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Case report

An unusual case of gastrointestinal basidiobolomycosis mimicking colon cancer; literature and review



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ABSTRACT

Gastrointestinal basidiobolomycosis (GIB), a rare fungal infection associated with high mortality, has been reported worldwide mainly from tropical and subtropical regions of Asia, USA, and Latin America. The clinical manifestations are highly diverse and non-specific depending on the underlying disease, but fever, abdominal pain, weight loss, diarrhea, constipation and chills have been observed. There are no prominent risk factors for GIB but climatic conditions and life style are related to this infection in arid and semi-arid regions. Therefore timely diagnosis and early treatment is a challenge. Herein, we present an unusual case of gastrointestinal basidiobolomycosis in a 54-year-old male, initially misdiagnosed as colon cancer. After follow-up, no evidence of relapse and the patient was successfully cured by liposomal amphotericin B. In addition, the differential diagnosis and histopathological findings are discussed with a review of the literature.

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1. Introduction

Basidiobolus, a member of the order basidiobolales in the family of basidiobolaceae, is encountered in human disease with infections ranging from mild sub-cutaneous lesions involving the buttocks, trunk, and limbs to systemic infections with gastrointestinal involvement [1]. *Basidiobolus ranarum* is found in dead plant material, rotten wood, soil, faeces of reptiles, insectivorous fish, and amphibians, mainly limited to tropical regions (Asia, Africa, and South America) [2–4]. The infection was first reported by Joe et al. [5] in Indonesia followed by cases from different parts of the world [6–8]. Although basidiobolomycosis mainly presents as subcutaneous lesions, gastrointestinal basidiobolomycosis (GIB) has been reported due to ingestion of soil, animal feces, and food [9–11]. The clinical

manifestations are diverse and nonspecific depending on the underlying disease, but fever, abdominal pain, weight loss, diarrhea, constipation and chills are hallmarks [10,11]. Most of the GIB cases have been misdiagnosed as inflammatory bowel disease, intestinal tuberculosis, sarcoidosis, amebiasis, malignancy or Crohn's disease [11]. GIB is well known in the Middle East, i.e., Saudi Arabia, Kuwait, Iraq and Iran [11–14]. GIB is an emerging fungal infection with around more than 100 cases reported worldwide, may lead to diagnostic confusion, and patient morbidity and mortality. Herein, we present an Iranian case of gastrointestinal basidiobolomycosis in a 54-year-old male that was initially misdiagnosed as an abdominal malignancy.

2. Case report

A 54-year-old male was admitted to a regional hospital in Kazerun, Fars Province, Iran, complaining of a painless abdominal

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mass in the right lower quadrant (RLQ). The patient had no fever, chills, pain, or gastrointestinal symptoms. He was not taking medication and he did not have any history of trauma. He was addicted to opium and cigarette abuse and experienced weight loss (4–5 kg) in a two-month-period. Initially, the abdominal mass was surgically resected elsewhere and after 10 days, the mass reappeared. After one week, he was transferred to the tertiary care Al-Zahra hospital in Isfahan, Iran. Peripheral blood counts and red blood cell indices indicated mild anemia, anisocytosis, leukocytosis ($16 \times 10^3/\text{mm}^3$; neutrophils: 60% and eosinophils: 15%), and thrombocytosis ($475 \times 10^3/\text{mm}^3$). Erythrocyte sedimentation rate (ESR) in the first 1 hr was 50 mm. An abdominal CT scan with contrast showed a soft tissue lesion of $58 \times 59 \times 21$ mm in the RLQ extending into the anterior wall of the caecum and abdominal wall muscles. The differential diagnosis included fungal infection or a malignant process (Fig. 1A-B). The retroperitoneal mass, two iliac lymph nodes, and a piece of small intestine were resected (Fig. 1C). The histopathologic findings showed granulation tissue with mixed inflammatory cells including giant cells (Fig. 2A), deep vein thrombosis (DVT) (Fig. 2B) and broad, non-septated, hyphae-like structures surrounded by an eosinophilic sheath, the so-called Splendore-Hoeppli phenomenon (Fig. 2A-B). The tissue samples were inoculated onto Sabouraud's dextrose agar (SDA; Difco), and SDA supplemented with chloramphenicol ($50 \mu\text{g}/\text{ml}$) and incubated at both 25°C and 30°C in the dark, but culture was negative. Ribbon-like aseptated hyphae were seen in direct microscopy (Fig. 1D). Immunohistochemical investigations were negative for CK, CD3, and CD20 markers suggesting no evidence of a malignant process. Postoperatively, the tentative diagnosis of *Basidiobolus* species was made and the patient was treated with liposomal amphotericin B (AmBisome) ($5 \text{ mg}/\text{kg}/\text{day}$) for 55 days, and finally the patient was discharged with a regimen of posaconazole oral solution ($10 \text{ ml}/12 \text{ h}$) for two months. He was discharged and after a follow up of 3 months, the patient was cured

without evidence of relapse. Publication of this case was approved by the ethics committee of Isfahan University of Medical Science and written informed consent was obtained from the patient.

