A rare fungal infection: Phaeohyphomycosis due to *Veronaea botryosa* and review of literature

Anne Wolfringer, Valérie Vuong, Nicolas Argy, Christian Chochillon, Lydia Deschamps, Guillaume Rollin, Stanislas Harent, Véronique Joly, William Vindrios, Vincent Descamps

**Abstract**

We report a rare case of phaeohyphomycosis in a 71-year-old heart transplant recipient Togo native patient. Four months after the transplant, he presented painless nodules on the right heel with superficial ulceration. The polyphasic identification uncovered a rare cause of phaeohyphomycosis: *V. botryosa*. The treatment combined surgical excision of the lesions and anti-fungal therapy with posaconazole. We discussed eleven reported cases in literature since 1990.

**1. Introduction**

Infectious complications, especially fungal, are common in transplant recipients due to the underlying immunosuppression. We report a rare case of phaeohyphomycosis *Veronaea* (*V.*) *botryosa* in a heart transplant recipient. The originality of this phaeohyphomycosis is the rarity of the species identified. In the literature, 11 other cases of *V. botryosa*-induced cutaneous phaeohyphomycosis have been reported since 1990 including 3 cases in transplant recipients. This case highlighted the importance of careful research of fungal infection in immunocompromised transplant recipients and monitoring of the immunosuppressive regimen.

**2. Case**

A 71 year old native Togo patient, who has been living in France since 1970 and has not been back to Africa for 20 years, also a heart transplant recipient, was hospitalized for nodules on his right heel. The nodules were painless and slowly progressive with superficial ulceration. In December 2014 (day 210), histological analysis of skin biopsy uncovered a rare cause of phaeohyphomycosis: *V. botryosa*. The treatment combined surgical excision of the lesions and anti-fungal therapy with posaconazole. We discussed eleven reported cases in literature since 1990.
3. Discussion

Phaeohyphomycosis is defined by the presence of melanized yeast-like cells or hyphae in tissues. Patients diagnosed with phaeohyphomycosis are often immunocompromised (diabetics, transplant recipients, patients on immunosuppressive drugs or steroids). These fungi induce subcutaneous and systemic opportunistic and cosmopolitan infections [2]. They are saprophyte of plants, water, and earth. Their transmission mode is land-based, through contaminated water or vegetable items. The melanin present in the cell wall is a known virulence factor. The physiopathology of the infection remains unclear, but some authors speculate that the organism is acquired previously, remained quiescent, and is reactivated due to immunosuppression [3]. [4]. The uniqueness of this phaeohyphomycosis case is that the species found is extremely rare. To date, only 11 cases of \textit{V. botryosa}-induced cutaneous phaeohyphomycosis have been reported since 1990. We report here the main characteristics of these patients (Table 1): most patients were natives from Asia, the mean (age: 51.7 years old, and most of them were males (8 men/12 cases with our case). This is the third reported case of \textit{V. botryosa} infection in a transplant-recipient. The clinical presentation was papulo-nodules or ulcerations, mainly on the lower limbs. All patients were treated by anti-fungals and four with surgery leading to a favorable outcome with resolution of the lesions for 7 patients.

\textit{V. botryosa} can induce both chromoblastomycosis (chronic disease of the skin and subcutaneous tissues in tropical regions characterized by the presence of fumagoid cells and phaeohyphomycosis). The clinical presentation of phaeohyphomycosis is polymorphic (only skin involvement, systemic, superficial, or deep infection). It requires both histopathological and mycological analysis. Histological diagnostic criteria include the presence of brown hyphae, septate vesicular thickened wall to dark brown accompanied by yeast-like elements poorly systematized in an inflammatory granuloma. The cell wall is pigmented and stained by Gomori Grocott. Histology displays a cystic abscess with granulomatous reaction. Identification of the species involved is essential since many different species can be responsible for phaeohyphomycosis. Lack of sporulation for the isolate prevented antifungal susceptibility testing. However, previous studies have shown that the species usually exhibits high minimal inhibitory concentrations (MIC) of amphotericin B, terbinafine, voriconazole and echinocandins with lower MICs of itraconazole and posaconazole [5]. The patient was thus prescribed posaconazole together with surgical resection of the lesion. Most of the cases reported were only prescribed antifungal drugs. Phaeohyphomycosis should be kept in mind in transplant recipients.

