

Diagnosis and Management of Basidiobolomycosis: A Comprehensive Review of Case Series and Reports

Mohammed Samannodi, MD, ABIM*

ABSTRACT

Basidiobolomycosis, especially gastrointestinal basidiobolomycosis, is challenging to diagnose due to its diverse and nonspecific manifestations, which can lead to misdiagnosis, delay in initiation of treatment, and increased risk of death. This review aimed to summarize the available literature on the diagnosis and management of basidiobolomycosis. This review showed that antifungal monotherapy was sufficient to manage most cases of subcutaneous basidiobolomycosis. However, combination antifungal therapy (mono or combination) with surgical intervention was used to treat most cases of gastrointestinal basidiobolomycosis. Itraconazole and voriconazole were the most used and effective antifungal treatments for basidiobolomycosis. However, in some cases that are resistant to treatment, deaths have occurred despite the use of medical and surgical treatment. Thus, more research is needed to develop a detailed therapeutic approach for this infection, especially in cases with comorbidities and/or treatment resistance.

Keywords: *basidiobolomycosis; case reports; case series; management*

INTRODUCTION

Basidiobolomycosis is an uncommon fungal infection resulting from the environmental saprophytic fungus *Basidiobolus ranarum*^{1,2}. It is generally found in some animals' gastrointestinal tracts, decaying vegetables and fruit matter, and soil^{3,4}. It can enter human hosts through traumatic inoculation or insect bites⁵. The prevalence of basidiobolomycosis is higher in tropical and subtropical places in Latin America, Asia, and Africa, with numerous cases reported in Iran, Australia, Kuwait, Saudi Arabia, Egypt, and the United States⁶⁻¹⁹.

Basidiobolomycosis often impacts immunocompetent individuals²⁰. Besides, it is more common among children and male individuals⁵. The first documented subcutaneous basidiobolomycosis case was among three children in Indonesia in 1956²¹. Although basidiobolomycosis predominantly influences skin and subcutaneous tissues, it can also involve the gastrointestinal tract²²; the first reported gastrointestinal basidiobolomycosis case was in a boy child in Nigeria in 1964²³. Furthermore, recent studies have declared a growing number of cases that affect the digestive system, involving organs like the intestines, liver, and stomach²².

The clinical signs and symptoms of basidiobolomycosis are varied and nonspecific, influenced by the underlying condition. For instance, the hallmark gastrointestinal basidiobolomycosis manifestations include chills, constipation, diarrhea, weight loss, abdominal pain, and fever²⁴. In addition to negative endoscopic biopsy and undefined risk factors, these varied and nonspecific manifestations lead to underdiagnosis and misdiagnosis of this fungal infection^{16,25-27}. The majority of patients with gastrointestinal basidiobolomycosis have been misdiagnosed with malignancy, amebiasis, sarcoidosis, tuberculosis, or inflammatory bowel disease (like ulcerative colitis or Chron's disease)^{14,26,28}. Generally, misdiagnosis of basidiobolomycosis results in diagnosis delays²⁶, consequently raising basidiobolomycosis-related mortality and morbidity^{25,29-32}.

Basidiobolomycosis is a severe and lethal infection³³ that requires efficacious treatment approaches for affected patients²². Regardless of basidiobolomycosis severity, understanding of its treatment regimens remains poor²². Therefore, this literature review aims to provide comprehensive knowledge about basidiobolomycosis management which may aid in preventing many serious complications.

Basidiobolomycosis management

Starting immediate basidiobolomycosis treatment can help prevent the spread of fungal infections and their associated complications and thus reduce their life-threatening risk³³. The pharmacological treatment currently includes potassium iodide, amphotericin B, itraconazole, voriconazole, posaconazole, cotrimoxazole, and terbinafine in combination or as monotherapy^{22,34,35}. Pharmacological treatment also includes antibiotics in superinfection cases. The best previously documented basidiobolomycosis treatment approach encompasses surgical resection and prolonged systemic antifungal therapy^{1,22,30,33}. Recently, the focus has been on treating this condition with antifungal medications (specifically, the azole group) without surgical intervention³⁶. A previous study highlighted that early diagnosis of basidiobolomycosis can prevent many adverse effects and is associated with effective treatment using antifungal therapy without needing surgical interventions³⁷. The patient's status and response to medication affect the decision of whether to perform surgery or not³⁶. Furthermore, studies have shown favorable outcomes in patients who have undergone medical treatment without surgical intervention for a period ranging from six months to a year^{9,11,35}.

