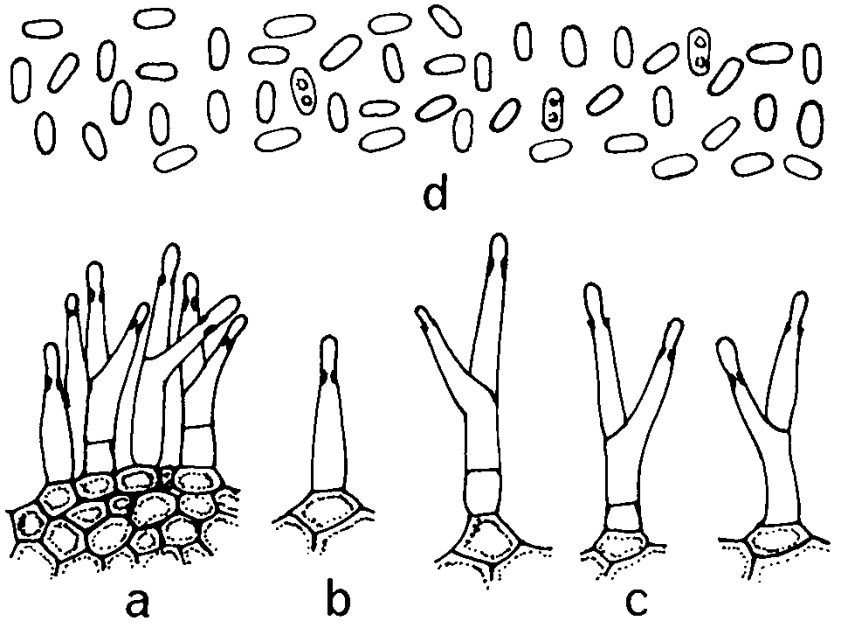

Fig. 11 (a) Part of conidiomatal wall, Conidiophores, conidiogenous cells. (b,c) Conidiophores and conidiogenous cells. (d) Conidia (× 2600).

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