![Fig. 1. painless nodules, with superficial ulceration (1A and 1B). (1C and 1D) original magnification ×400 Histological analysis of skin biopsy demonstrated multinucleated giant cells containing pigmented spores, (hematoxylin eosin stain) (1C) Grocott staining showed numerous spores (1D).](image1)

![Fig. 2. Culture on Sabouraud chloramphenicol at 27 °C (2A). Micromorphology of conidiophores, conidiogenous cells and conidia of \textit{V. botryose} (2B).](image2)
### Table 1
Reported cases of *V. botryosa* induced cutaneous phaeohyphomycosis.

| Case (ref.) | Years | Age/Sex | Country origin | Immunosuppression/comorbidities | Soil or plant exposure | Clinical presentation | Treatment | Follow-up |
|------------|-------|---------|----------------|-------------------------------|------------------------|----------------------|------------|-----------|
| 1/[6]      | 1990  | 24M     | China          | NA                            | Farmer                 | Black, verrucous nodules and cysts on back of hands, cheeks, and forearm and ear | AmB and lesional excision without efficacy; NA | NA        |
| 2/[7]      | 1995  | 28F     | Libya          | NA                            | NA                     | Nodule-like nodular lesions on thumb and fifth finger, upper limb, nasal mucosa, and palate erythematous, pruritic papules on the right deltoid and left shin | NA         | NA        |
| 3/[8]      | 1998  | 37M     | Philippines    | NA                            | No                     | Nodular-ulceronodular lesions on thumb and fifth finger, upper limb, nasal mucosa, and palate erythematous, pruritic papules on the right deltoid and left shin | Itraconazole | Healing   |
| 4/[3]      | 1999  | 57M     | France         | Liver transplant: appearance of lesions 11 weeks after transplantation | No                     | Multiple painless dermal nodules that coalesced and spontaneously yielded pus | Itraconazole | Healing   |
| 5/[9]      | 2003  | 81M     | Taiwan         | No/Chronic renal failure      | No                     | Swelling plaque, papulonodules on Left leg and dorsal foot | Debridement and Itraconazole | Healing   |
| 6/[10]     | 2003  | 12M     | China          | Unknown                       | No                     | Disseminated nodular lesions on face, upper limbs, legs, scrotum, and buttocks | Herbal medication thermotherapy, local AmB injection, Terbinafine, Itraconazole | No effect |
| 7/[4]      | 2004  | 62M     | USA            | Heart transplant              | No                     | Area of chronic induration and tenderness over the dorsum of the right hand | Itraconazole and Voriconazole (gastrointestinal complaints) and incision | Healing   |
| 8/[11]     | 2006  | 76M     | Taiwan         | No                            | Farmer                 | Crusted nodules and plaques. Right forearm and knee, left upper limb | Itraconazole/amB | No effect |
| 9/[12]     | 2007  | 65F     | Japan          | VHC                           | Farmer                 | A erythematous, slightly scaly, indurated plaque on the dorsum of the left foot, duration of more than 3 years’ duration crusted, verrucous lesions, initially on the left ear and later on the left buttock | Surgical excision | Healing   |
| 10/[13]    | 2010  | 16F     | China          | No                            | No                     | Chronic dermatitis which started 10 years earlier with multiple Exophytic, multilobulated, soft, and pendunculated or sessile neoformations of diverse sizes from 2 to 10 cm in diameter, which became verrucous and increased in size. | Itraconazole | Healing   |
| 11/[14]    | 2012  | 32F     | Mexico         | No                            | No                     | Chronic dermatitis which started 10 years earlier with multiple Exophytic, multilobulated, soft, and pendunculated or sessile neoformations of diverse sizes from 2 to 10 cm in diameter, which became verrucous and increased in size. | Posaconazole | Improvement of the lesions |
| 12/[15]: Case reported in this article | 2015  | 71M     | France         | Heart Transplant, four months after the transplant | No                     | Painless, slowly progressive on the leg with superficial ulceration | Excision and Posaconazole | Death     |
Conflict of Interest

There are none.

Acknowledgements

We thank Dea Garcia-Hermoso (National Reference Center for Invasive Mycoses & Antifungals, Molecular Mycology unit, Institut Pasteur, Paris, France) for identification of the isolate and for the picture.

