Fatal hyalohyphomycosis with cutaneous involvement caused by *Purpureocillium lilacinum* in an immunocompromised patient with bullous pemphigoid

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To the Editor,

Emergent pathogen as *Purpureocillium lilacinum* are becoming cause of morbidity and mortality in our population, especially in immunocompromised patients (1). *Purpureocillium lilacinum* (P.L.) (formerly known as *Paecilomyces lilacinus*) is a ubiquitous saprophytic, asexual and filamentous fungus found in the environment, especially in the soil, air and water. It is best known for its entomopathogenicity and has been widely used as an agricultural biocontrol agent, killing the eggs of a broad range of plant parasitic nematodes, infesting the roots of fruits and vegetables (2). In humans, it causes ocular mycosis or skin and soft tissue infections and sometimes deep-seated infection (1). Cutaneous infections can present with macules, papules, vesicles and nodules, both in a solitary and disseminated fashion. Diagnosis is often misleading and treatment, especially in immunocompromised patients is challenging. We present the case of a 79-year-old man with a previous medical history of bullous pemphigoid, insulin-dependent diabetes mellitus, hypertension, and hyperuricemia. He presented with a progressive, erythematous warm and tender plaque surmounted by multiple pustules located on the dorsal surface of his right hand and wrist that developed over a period of 2 weeks (Fig. 1a). Under the initial suspect of cellulitis, a cutaneous swab was performed and empiric treatment with ceftriaxone 1 gr i.m. bid was initiated. Cultures from intact pustules on Sabouraud-dextrose-agar medium containing chloramphenicol revealed floccose whitish colonies with central mauve-lilac discoloration, brownish on the reverse side (Fig. 1d,e), identified as P.L. with MALDI-TOF Mass Spectrometry. Microscopical examination showed hyaline, septate hyphae, branched conidiophores stipes and brush-like clusters of phialides (Fig. 1f).

Histopathological examination from a skin biopsy revealed a granulomatous mixed inflammatory infiltrate containing histocytes and Periodic acid–Schiff (PAS) stain positive hyphal elements and spores (Fig. 1b,c). Despite initiation of treatment with Itraconazole (200 mg bid) the patient started complaining bilateral leg and ankle swelling. Doppler ultrasound showed bilateral oedema of soft tissues. General conditions progressively deteriorate, and he developed congestive heart failure, elevated levels of serum Ca 19.9, LDH, ferritin and positivity of faecal occult blood test, that raised the suspect of a neoplastic disease and lead to the admission to an internal medicine ward. Esophagogastroduodenoscopy and colonoscopy were performed with negative results. Afterwards he manifested dizziness, mood swings, unsteady gait and rapid cognitive deterioration. Despite treatment, his clinical status continued to worsen, itraconazole therapy was switched to voriconazole 6 mg/kg IV every 12 hours. A brain MRI was performed, showing an extra-axial mass, initially misinterpreted as meningioma, and then re-evaluated as a localization of the P.L. infection. The patient died few weeks later and the family refused post-mortem investigations.

P.L. cutaneous infection can be highly mortal, due to its ability to sporulate in tissues, though fatal out-
come can be related to an immunocompromised status. Treatment is controversial, in very early and limited infections surgical debridement is adequate, but often a systemic therapy is required. Conventional antifungals (amphotericin, terbinafine) and first-generation azoles (fluconazole, itraconazole) are in some cases effective (3). Second-generation triazoles (voriconazole, posaconazole, isavuconazole, and ravuconazole) are promising alternatives (4).

In our case despite the expedite diagnosis and an immediate aggressive treatment we could not avoid the dissemination of the infection as the brain localization has been at first misinterpreted as a meningioma. Voriconazole was initiated when the central nervous system (CNS) dissemination was ineluctable and patient’s general condition was already deteriorated.

When facing rapidly disseminating cutaneous infections with refractory cellulitis-like presentation, sustained by moulds, it is important to initiate treatment aggressively with appropriate antimycotics especially when dealing with critically ill immunocompromised patients. CNS mold infections should be considered to choose dedicated medications like voriconazole, able to cross the blood-brain barrier and reach appropriate concentrations (5,6) to prevent neurologic sequelae and ultimately save patient’s life.

In addition, due to their natural origin, the use of bio-pesticides like P.L. is considered safe, but there is now overwhelming evidence, that some of them can harm animals or human beings and researchers should address the lack of experimental evidence on their impact both on soil microbes, animal and human health (2). The aim of this letter is to increase awareness of clinicians about this uncommon, but frequently fatal refractory mycotic infection.

**Conflict of Interest:** Each author declares that he or she has no commercial associations that might pose a conflict of interest in connection with the submitted article.
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