Case Report
Successful Treatment of Gastrointestinal Basidiobolomycosis with Voriconazole without Surgical Intervention

by Bandar A. Albaradi,1,2 Amir M. I. Babiker,2 and Hadi S. Al-Qahtani1
1Paediatric Department, Infectious diseases division, King Fahad Specialist Hospital, Dammam, Saudi Arabia
2Paediatric Department, College of medicine, King Khalid University Hospital and King Saud University, Riyadh, Saudi Arabia

Correspondence: Bandar A. Albaradi, Paediatric Department, Infectious diseases division, King Fahad Specialist Hospital, P.O. Box 15215, Dammam 31444, Saudi Arabia. E-mail <bandar.baradi@hotmail.com>.

Summary
Basidiobolomycosis is a rare disease due to fungus Basidiobolus ranarum, an environmental saprophyte that is found worldwide, though mainly reported in the tropical and subtropical regions. Basidiobolomycosis is an unusual fungal skin infection, rarely involves the gastrointestinal (GI) tract. Most of the cases of paediatric GI basidiobolomycosis (GIB) were reported from the southern region of Saudi Arabia. We report an 11-year-old Saudi boy. He presented with a huge right lower quadrant abdominal mass and marked eosinophilia. Abdominal computed tomography scan revealed a large caecal mass. A biopsy was taken and it showed transmural granulomatous inflammation. A diagnosis of GIB was confirmed by specific features in histopathology. Most of the reported paediatric cases with GIB required adjuvant therapy of antifungal and surgical resection. In our case, treatment with voriconazole alone for 1 year was successful with complete recovery and with no recurrence after a year of discontinuing the treatment.

Key words: basidiobolomycosis, Basidiobolus ranarum, gastrointestinal, granulomatous, Saudi Arabia, voriconazole.

Introduction
Basidiobolomycosis is a rare disease caused by the fungus Basidiobolus ranarum, an environmental saprophyte found worldwide. Basidiobolus ranarum belongs to the Entomophthoraceae family of the class Zygomycetes and is mainly associated with subcutaneous fat tissue infection involving the limbs, trunk or buttocks. It is presumed that this infection is acquired after minor trauma to the skin or following insect bites. Most cases of basidiobolomycosis have been reported from Africa, South America and Asia [1–17].

Patients with B. ranarum infection may present with subcutaneous, gastrointestinal or systemic lesions. Recently, an aetiologic role of B. ranarum in gastrointestinal infections has been increasingly recognized. Gastrointestinal basidiobolomycosis (GIB) is a rare condition resulting from B. ranarum infection of the gastrointestinal tract. Ingestion of soil, animal faeces or contaminated food is the most likely route of infection [2]. All age groups are susceptible, and the condition is reported in both children and adults [2–4]. Several paediatric cases have been reported with GIB, most often involving the colon. Most of these cases have been reported from Saudi Arabia, and the majority came from the southern region of the country. Clinical features of GIB include fever, abdominal pain, diarrhoea, constipation, weight loss and/or abdominal mass.

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Consent
The parents of the index patient were consented for using their child’s clinical information for publication in this journal.
GIB poses diagnostic difficulties, as the clinical presentation is non-specific, with no identifiable risk factors. A definitive diagnosis requires a biopsy from the involved site, with characteristic findings of broad, sparsely septated hyphae surrounded by eosinophilic granular material (Splendore–Hoeppli phenomenon). Tissue eosinophilia and granulomatous inflammation are also usual findings [3].

Almost all of the previously reported cases in literature were treated by a combination of surgery and antifungal medications [4–15]. Our report is one of the first few reports on a Saudi child with GIB who was treated successfully with antifungal medication alone without surgical intervention [16, 17].

**Case Report**

A previously healthy 11-year-old Saudi boy presented to a private hospital in Aseer province, southwest Saudi Arabia, with a history of 3 weeks duration of abdominal pain. He did not have fever, weight loss or any other symptom. His medical history was unremarkable. On physical examination, a large mass was noted in his right iliac fossa, which was confirmed by abdominal ultrasound. He was, therefore, referred to our tertiary hospital for further evaluation and management. On a review in our institute, he looked well, with normal vital signs and average body built. He had tenderness in the right iliac fossa with a palpable mass measuring 5 × 5 cm that was firm, mobile and with no overlying skin changes. There was no organomegaly and no palpable inguinal lymph nodes. Other systemic examination was unremarkable.

The initial laboratory workup showed white blood cells 8.34 × 10³/mm³, with 45.3% neutrophils, 33.6% lymphocytes, 11.2% eosinophils and 5.3% monocytes, Haemoglobin 10.9 g/dL and platelets 485 × 10³/mm³. His erythrocyte sedimentation rate (ESR) was 48 mm/hour and test results indicated that he had normal liver function. Abdominal ultrasound showed a heterogeneous mass around the abdominal aorta measuring 7 × 3 × 3 cm with multiple enlarged lymph nodes as well as a small amount of free fluid in the pelvis (Fig. 1). A subsequent computed tomography (CT) scan of the abdomen showed several enlarged regional lymph nodes with a large mass at the right iliac fossa that resulted in significant thickening of circumferential caecal wall extending into the terminal ileum but no signs of luminal obstruction (Fig. 2). He underwent colonoscopy and was found to have a large ulcerating and fragile mass at the end of terminal ileum (Fig. 3). Because the patient was initially admitted with a suspicion of Crohn’s disease, the colonoscopic sample was sent for histopathology but not for culture. The biopsy showed granulomatous inflammation around a fungal structure that appeared as a broad, non-septated, hyphae-like structure with thin wall surrounded by eosinophilic material (Splendore–Hoeppli phenomenon) with several multi-nucleated giant cells (Fig. 4). Based on these specific histopathological features, a diagnosis of GIB was established.

