CASE REPORT

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Subcutaneous Basidiobolomycosis: A Rare and Underdiagnosed but Curable Fungal Infection - A Case Report

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Basidiobolomycosis is a rare deep fungal infection caused by *Basidiobolus ranarum* and characterized by the development of swollen erythematous nodular lesions. Several azoles have been shown to be an effective treatment for this condition. Herein, we report a case of basidiobolomycosis that was initially misdiagnosed as a different disease and resolved after itraconazole medication. A 25-year-old man presented with a 2.5-year history of extensive swelling on his right arm, face, and neck. Initially, he was diagnosed with lipoma and scapular tuberculosis; however, no improvements were observed post-surgery and with tuberculosis medication. Histopathological examinations revealed giant cells, aseptate hyphae, and the Splendore-Hoeppli phenomenon. Fungal culture confirmed the isolate to be *Basidiobolus ranarum*. The patient was given oral itraconazole 200 mg twice daily, and the complete resolution was achieved after 25 months of treatment.

Key Words: Basidiobolomycosis, *Basidiobolus ranarum*, Infectious disease, Itraconazole

INTRODUCTION

Basidiobolomycosis is a rare deep fungal infection caused by *Basidiobolus ranarum* that usually affects immunocompetent individuals, particularly children and young people. *Basidiobolus ranarum* infection can cause a range of clinical presentations, including subcutaneous, gastrointestinal, retroperitoneal, and pulmonary basidiobolomycosis, with the most typical clinical form being subcutaneous basidiobolomycosis that is characterized by the development of swollen erythematous nodular lesions with gradual peripheral extension and enlargement, generally on extremities and trunk[1,2].

The accurate identification of basidiobolomycosis requires high clinical suspicion. Given the rarity of the disease, this infection is often misdiagnosed as tuberculosis, chronic abscess, soft tissue tumor, malignancy, and others. For this invasive species of fungi, such misdiagnosis often delays definitive diagnosis and subsequent effective care, thereby

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Fig. 1. (A) Photograph of the patient when he first time came to the dermatology outpatient clinic (B) Complete resolution after 25 months itraconazole medication

increasing disease morbidity and mortality. The treatment includes medical therapy with or without surgical intervention[1,3,4].

Herein, we report a case of a 25-year-old male with basidiobolomycosis, who was initially misdiagnosed with lipoma and scapular tuberculosis and showed complete resolution after itraconazole medication.

CASE REPORT

A 25-year-old male presented with a 2.5-year history of extensive swelling in his right arm, face, and neck. Lesions initially appeared as a painless nodule on his upper back

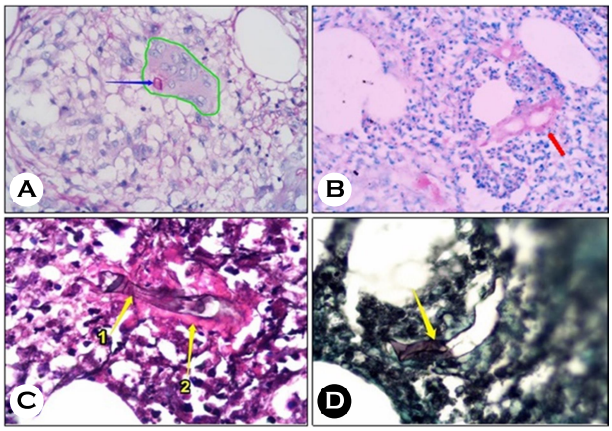

Fig. 2. Histopathology examination of the patient (A) Giant cell (green line) internalizing hyphae (PAS, ×40) (B) Rare Splendore-Hoeppli phenomenon appeared in acid fast staining (red arrow) (AFS, ×40) (C) 1. Aseptate hyphae, 2. Splendore-Hoeppli phenomenon (GMS with H&E Counterstain, ×100) (D) Aseptate hyphae (GMS, ×100)

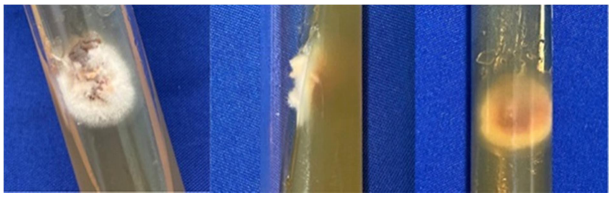

Fig. 3. Fungal culture showed growth of colony that appear flat and grooved, yellowish gray in color with pale reverse after 5 days of incubation at room temperature.