REVIEW OF THE LITERATURE

Table 1 summarizes the published basidiobolomycosis case reports and series. The management of basidiobolomycosis and its outcomes differed depending on demographics, country, and site of infection. Subcutaneous basidiobolomycosis was more common among younger patients. Besides, most subcutaneous basidiobolomycosis

* Department of Medicine
College of Medicine, Umm Al-Qura University
Makkah 24382, Saudi Arabia.
Email: mssamannodi@uqu.edu.sa

Table 1. Summary of published basidiobolomycosis case reports and series.

Site(s) involved basidiobolomycosis	Sex/Age (years)	Country	Basidiobolomycosis management	Outcome(s)	PY, Ref.
Subcutaneous	F/8	India	Potassium iodide Itraconazole	Response was poor with potassium iodide. Cured with itraconazole.	2005, ³⁸
Gastrointestinal *There was difficulty in reaching the diagnosis	M/61	Netherlands	Amphotericin B *Because the patient suffers from renal failure, itraconazole is contraindicated.	The septic shock occurred, and then the patient died.	2006, ¹⁹
Gastrointestinal (intestinal)	M/13	Saudi Arabia	Itraconazole Surgical resection of the lesion	Considerably improved. On long-term follow-up the patient remained well.	2007, ⁵⁴
Subcutaneous	F/1.5	India	Potassium iodide Itraconazole	Cured	2009, ⁴⁹
Nose and subcutaneous tissues of the face	M/35	India	Itraconazole, Terbinafine	Cured	2010, ³⁴
Gastrointestinal and retroperitoneal	M/2.5	Saudi Arabia	Amphotericin B	A promising response was seen	2010, ⁵⁵
Subcutaneous	M/9	Togo	Ketoconazole	Cured	2010, ³⁹
Subcutaneous	M/3	India	Excision Oral potassium iodide Itraconazole	Cured	2010, ¹⁷
Gastrointestinal	C1: M/6	Saudi Arabia	C1: Amphotericin-B Itraconazole	C1: Cured	2011, ¹⁴
	C2: F/13		C2: Right hemicolectomy with partial resection of the mass. Amphotericin-B Itraconazole	C2: Cured	
	C3: F/8		C3: Amphotericin-B Itraconazole	C3: Cured	
	C4: M/8		C4: Tracheostomy Amphotericin-B Itraconazole	C4: Cured	
	C5: M/10		C5: Amphotericin-B Voriconazole	C5: Cured	
Gastrointestinal (colon)	F/25	Saudi Arabia	Subtotal colectomy Itraconazole	The patient remained well during follow-up but was still under itraconazole treatment.	2011, ¹⁶
Gastrointestinal	M/2	Saudi Arabia	Amphotericin B Voriconazole	Responded well to voriconazole treatment.	2012, ⁵⁶
Subcutaneous	M/46	India	Potassium iodide	Cured	2013, ⁴⁰
Gastrointestinal	C1: F/12	Saudi Arabia	C1: Hemicolectomy Itraconazole	C1: Improved but still under follow-up	2013, ⁵⁷
	C2: M/1.5		C2: Itraconazole	C2: Died shortly after hospitalization	
	C3: F/9		C3: Itraconazole	C3: Improved	
Gastrointestinal accompanied by liver involvement	F/41	Iran	Itraconazole	Cured	2014, ⁵⁸
Gastrointestinal (colon)	M/3	Iran	Surgical excision Posaconazole Itraconazole	Cured	2014, ¹⁰
Gastrointestinal with hepatic dissemination	M/12	Saudi Arabia	Itraconazole	Cured	2014, ⁵⁹
Gastrointestinal	M/11	Saudi Arabia	Voriconazole	Cured	2014, ⁹
Gastrointestinal	M/36	Saudi Arabia	Itraconazole Voriconazole	Resistance to itraconazole. Treated with voriconazole.	2015, ⁶⁰
Gastrointestinal accompanied by liver involvement	F/2	Iran	Resection of the mass. Amphotericin B.	Improved but still under treatment and follow-up	2015, ⁶¹
Visceral	F/4	Qatar	Voriconazole Oral antifungal therapy Surgical intervention	She remained asymptomatic during the follow-up.	2015, ⁶²
Subcutaneous with multiple swellings	M/12	India	Misdiagnosed: surgical resection and anti-tuberculous. Diagnosis: itraconazole.	Cured	2016, ⁴¹
Gastrointestinal	M/7	Saudi Arabia	Voriconazole	Improved. He remained asymptomatic during the follow-up.	2017, ⁶³
Gastrointestinal	F/7	Saudi Arabia	Voriconazole	Cured	2017, ⁶⁴