**Fig. 1.** Abdominal ultrasound showed heterogeneous mass around abdominal aorta measuring 7 × 3 × 3 cm.

**Fig. 2.** Contrast-enhanced CT scan of abdomen showed a large mass of terminal ileum and caecum.

**Fig. 3.** Colonoscopy study; a mass at the end of terminal ileum fungating to the lumen and bleeding.
The patient was therefore started on oral voriconazole 150 mg twice daily. By the end of the first month of therapy, there was significant reduction in the size of the mass (half the original size), with disappearance of blood eosinophilia and normalization of ESR. During subsequent outpatient visits, the patient continued to improve and had no symptoms. Voriconazole was discontinued after 1 year following complete clinical recovery and radiological resolution of the disease. Ultrasound abdomen was repeated at 1 month with reduction in the mass size to half the original size; at 3 months, the mass disappeared and this was again confirmed at 6 months and 1 year of treatment. To date, the patient did not have recurrence of the illness or reappearance of the mass after >1 year following discontinuation of the antifungal therapy.

Discussion

GIB is a rare infection caused by the fungus *B. ranarum*, of the order Entomophthorales [19]. The pathogenesis and risk factors of GIB remain poorly understood. It is suspected that GIB is acquired through ingestion of soil, animal faeces or contaminated food. Although *B. ranarum* may be found worldwide, the GIB form of the disease has been predominately reported in Saudi Arabia, the United States and some few cases in Brazil and Iran [20]. The organism has also been found in decaying plant material, compost heaps and leaves of deciduous trees, and as intestinal carriage among lizards and other amphibians [21].

Several cases of otherwise healthy children with GIB have been reported, most often involving the colon. They either presented as obstruction or mimicking the presentation of Crohn’s disease [22]. Clinical features of GIB, in a recent review, include abdominal pain as the most common presenting symptom (84%), followed by abdominal mass (43%) and constipation (39%); fever was only present in 32% of cases [20]. The diagnosis is often suspected from the clinical presentation and the geographical origin of the patient.

Peripheral eosinophilia appears to be a prominent feature; in a review of paediatric cases by El-Shabrawi and Kamal, all had eosinophilia [23]. More recently, the review by Vikram et al. found peripheral eosinophilia in 76% of cases [20]. For definitive diagnosis, culture of *B. ranarum* is considered as the gold standard [21]. The usual histopathological findings include tissue eosinophilia and granulomatous inflammation with characteristic findings of broad, sparsely septated hyphae surrounded by eosinophilic granular material (Splendore–Hoeppli phenomenon) [3].

An optimal standardized treatment regimen for this uncommon infection has not yet been established. Most patients have received a combination of surgical and medical therapies. Of the antifungal agents, Itraconazole has been used most frequently (73%), followed by Amphotericin (22%), Ketoconazole (8%) and Voriconazole (5%) [20]. On average, an overall survival is estimated at 80% when antifungal therapy is implemented for 8 months [20]. Notably, the use of Amphotericin has been associated with several clinical failures [3, 20, 24], and susceptibility testing has confirmed Amphotericin resistance in some of these cases [20, 25]. Our patient was successfully treated by voriconazole alone without surgical resection of the mass. We chose voriconazole because of its relatively high safety profile and the ability to monitor drug level during treatment. Voriconazole is a second-generation triazole with a broad-spectrum antifungal activity. It works through the inhibition of synthesis of ergosterol, a major sterol component of the fungal cell membrane. It is available in oral and parenteral formulations. It is widely distributed throughout the body, with high concentrations obtained in the liver, kidney, lung, heart, spleen, brain and cerebrospinal fluid [26, 27].

All of the previously reported paediatric GIB cases were treated by adjuvant antifungal therapy and surgery [4–15]. To our knowledge, this is one of the very first case reports of paediatric GIB treated with oral voriconazole alone without surgical intervention and with no documented side effects related to voriconazole during or after the period of treatment. This approach with close monitoring of our patient enabled us to avoid prolonged hospitalization as well as possible surgical complications including

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**FIG. 4.** Fungal hyphae (arrow 1) and zygospores (arrow 2) of basidiobolomycosis. Note the eosinophilic amorphous material (Splendore–Hoeppli phenomenon) surrounding the fungal elements.
bleeding, secondary infection, anastomotic leak or wound dehiscence. Moreover, the case demonstrates the importance of antifungal therapy in treating this infection.

Conclusion

GIB is an emerging disease in Saudi Arabia. There are few reports from other parts of the world but most of the paediatric GIB cases were reported in the south-west part of Saudi Arabia. Diagnosis of GIB requires high index of suspicion. An increased awareness of this rare disease helps to reach an early diagnosis and initiation of treatment. In our case, voriconazole alone was effective in treating the condition with less risk of complications compared with combined antifungal therapy and surgical treatment.

References