3. Discussion

Previously *Basidiobolus* was classified as *B. ranarum*, *B. haptosporus*, and *B. meristosporus*, however recent taxonomic classifications based on isoenzyme banding, antigenic analysis, and analysis of rDNA reveal that all human pathogens belong to *B. ranarum* [15–18]. *B. ranarum* is a saprophyte in dead plant material, vegetations and soil, and is also isolated from several species of reptiles and amphibians [2,18]. The review process involved study of existing English literature of all reported cases with gastrointestinal basidiobolomycosis using Medline database through PubMed, Embase through Scopus, ISI Web of Science, Science Direct and Google Scholar between 1997 and 2018. Although GIB is a rare infection, more than 100 cases of GIB due *Basidiobolus* species have been reported in the English language literature, i.e., Asia [3,15,19], USA [20], and Latin America [21]. So far, the majority of cases have been reported from the Middle East. Interestingly, Saudi Arabia ($n=62$) and Iran ($n=24$) had the majority of cases (Fig. 3) followed by USA ($n=21$) and Iraq ($n=6$) [11,14,19,22–64]. Although, the risk factors of GIB are poorly understood, climatic conditions and life style are related to this infection in arid and semi-arid regions. Most of the cases in the USA were reported from Arizona, a state with a hot and dry climate similar to the Middle Eastern climate. Therefore, understanding of factors that contribute to disease in various local climatic conditions may aid in identifying sources of infection and epidemiology [20,61].

In contrast to the present case, infections often occur in children with most cases of the disease reported in male children. The latter may be due to habits like lying on the ground, playing with

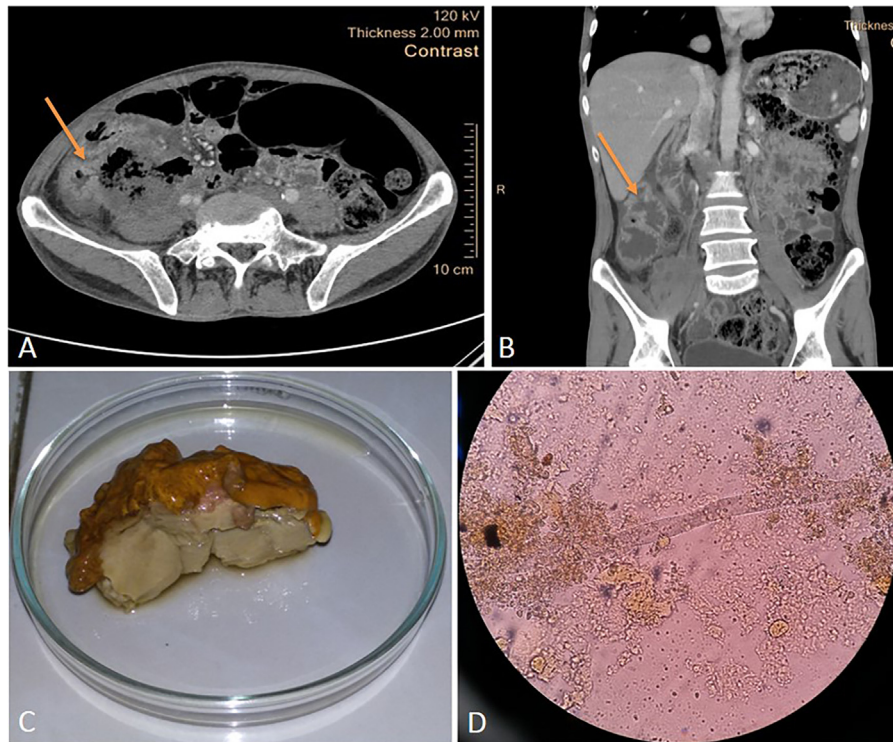


Fig. 1. A-B. Abdominopelvic C.T scan with contrast showed (arrow) a soft tissue lesion of $58 \times 59 \times 21$ mm in the right lower quadrant (RLQ) with extension into the anterior wall of the caecum and Rt abdominal wall muscle. C. Segments of the intestine showing diffuse thickening of the wall. D. Direct microscopic examination showing aseptated hyphae.