Gastrointestinal	M/42	Iran	Itraconazole, voriconazole, and amphotericin B	Antifungal resistant. The septic shock occurred, and then the patient died.	2017, ⁶⁵
The skin over the buttock, back, and right flank	M/5	Togo	Ketoconazole	Cured	2017, ⁸
Gastrointestinal	M/2.5	Iran	Amphotericin B and itraconazole. Four operative procedures. Potassium iodide	Infection progressed and spread after Amphotericin B and itraconazole. The addition of potassium iodide resulted in a complete cure.	2018, ⁶⁶
Ocular	M/47	Thailand	Topical ketoconazole, subconjunctival fluconazole injection, and oral itraconazole	Partial response. The patient did not continue treatment and did not return for follow-up.	2018, ⁸¹
Gastrointestinal	M/25	Italy	Surgical intervention Itraconazole	Good outcome	2019, ⁶⁷
Gastrointestinal	M/29	Oman	Surgical intervention Prolonged azole antifungal therapy	Cured	2019, ⁶⁸
Gastrointestinal	M/78	Italy	Surgical intervention Itraconazole	Cured	2019, ⁶⁹
Subcutaneous	M/2	India	Itraconazole	Cured	2019, ⁴²
Gastrointestinal	M/70	Saudi Arabia	Surgical intervention Prolonged voriconazole treatment	He remained asymptomatic during the follow-up.	2019, ²
Retroperitoneal	F/29	Saudi Arabia	Itraconazole	Treated successfully. She was still under treatment and follow-up.	2020, ³⁶
Subcutaneous	M/12	Filipinos	Itraconazole	Cured	2020, ⁴³
Skin and soft tissue	F/4	Australia	Surgical intervention Liposomal amphotericin B Voriconazole Itraconazole	Cured	2020, ⁵⁰
Subcutaneous	F/5	Benin	Ketoconazole Surgical intervention Physiotherapy	Cured	2020, ⁵¹
Gastrointestinal	F/36	Saudi Arabia	Liposomal amphotericin B Surgical intervention	Died on day 24 post admission	2020, ⁷⁰
Gastrointestinal	C1: M/53	Sudan	C1: Surgical intervention Voriconazole	C1: Died	2020 ⁷¹
	C2: F/17		C2: Surgical intervention Voriconazole	C2: Cured	
	C3: M/13		C3: Surgical intervention	C3: Cured	
	C4: F/56		C4: Surgical intervention Voriconazole	C4: Died	
	C5: M/58		C5: Surgical intervention	C5: Cured	
	C6: M/50		C6: Surgical intervention	C6: Cured	
	C7: F/6		C7: Surgical intervention Voriconazole	C7: Cured	
Gastrointestinal	M/1.8	United Arab Emirates	Surgical intervention Prolonged antifungal medication	Cured	2020 ⁷²
Subcutaneous	M/3	India	Potassium Iodide	Completely melted the swelling. He was still under follow-up.	2020, ⁴⁴
Dorsum of the left knee	F/7	India	Itraconazole	Cured	2021, ⁴⁵
Gastrointestinal with multi-organ involvement	M/1.9	Iran	Trimethoprim/sulfamethoxazole Liposomal amphotericin B Potassium iodide Itraconazole Surgical intervention	Improved.He remained asymptomatic during the follow-up.	2021 ⁷³
Gastrointestinal	M/1.3	Iran	Liposomal amphotericin B Potassium iodide Co-trimoxazole	Cured	2021, ⁷⁴
Gastrointestinal	C1: M/9	Oman	C1: Antibiotics	C1: Died	2021, ³²
	C2: F/19		C2: Antibiotics Caspofungin Amphotericin B	C2: Hyperkalemia, Metabolic acidosis Disseminated fungal infection Severe sepsis	
	C3: M/45		C3: Right hemicolectomy Antibiotics Amphotericin B	C3: Died	
	C4: F/5		C4: Right hemicolectomy Voriconazole	C4: Improved	
	C5: M/10		C5: Right hemicolectomy Voriconazole	C5: Improved	
Gastrointestinal	M/8	Oman	Voriconazole	Cured	2021, ⁷⁵

