Dermatology Reports

https://www.pagepress.org/journals/index.php/dr/index

eISSN 2036-7406

Please cite this article as: Farina C, Cavallini M, Gambini D, et al. Autochtonous *Emergomyces pasteurianus* subcutaneous infection in an Italian immunocompromised patient: a case report and review. *Dermatol Rep 2025 [Epub Ahead of Print] doi: 10.4081/dr.2025.10251*

Submitted 05/01/25 - Accepted 26/01/25

Autochtonous *Emergomyces pasteurianus* subcutaneous infection in an Italian immunocompromised patient: a case report and review

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Key words: *Emergomyces pasteurianus*; mycoses; immunocompromised.

Contributions: CF, writing, conceptualization; methodology; CF, DG, AT, data curation; MC, writing—original draft preparation; DG, supervision. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest: the authors certify that they have no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Ethics approval and consent for publication: the patient in this manuscript has given written informed consent to the publication of this case details. No further steps were required by the ethics committee for this case report.

Availability of data and materials: data are available upon request to the corresponding author.

Abstract

We describe the second case of infection by *Emergomyces pasteurianus* that occurred in Italy. The patient presented ulcerated nodular lesions primarily in the forehead, beneath the orbital and nasal areas, but also in the neck and fingers in the early stages. Treatment involved amphotericin B, followed by long-term itraconazole, which resulted in complete clinical resolution. A review of the literature is also included.

Introduction

Emergomyces pasteurianus is a recently identified dimorphic fungus. It was initially classified in the *Emmonsia* genus but recently transferred to the *Emergomyces* genus.[1,2] *Emergomyces* species cause disease in immunocompromised hosts, probably infected by inhaling dust-borne conidia. The genus *Emergomyces* includes five described species: *E. africanus, E. pasteurianus, E. europaeus, E. orientalis,* and *E. canadensis*. All *Emergomyces* species differ from *Emmonsia* genus by the lack of adiaspores.[2]

The first case in Italy was described in a 40-year-old Italian woman who had never traveled abroad.[3,4] She was an intravenous drug user who had been HIV-positive for ten years. She developed erythematous, papular, ulcerated cutaneous lesions, emaciation, and vomiting. CD4 counts were at 7/mm^3. Skin biopsies indicated that the patient was suffering from histoplasmosis, and she was placed on a short course of amphotericin B before she died without autopsy. Slow-growing cultures were obtained from the last cutaneous biopsy: a) at 25°C on Sabouraud agar in a mycelial phase with a delicate conidial apparatus similar to that of the two onygenalean dimorphic genera *Blastomyces* and *Emmonsia*; b) at 37°C on BHI medium in a yeast phase similar to that of the cutaneous biopsy. There were no adiaspores, like those produced *in vivo* by *Emmonsia parva* or *E. crescens.*

Case Report

The patient was a 37-year-old man suffering from AIDS. No trips abroad were reported.

He was hospitalized in the Infectious Diseases Department for the appearance of ulcerated nodular lesions mainly in the forehead, under the orbital and nasal areas, but also, still in the initial phase, in the neck and fingers (Figure 1).

Blood chemistry tests show: HIV-RNA 42090 copies/mL; T helper $CD4^+$ 32cell/mmc; CD4/CD8 ratio 0.15; ESR 35. Double immunodiffusion tests for the detection of antibodies anti-*Aspergillus* and anti-dimorphic fungi (*H. capsulatum*, *C. immitis,* and *B. dermatitidis*) were negative.
The histological examination of the skin biopsy shows rounded intracellular structures, while the culture examination highlighted the growth of filamentous fungi (Figure 2).

The subculture of the skin biopsy on Sabouraud Dextrose Agar allowed the growth of yeast-like, then finely fluffy, white, yellowish, and restricted colonies in 2 weeks of incubation. The microscopic examination revealed the presence of thin hyphae producing wide, yeast-shaped conidia with uni- and bipolar budding (Figure 3). Genotypic identification (amplification and sequencing of the rDNA internal transcribed spacer, Applied Biosystem, USA) allowed the confirmation of *E. pasteurianus.*

The patient underwent HAART therapy for HIV infection and antifungal treatment with amphotericin B 3 mg/kg e.v. for 15 days, followed by itraconazole 200 mg/day for 6 months, with complete clinical resolution of disseminated mycoses. The patient showed no signs of recurrence after five years.