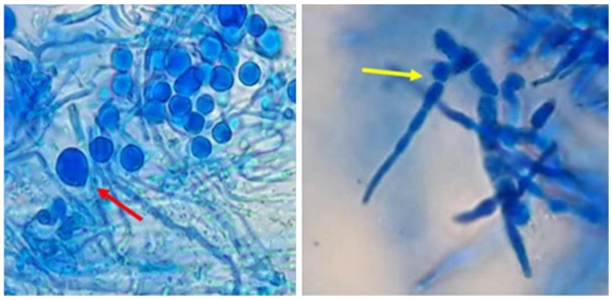

Fig. 4. Five days-old culture showed a aseptate hyphae and zygospores with conjugation beaks (red arrow), and club-shaped spores with a knoblike tip (yellow arrow) (lacto-phenol cotton blue preparation, ×400).

and were diagnosed as a lipoma, for which he underwent excisional surgery. The rapid growth of the lesions was observed post-surgery. The swelling began in his right arm and then gradually spread to his face and neck along the region of right lymphatic circulation. Histopathological examination of his arm lesion indicated granulomatous inflammation, which suggested tuberculosis. However, tissue culture and fungal staining were not performed. Therefore, the patient was suspected of scapular tuberculosis and given six months of tuberculosis medication; however, no clinical improvement occurred. After a multidisciplinary discussion, deep fungal infection was suspected, and the patient was then referred to the Dermatovenereology Department.

Dermatological examination of the face, neck, and upper right extremities area revealed massive nonpitting edema on the right part of the face and arm, impairing the patient's ability to open his eyes and restricting movement of the right hand. The examination also revealed multiple painless,

Table 1. Summary of published basidiobolomycosis cases

Reference	Year	Age	Site of infection	Lesional size	Disease duration	Antifungal therapy/duration	Outcome
Anaparthy[14]	2014	6 month-old	Left knee	3 × 4 cm	4 months	Saturated solution of oral potassium iodide/8 weeks	Complete resolution
Kumaravel[15]	2016	7-year-old	Left thigh and leg	Not known	1.5 years	Saturated solution of oral potassium iodide continue with itraconazole/4 weeks (itraconazole)	Complete resolution
		4-year-old	Left gluteal	Not known	4 months	Itraconazole/4 weeks	Complete resolution
		2-year-old	Right gluteal	Not known	1 months	Itraconazole/4 weeks	Complete resolution
		1-year-old	Left hemi scrotum	Not known	1 months	Fluconazole/4 weeks	Complete resolution
		6-year-old	Left gluteal	Not known	4 months	Itraconazole/4 weeks	Complete resolution
		6-year-old	Right gluteal and thigh	Not known	3 months	Itraconazole/4 weeks	Complete resolution
		5-year-old	Right lateral thigh	Not known	1 months	Itraconazole/4 weeks	Complete resolution
		2-year-old	Left gluteal	12 × 10 cm	5 months	Itraconazole/4 weeks	Complete resolution
Sackey[13]	2017	3-year-old	Right leg and buttock swelling, right thigh ulceration	The right leg 24.4 cm, the left leg 15 cm, ulcer 2 × 3 cm, 1 × 1.5 cm	6 months	Itraconazole/ several weeks	Lost of follow up
Patro[16]	2019	4-year-old	Right distal arm	6 × 5 cm	4 months	Itraconazole/2 months	Lesion started to resolve within first month
Shety[17]	2021	7-year-old	Left knee	5 × 4 cm	6 months	Itraconazole/12 weeks	Complete resolution after 8 weeks
Pramitha[18]	2021	23-years-old	Back, chest, and arm	Multiple nodules vary in size between 1.5 × 2 cm to 2.5 × 3 cm	2 years	Itraconazole/12 weeks	Complete resolution

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firm, mobile, and well-circumscribed subcutaneous nodules on the right periorbital, cheek, neck, upper arm, and lower arm area (Fig. 1A). Liver and kidney function tests were normal, and HbsAg and HIV tests were negative.

We performed fungal culture and histopathological examination of subcutaneous tissue on the right arm region using excision biopsy. Histopathological examination using periodic acid-Schiff staining revealed giant cells and aseptate hyphae (Fig. 2A). Acid-fast staining (AFS) demonstrated the Splendore-Hoeppli phenomenon and aseptate hyphae; however, no acid-fast bacilli were found (Fig. 2B). These findings were confirmed using a Gomorri-methenamine silver (GMS) stain with hematoxylin-eosin (H&E) counterstain, which enhances hyphal appearance (Fig. 2C, D). Tissue material cultured on Sabouraud's dextrose agar confirmed the isolate to be *Basidiobolus ranarum* (Fig. 3 and 4). In this case, we performed AFS using the optimized method for histopathological staining. The carbol fuchsin 1% was heated for 15 min, 1% HCl-alcohol was used, and 0.25% methylene blue was used as a counter stain.

After the microbiological result confirmed the diagnosis of basidiobolomycosis, itraconazole was started with a dosage of 200 mg twice a day. Post nine months of itraconazole medication, swelling in the face disappeared, and upper and lower arm circumferences decreased but were still firm on palpation on his right face, neck, and arm. However, the growth of *Basidiobolus ranarum* was still observed via biopsy and culture; therefore, itraconazole therapy continued. At the 25th month of the treatment, the affected areas became soft in consistency and had no palpable mass (Fig. 1B). Further, excisional biopsy and culture evaluation were performed; however, no spores, hyphae, or granuloma were found. No fungal growth was observed in the culture. Itraconazole continued for a month after complete resolution, with no recurrence observed after one year.