Gastrointestinal (colonic perforation and concomitant liver involvement)	M/65	Saudi Arabia	Voriconazole Itraconazole Amphotericin B Surgical intervention	Cured	2022, ⁷⁶
Subcutaneous	M/23	India	Itraconazole	Improved	2022, ⁴⁶
Bladder and gluteal	M/8	Saudi Arabia	Voriconazole	Cured	2022, ⁷⁷
Gastrointestinal	C1: M/5	Saudi Arabia	C1: Medical management Surgical intervention	C1: Survived	2022, ⁷⁸
	C2: M/2.5		C2: Medical management Surgical intervention	C2: Survived	
	C3: M/5		C3: Medical management	C3: Survived	
	C4: F/6		C4: Medical management Surgical intervention	C4: Survived	
	C5: M/6		C5: Medical management Surgical intervention	C5: Survived	
	C6: M/1.5		C6: Medical management	C6: Survived	
Subcutaneous	M/18	India	Itraconazole	Cured	2022, ⁴⁷
Right arm, right upper arm, neck, and face	M/24	Indonesia	Itraconazole	Cured	2022, ⁴⁸
Subcutaneous	F/6	India	Potassium iodide Co-trimoxazole	Cured	2023, ⁵²
Subcutaneous (Right upper buttock)	F/5	India	Potassium iodide Itraconazole	Cured	2023, ⁵³
Gastrointestinal *Misdiagnosed as colon cancer with liver metastasis; delayed diagnosis and treatment	M/50	Saudi Arabia	Surgical intervention Antifungal therapy	Died	2023 ²⁴
Gastrointestinal	M/69	Saudi Arabia	Surgical intervention Liposomal amphotericin B Itraconazole Antibacterial agents	Died due to refractory septic shock	2023 ⁷⁹
Gastrointestinal	C1: M/23	Saudi Arabia	C1: Itraconazole	C1: Cured	2024, ⁸⁰
	C2: M/52		C2: Voriconazole	C2: Improved	
	C3: F/41		C3: Itraconazole	C3: Improved and asymptomatic during the follow-up	
	C4: M/54		C4: Voriconazole Surgical intervention	C4: Well and asymptomatic during the follow-up	
	C5: F/58		C5: Voriconazole Surgical intervention	C5: Good and asymptomatic during the follow-up	
Gastrointestinal	M/3	Oman	Surgical intervention Antifungal therapy	Died	2024, ²⁰

PY, publication year; Ref., reference; F, female; M, male; C, case.

Included surgery for management, not for diagnosis.

cases were successfully treated using mono-antifungal therapy, like potassium iodide, ketoconazole, or itraconazole^{8,38-48}. Moreover, combination antifungal therapy or antifungal therapy (mono or combined) with surgical intervention was used to manage some subcutaneous basidiobolomycosis cases^{17,34,49-53}. On the other hand, most gastrointestinal basidiobolomycosis cases^{2,9,10,14,16,19,20,24,32,36,54-80} were treated with combination antifungal therapy (mono or combined) with surgical intervention; however, several cases were managed with mono or combined antifungal medications, especially with itraconazole and voriconazole. Factors such as misdiagnosis, delayed diagnosis, comorbidities, and treatment resistance may contribute to poor outcomes and may lead to death^{19,24,65,70}.

Basidiobolomycosis diagnosis

Definitive diagnosis of Basidiobolomycosis relies on a combination of histopathological examination, microbiological culture, clinical

suspicion, and imaging studies⁸²⁻⁸⁴. Histologically, the infection is characterized by granulomatous inflammation with a notable eosinophilic infiltrate and the presence of broad, thin-walled fungal hyphae surrounded by eosinophilic material, known as the Splendore-Hoeppli phenomenon. Microbial culture can confirm *Basidiobolus ranarum* as the causative agent, although cultures may sometimes be negative. Molecular techniques, such as panfungal polymerase chain reaction, have proven valuable in identifying the organism when cultures are inconclusive.

In conclusion, although basidiobolomycosis is rare, it is associated with several adverse events that can lead to death. Often, basidiobolomycosis, especially gastrointestinal basidiobolomycosis, is challenging to diagnose due to its diverse and nonspecific manifestations, which can lead to misdiagnosis, delays in the initiation of treatment, and increased risk of death. The early diagnosis of basidiobolomycosis can prevent

adverse events and improve patient survival rates. Therefore, there is a need to raise awareness of the diagnosis of this infection among health system members and to find faster and more precise methods of diagnosis. This review has shown that antifungal monotherapy can be sufficient to manage most cases of subcutaneous basidiobolomycosis. However, a combination of antifungal therapy (mono or combination) with surgical intervention was used to treat most cases of gastrointestinal basidiobolomycosis.

CONCLUSION

Itraconazole and voriconazole were the most used and effective antifungal treatments for basidiobolomycosis. However, in some cases that are resistant to treatment, deaths have occurred despite the use of medical and surgical treatment. Thus, more research is needed to develop a detailed therapeutic approach for this infection, especially in cases with comorbidities and/or treatment resistance.

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