Discussion

Five species belong to the genus *Emergomyces*, all characterized by the absence of adiasporas, classically characterizing the *Emmonsia* genus in which all the species were previously included. In addition to *E. africanus, E. europeaus, E. orientalis,* and *E. canadensis*, *Emergomyces pasteurianus* was identified for the first time (1998) in the skin biopsy of an HIV-positive Italian woman who had disseminated mycosis.[3] Since then, only a few sporadic cases have been reported in the scientific literature: a review of more than 60 cases in the scientific literature shows that adiaspiromycosis is a rare infection and *Emmonsia* is a difficult-to-grow dimorphic fungus.[5]

Since the 1970s, novel pathogens have emerged with phylogenetic, morphological, and clinical similarities to known members of the Ajellomycetaceae. Schwartz *et al*. summarized reports of numerous additional human cases due to novel species in the family Ajellomycetaceae, most of which remained undescribed. Several of these novel taxa are opportunistic pathogens of immunocompromised hosts, primarily persons infected with HIV. An important emerging species associated with disease in advanced HIV infection was found in South Africa, with at least 56 cases reported since being correctly identified in 2008. The agent causing this mycosis was closely related to *Emmonsia pasteuriana*, which is also known to infect patients with AIDS and patients with other immune disorders.[6-8]

Between 2015 and 2019, a small number of cases were reported. The patients were always immunocompromised and showed cutaneous lesions, often accompanied by pulmonary involvement.[9-17]

Conclusions

Emergomycosis caused by *E. pasteurianus* is a new fungal pathology that affects immunocompromised people, particularly those with AIDS, but also transplanted patients and those on long-term steroid therapy. The cutaneous presentation occurs in more than 90% of cases, and it is almost pathognomonic because ulcerated nodular lesions are very often present. The diagnosis needs to be confirmed by histology and culture of the skin and all the other tissues. The molecular identification by sequencing the ITS region of the rDNA is mandatory to distinguish it from *Histoplasma* spp. and permit the species identification, even if the classical diagnostic approach (direct examination of sample, histology, and culture) continues to help microbiologists and clinicians to orient diagnosis and treatment.[18] This diagnostic approach is not yet widespread, which is why it is not easy to define the epidemiology of emergomycosis. Schwartz and colleagues say that the published case reports represent the “ear of the hippo” in Africa (and in other parts of the world).[19,20] Therapy with amphotericin B followed by an azole (itraconazole, voriconazole, or posaconazole) assures the best outcome, even if new drugs, like manogepix, seem to be active.

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Figure 1. Nodular lesions ulcerated mainly in the forehead, under orbital and nasal areas.

Figure 2. Histological examination of the skin biopsy highlights the presence of round intracellular structures.

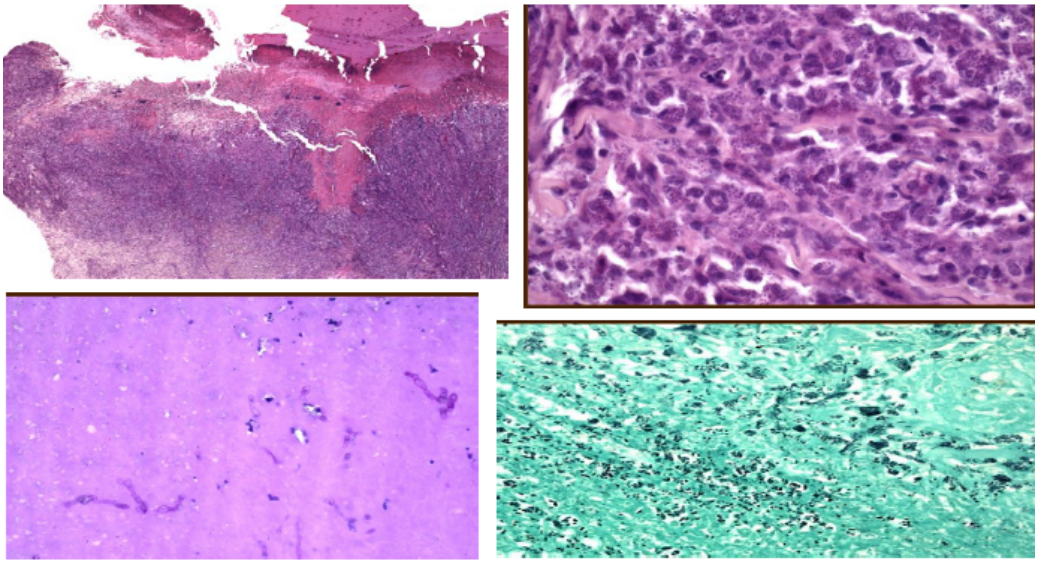

Figure 3. Presence of restricted colonies, initially yeast-like, then finely fluffy, white, and yellowish on Sabouraud Dextrose Agar after 2 weeks of incubation.