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Case Report

Subcutaneous Basidiobolomycosis Associated with an Uncommon Cycloheximide-Resistant *Basidiobolus ranarum* Isolate

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Abstract

Introduction: Basidiobolomycosis is an unusual mycosis caused by *Basidiobolus ranarum*. It affects preferentially rural tropical and subtropical children. The diagnosis is suggested by histological examination and provided by the culture of the biopsy products on Sabouraud's medium without cycloheximide; this latter generally inhibiting the growth of *Basidiobolus ranarum*. We report a case of basidiobolomycosis due to a cycloheximide resistant isolate of *Basidiobolus ranarum*.

Patient: The patient was a 7-years-old female patient living in a village about 50 km from Abidjan. She had presented, for more than 6 months, a dermo-hypodermic plaque located in the abdomen and evolving slowly towards the thorax. Thus, she benefited cutaneous biopsies for anatomopathological and mycological examinations. The biopsy fragments were cultured on Sabouraud-Chloramphenicol agar and Sabouraud-Chloramphenicol agar supplemented with cycloheximide and incubated at 30°C for 15 days.

Results: Histological examination revealed hyphal fragments surrounded by an eosinophilic reaction (Splendore-Hoeppli Phenomenon) which could suggest the diagnosis of basidiobolomycosis. From a mycological point of view, only one type of colony was found on the 2 agars. Microscopic examination of these colonies identified *Basidiobolus ranarum* by morphological characters. The evolution of the symptomatology under treatment with ketoconazole was favorable after one month.

Conclusion: The growth of *Basidiobolus ranarum* is generally inhibited by cycloheximide. However, some isolates would be resistant to this antiseptic.

Keywords: *Basidiobolomycosis; Basidiobolus ranarum; Cycloheximide; Côte d'Ivoire*

Introduction

Basidiobolomycosis is a rare deep mycosis. Indeed, only 179 cases have been reported worldwide in 40 years with an annual prevalence of 4 cases per year [1,2]. In Côte d'Ivoire, 20 cases have been reported in 21 years by Ahogo., *et al.* at the Dermatology Department of the University and Hospital Center in Treichville [3]. The etiological agent is a fungus of the Phycomycete class, saprophyte of reptiles, amphibians, decaying soils and plants called *Basidiobolus ranarum* (*B. ranarum*) [4-6]. It is well known to cause cutaneous and subcutaneous involvement in healthy individuals [7,8]. However, this fungus can also infect other tissue including eyes, gastrointestinal tract, lungs, maxillary sinus, palate and nasal turbinates [5,7]. Human contamination is transcutaneous through microtrauma, stinging of thorn prick or insect bites [5,9,10]. Basidiobolomycosis is mostly found in the tropical and subtropical Africa, south America and Asia [9,11,12] where it usually affects children, less commonly teenagers and rarely adults. In these endemic areas, the most at risk are rural populations [1,13].

Histological examination of biopsies is essential for diagnosis. However, the confirmation of the diagnosis is based on the demonstration of *B. ranarum* colonies after seeding the biopsies on Sabouraud's medium without cycloheximide [1,13,14]. Indeed, the growth of *B. ranarum* is generally inhibited by this antiseptic. The objective of this study was to report a case of subcutaneous basidiobolomycosis with a cycloheximide-resistant isolate of *B. ranarum*.

Case Report

The patient was a 7-years-old rural female patient living at about 50 km from Abidjan and having an undocumented family history of elder brother's death due to symptoms similar to that of the patient. The history of the disease reveals the insidious appearance of cutaneous induration of the abdominal seat. The evolution the case was marked by a slow extension of induration to the entire abdomen and then to the thorax. This induration was associated with spontaneously resolving pains. The patient received an unsuccessful traditional treatment made of poultices. Due to the aggravation of signs and recollection of the death of the elder brother that the parents made the decision to consult University Health Center (UHC) of Treichville.

Initially, the patient presented with a dermo-hypodermic plaque that extended from the abdomen to the chest. It was a cold, painless, shiny, tense, smooth-surface, firm-consistency, non-scooping swelling. This closet was adhering to the superficial plane but movable in relation to the deep plane with sharp and stiff edges (Figure 1). His general condition was preserved, she had no fever, neither satellite lymphadenopathy nor ulceration.