We thank Virginia Nguyen (Department of cardiology, Hospital Bichat, University Paris Diderot, Paris).

References

[1] E. Alvarez, D. Garcia-Hermoso, D.A. Sutton, J.F. Cano, A.M. Stchigel, D. Hoinard, et al., Molecular phylogeny and proposal of two new species of the emerging pathogenic fungus Saksenaea, J. Clin. Microbiol. 48 (12) (2010) 4410–4416.
[2] K. Nishimura, M. Miyaji, H. Taguchi, D. L. Wang, R. Y. Li, and Z. H. Meng. An ecological study on pathogenic dematiaceous fungi in China, p. 17-20. In Current problems of opportunistic fungal infections, 1989
[3] F. Foulet, C. Davoust, C. de Bièvre, C. Hézode, S. Bretagne, Cutaneous phaeohyphomycosis caused by Veronaea botryosa in a liver transplant recipient successfully treated with itraconazole, Clin. Infect. Dis. Publ. Infect. Dis. Soc. Am. 29 (3) (1999) 689–690.
[4] D.A. Sutton, M.G. Rinaldi, M. Kielhofner, First U.S. report of subcutaneous phaeohyphomycosis caused by Veronaea botryosa in a heart transplant recipient and review of the literature, J. Clin. Microbiol 42 (6) (2004) 2843–2846.
[5] H. Badali, S.A. Yazdanparast, A. Bonifaz, B. Mousavi, G.S. de Hoog, C.H.W. Klaassen, et al., Veronaea botryosa: molecular identification with amplified fragment length polymorphism (AFLP) and in vitro antifungal susceptibility, Mycopathologia 175 (5–6) (2013) 505–513.
[6] H.E. Zhang, D.L. Wang, R.Y. Li, Report of the case of phaeohyphomycosis caused by Veronaea botryosa, Chin. J. Dermatol. 23 (1990) 96–98.
[7] A. Ayadi, M.R. Huerre, C. de Bièvre, Phaeohyphomycosis caused by Veronaea botryosa, Lancet Lond. Engl. 23 346 (8991–8992) (1995) 1703–1704.
[8] A.L. Medina, J.A.D. Redondo, L.M. Nebrida, Two unusual cases of mycoses in the Philippines, p. 88. In Proceedings of the 4th China Japan International Congress on Mycology, 1998.
[9] C. Chen, Y. Tsai, S. Hu Cutaneous Veronaea botryosa phaeohyphomycosis manifested as lymphocutaneous syndrome, 21, pp. 375–383
[10] A. Matsushita, L. Jilong, M. Hiruma, M. Kobayashi, T. Matsumoto, H. Ogawa, et al., Subcutaneous phaeohyphomycosis caused by Veronaea botryosa in the People’s Republic of China, J. Clin. Microbiol 41 (5) (2003) 2219–2222.
[11] Y.-T. Chen, H.-C. Lin, C.-C. Huang, Y.-H. Lo, Cutaneous phaeohyphomycosis caused by an Itraconazole and Amphotericin B resistant strain of Veronaeae botryosa, Int. J. Dermatol 45 (4) (2006) 429–432.
[12] Y. Kondo, M. Hiruma, A. Matsushita, S. Matsuba, K. Nishimura, K. Takamori, Cutaneous phaeohyphomycosis caused by Veronaea botryosa observed as sclerotic cells in tissue, Int J. Dermatol 46 (6) (2007) 625–627.
[13] H. Sang, X.E. Zheng, Q.T. Kong, W.Q. Zhou, W. He, G.X. Lv, et al., A rare complication of ear piercing: a case of subcutaneous phaeohyphomycosis caused by Veronaea botryosa in China, Med Mycol. 49 (3) (2011) 296–302.
[14] A. Bonifaz, M.M. Davoudi, G.S. de Hoog, C. Patilla-Desgreniers, D. Vázquez-González, G. Navarrete, et al., Severe disseminated phaeohyphomycosis in an immunocompetent patient caused by Veronaea botryosa, Mycopathologia 175 (5–6) (2013) 497–503.
[15] C. Chochillon, F. Lorme, W. Vindrios, L. Descamps, F. Dromer, S. Houze, Phaeohyphomycosis: un cas à Veronaea botryosa, J. Med Mycol. 25 (3) (2015) 239.