DISCUSSION

Basidiobolus ranarum is a saprophytic fungus found in decaying plants and soil and is a resident flora in the gastrointestinal tracts of various animals (amphibians, fish, bats, reptiles, and insects). *Basidiobolus* propagules can come into contact with humans through open skin exposure, interaction with amphibian and lizard droppings, organic material, insect bites, and soil. In this case, the patient lived near rice fields where amphibians and reptiles are natural inhabitants. He often wore sleeveless shirt at home and slept on the floor, thus likely contracting the infection due to minor trauma on his skin and exposure to *Basidiobolus* propagules.

A solitary, mobile, painless, and firm subcutaneous nodule emerges at the inoculation site, with progressive peripheral expansion and growth. *Basidiobolus* impairs the lymphatic circulation, causing lymphedema in the affected area[2,5,6]. Our case displayed typical clinical signs, aligning with existing literature.

Diagnosing cutaneous basidiobolomycosis is challenging due to its nonspecific symptoms, which can resemble other conditions[7]. Initially, our case was misdiagnosed as lipoma and scapular tuberculosis. Lipomas are painless, mobile masses in the soft tissue with a doughy consistency[8]. Based on clinical appearance, they are similar with the initial nodules in the patient; however, the difference is that basidiobolomycosis nodule exhibits a firm consistency. Scapular tuberculosis involves swelling, muscle pain, potential abscess formation, and joint stiffness. On palpation, it is soft, cystic, globular, and minimally tender, while in the patient, the nodule was painless, firm, and well-circumscribed[9]. Tuberculosis is an endemic granulomatous infection in Indonesia, and the similarities in predilection area and histopathological findings in tuberculosis and basidiobolomycosis frequently lead to misdiagnosis and improper treatment.

Diagnostic culture results and the presence of fungal components are essential for a definitive diagnosis[1]. *Basidiobolus ranarum* differs from other fungi in tissue sections owing to its distinctive hyphal shape, which can be right- or wide-angled, broad, aseptate, or minimally septate. This infection is characterized by a critical histological finding in the form of eosinophilic hyaline material around the hyphae (Splendore-Hoeppli phenomenon). This phenomenon has also been found in other granulomatous infections, such as other mycoses, bacterial and parasite invasion[3]. Tissue samples for culture are grown on Sabouraud's dextrose agar. Macroscopically, it appears as flat, waxy, greyish-yellow colonies with radial folds. The reverse of the colony is white. Microscopically, they exhibit intercalary zygospores with "beak-like" protrusions and club-shaped spores with knoblike tips[2,10].

Our case highlights the Splendore-Hoeppli phenomenon in AFS. The Spendore-Hoeppli is eosinophilic; therefore, it has a higher pH level, thus neutralizing the acid in 1% HCl-alcohol but not in 3% HCl-alcohol. Lowering the acid concentration helps preserve the aseptate hyphal structure. The GMS stain with H&E counterstaining better accentuates the Splendore-Hoeppli phenomenon than green counterstaining.

The treatment for basidiobolomycosis involves medical therapy with or without surgical intervention. Surgery should be carefully considered because any attempt at curative excision can be counterproductive and risks seeding the

fungus into the excision margins. However, if it must be done, a prolonged course of antifungal therapy is required after surgery[11,12]. In our case, the patient previously underwent surgical excision without antifungal treatment, resulting in rapid lesion growth post-surgery.

The optimal choice of antifungal treatment and duration of therapy for basidiobolomycosis remains unclear. Treatment should be continued for a month after lesions disappear. Several azoles, amphotericin-B, and potassium iodide have been used with varying outcomes[2,13]. Most patients with basidiobolomycosis respond well to azoles, with the most commonly used agents being ketoconazole (7 mg/kg/day) and itraconazole (5 mg/kg/day)[7]. Table 1 summarizes published basidiobolomycosis case reports. In our case, treatment with itraconazole was favorable. Complete resolution was achieved after 25 months of treatment, with no recurrence after a year. This patient had extensive lesions and a long disease duration compared to published case reports; therefore, a long duration of therapy was required.

CONCLUSION

Basidiobolomycosis is a rare deep fungal infection with an excellent response to antifungal therapy. In this case, the administration of oral itraconazole gave a remarkable outcome. Misdiagnosis is common in daily practice and may lead to unnecessary patient morbidity. However, accurate recognition of this entity will result in a more timely diagnosis and appropriate treatment for the patient.

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CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

PATIENT CONSENT STATEMENT

The patient provided written informed consent for the publication and the use of his images.

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