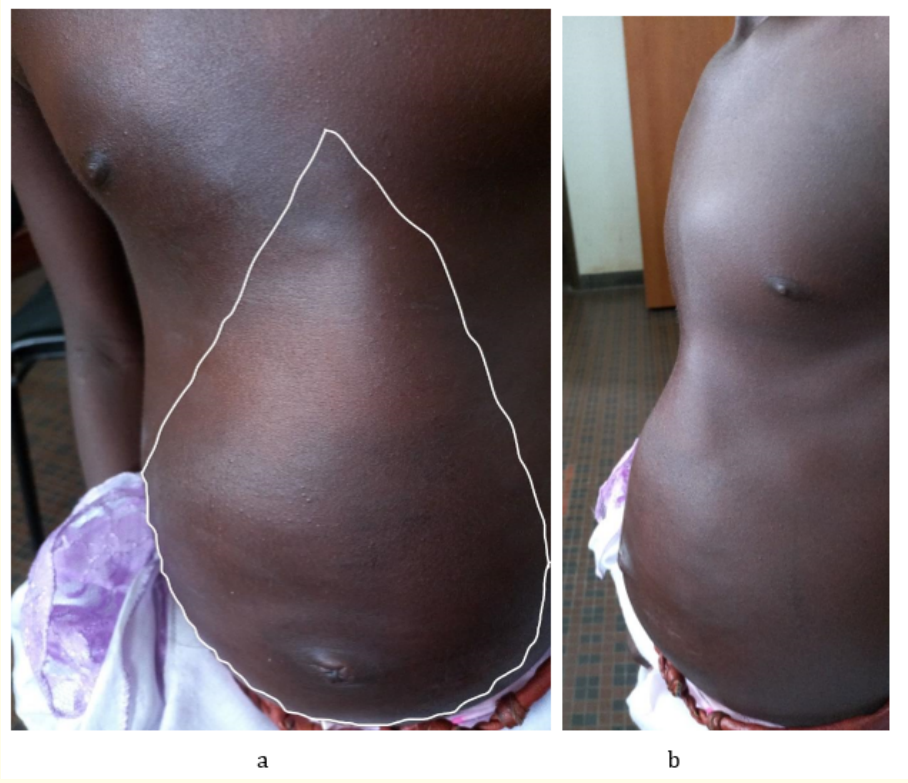

Figure 1: *Extent of dermohypodermal closet (a: Front view; b: Profile view).*

Faced with this table, cutaneous biopsies were carried out for anatomo-pathological and mycological examinations.

Histological examination revealed an inflammatory dermo-hypodermic granulomatous reaction with broad non-septate hyphal fragments surrounded by an eosinophilic reaction. This is the phenomenon of Splendore-Hoeppli that could suggest the diagnosis of basidiobolomycosis in this context of painless induration of the subcutaneous tissue (Figure 2).

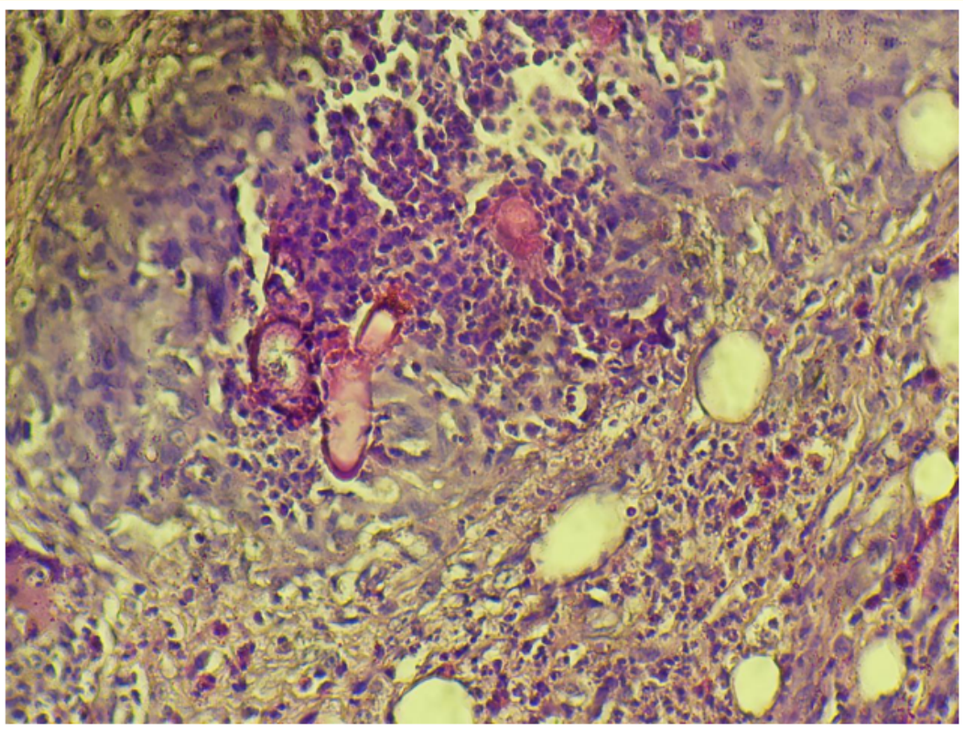

Figure 2: *(Hemalun Eosine, x 40) subcutaneous infiltrate with Splendore-Hoeppli phenomenon.*

The biopsy fragments were cultured on Sabouraud-Chloramphenicol (SC) agar and Sabouraud-Chloramphenicol-Cycloheximide agar (SCC) and incubated at 30°C for 15 days.

On SC agar, after 4 days of incubation, it was noted the appearance of a single type of colonies: they were flat, glabrous, whitish-colored colonies pleated in the center with a pale reverse. From the 16th day, these colonies turned greyish with a buff reverse (Figure 3a and 3b).

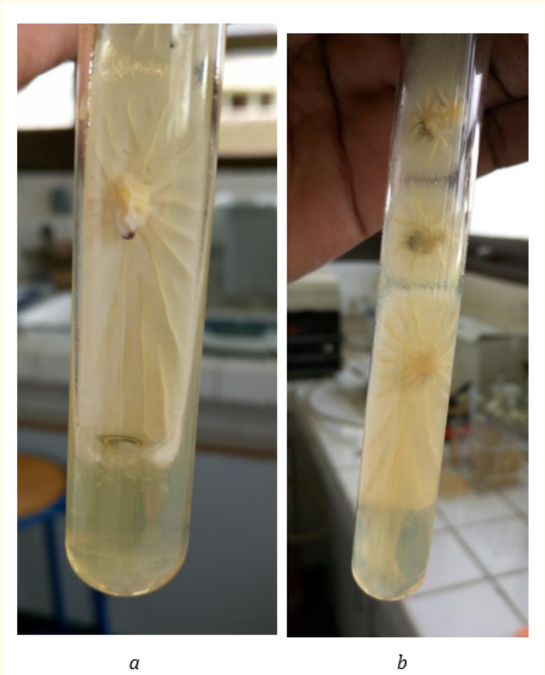

Figure 3: *Basidiobolus ranarum colonies on Sabouraud-Chloramphenicol agar after 7 days (a: Recto; b: Verso).*

On SCC agar, it was only after 15 days of incubation that the first colonies appeared. They were also flat, glabrous, whitish-colored colonies pleated in the center with a pale reverse. We therefore decided to keep the cultures after 15 days to assess the fate of the colonies. From the 30th day, these colonies became greyish with a buff reverse.

Microscopic examinations of these colonies on these 2 types of agar, revealed identical hyphae: they were broad, non-septate hyphal fragments with the presence of globoses zygospores with thick and smooth-walls as well as conjugation beaks (Figure 4a and 4b).

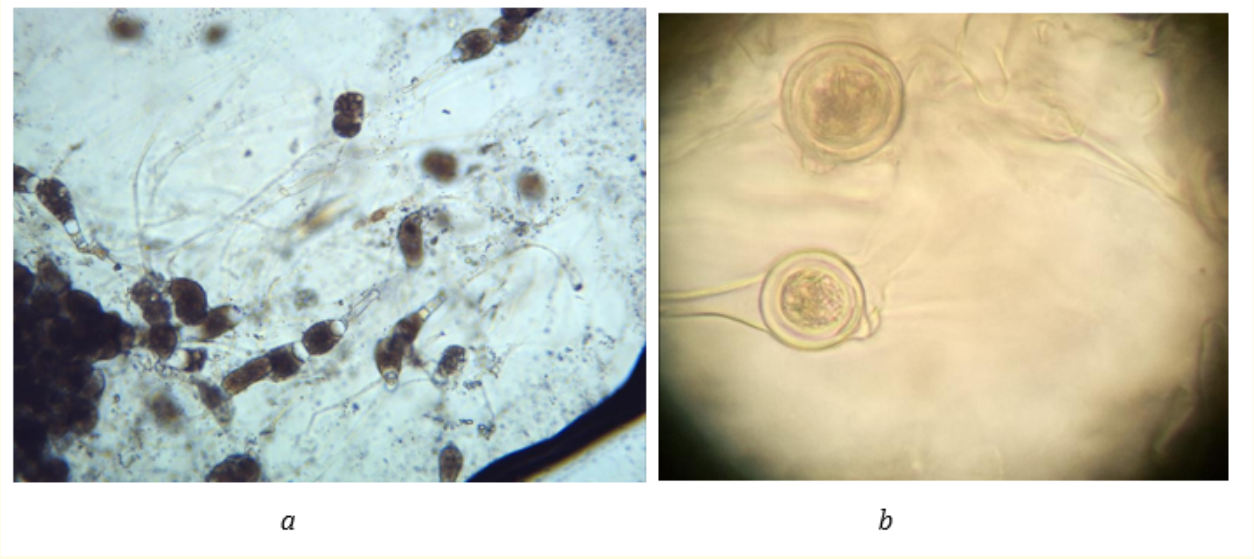

Figure 4: *Hyphae and zygospores of Basidiobolus ranarum (a: Young culture; b: Old culture).*

These macroscopic and microscopic morphological characters allowed us to conclude that *B. ranarum* was the etiologic agent.

Following this diagnosis, the patient was put on treatment with ketoconazole (7 mg/kg/day) with a favorable evolution after one month of treatment. The patient was lost to follow-up after one month.

Discussion

Basidiobolomycosis is a rarely reported chronic mycosis. However, it is the most common of the entomophtoramycosis [3,5]. The infection is caused by the filamentous fungus *B. ranarum*, belonging to the class zygomycetes and entomophthoral order [2]. The disease is endemic in rural intertropical areas, particularly in Indonesia, Burma, India and sub-Saharan Africa [2] where it usually affects children [3,11,12]. In Côte d'Ivoire, cases of basiodiobolomycosis have previously been described with children aged between 3 to 15, all living in rural areas [3]. In the clinical case described, the patient was 7 years old and lived in a village about 50 km from Abidjan. Moreover, the infection occurred in a female patient whereas this infection is reported more in males [3,15,16].

The clinical manifestations described in our patient corroborate the data of the literature. Subcutaneous basidiobolomycosis is generally manifested by firm, very clearly circumscribed, dermohypodermic plaques, generally cold and painless, adhering to deep planes with sharp and abrupt edges [2,14]. In addition, the general condition of affected children is often well preserved, and there is usually no lymphadenopathy [1,2]. Apart from the skin and subcutaneous tissue, *B. ranarum* can affect other tissues including gastrointestinal tract [5,8], lungs, sinus, palate and eyes [7]; systemic and invasive forms have also been described [1,15-18].

The clinical presentation of subcutaneous basidiobolomycosis is quite characteristic but it is not very specific and several other diseases may in fact mimic the clinical signs [14]. The diagnosis of basidiobolomycosis is based on histology and mycology [1,2,14,15]. However, cultivation of the *B. ranarum* fungus is difficult [2]. In our case, the histology revealed a dermo-hypodermic granuloma with non-septal mycelial hyphae surrounded by an eosinophilic reaction (Splendore-Hoeppli phenomenon). This description is similar to that of the literature [1,2,15,16]. Nonetheless, the Splendore-Hoeppli phenomenon itself is not specific for Basidiolomycosis and can also be observed in other infections, such as mycetoma, aspergillosis, sporotrichosis and cutaneous Malassezia folliculitis [2]. The diagnosis of basidiobolomycosis is therefore suggested by histology in front of clinical signs in favor.

Cultured skin biopsies on SC agar and SCC agar showed colonies whose macroscopic and microscopic characters identified *B. ranarum* [7,13,15]. On SC agar, the colonies appeared in 4 days, joining the results of Darré., *et al*, Angora., *et al*. and Singh., *et al*. which found 3, 4 and 5 days respectively [2,13,15]. *B. ranarum* grows rapidly at 30°C. and is capable of growth at 37°C [16]. However, colonies did not appear on SCC agar until after 15 days. Cycloheximide therefore slowed down the growth of the germ. In our case, if the cultures were removed strictly on the 15th day, we would have said that *B. ranarum* does not grow on medium supplemented with cycloheximide. The growth of *B. ranarum* being inhibited by cycloheximide, in the literature, the culture is done on Sabouraud's medium without cycloheximide [13,19]. However, our isolate gave colonies on Sabouraud's agar supplemented with cycloheximide. In India, Singh also reported a case of basidiobolomycosis with an isolate of *B. ranarum* that gave colonies on Sabouraud medium supplemented with cycloheximide; colonies appeared quickly, in less than 5 days [15]. But this isolate was responsible for a nasal manifestation.

Specific serology immunodiffusion tests and polymerase chain reaction (PCR) are also available to diagnose basidiobolomycosis [8]. But they are not often available in endemic areas and have varying sensitivity [2].

The treatment of our case was done with ketoconazole (7 mg/Kg/day) with a favorable evolution after four weeks. In several studies, azole derivatives including ketoconazole, are molecules of choice in the treatment of this condition [1,3,20]. Indeed, the latter are effective and well tolerated, unlike potassium iodide and trimethoprim-sulfamethoxazole [1]. Other molecules are commonly used successfully. these are itraconazole, voriconazole and posaconazole [3,19]. Amphotericin B or potassium iodide remain more readily available in developing countries. However, they have an inconsistent action, relapses on stopping treatment are frequent and side effects numerous [2,19].

Conclusion

Côte d'Ivoire is an endemic area of basidiobolomycosis. *B. ranarum*, the etiological agent of this condition, has a growth generally inhibited by cycloheximide; hence its culture on medium without this antiseptic. However, some isolates manage to grow despite this antiseptic. It is therefore interesting to keep the cultures on SCC agar beyond 15 days.

Conflict of Interest

The authors have no conflict of interest.

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