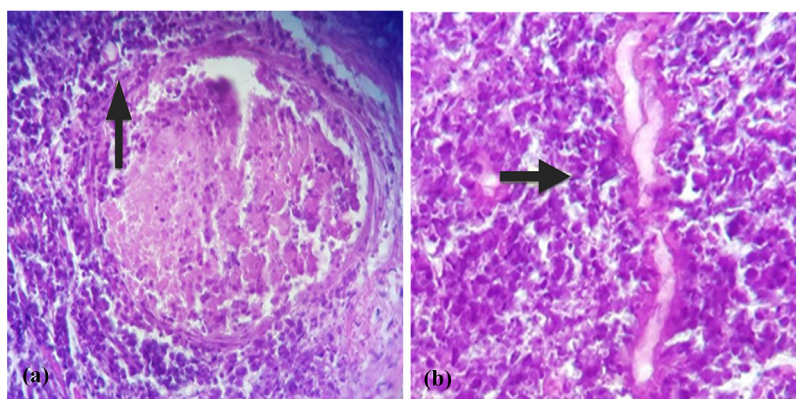


Fig. 2. A-B. The pathologic findings revealed granulation tissue with mixed inflammatory cells including giant cells, deep venous thrombosis and broad, non-septated, hyphae-like structures surrounded by an eosinophilic sheath, the so-called Splendore–Hoepli phenomenon (Periodic acid–Schiff \times 400).

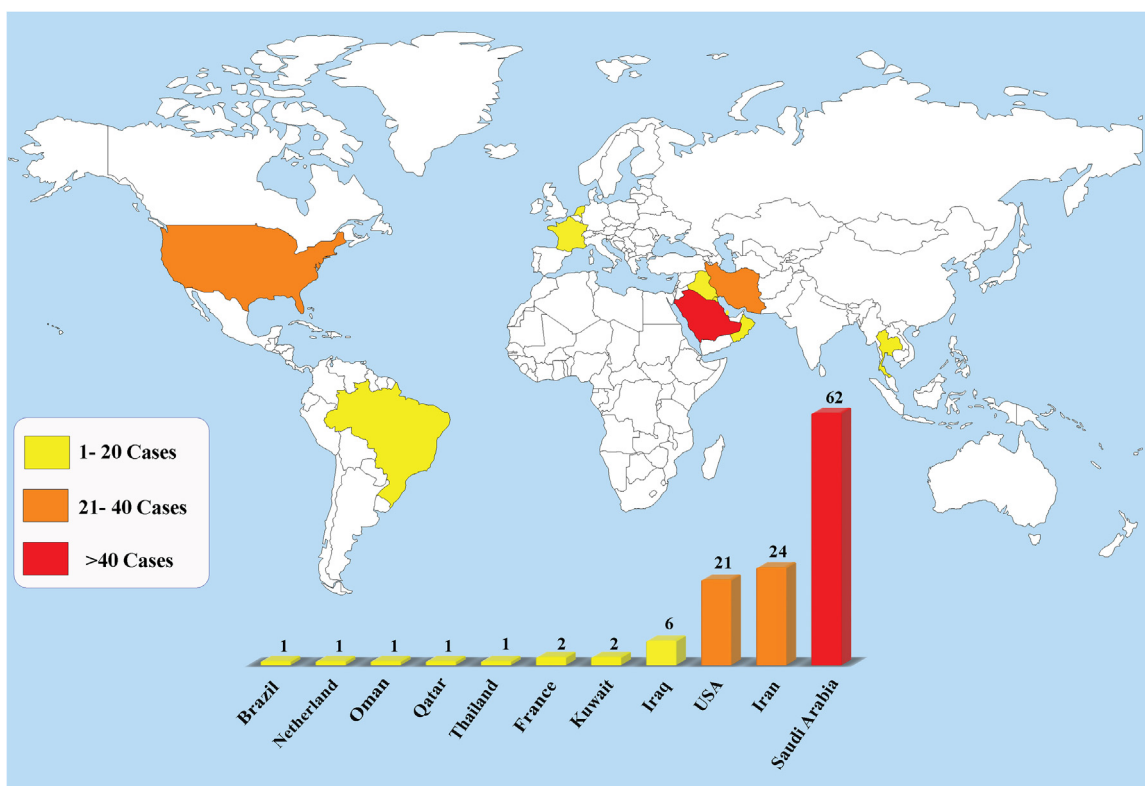


Fig. 3. Distribution and number of reported cases of gastrointestinal basidiobolomycosis due to *Basidiobolus* species in the world.

decaying plants, and the use of leaves as toilet papers [62]. The occupation of the current case was food provider for livestock and he handled large amounts of dried grass daily. In addition there appears to be a relation between GIB, smoking and ranitidine consumption [20]. Remarkably, ranitidine may contribute to GIB by lowering stomach acidity and allowing the fungus to survive [20,63]. Smoking unfavorably influences mucosal WBC function [14]. Our patient was addicted to opium use and cigarette smoking. Several studies reported that cases of GIB were initially diagnosed as inflammatory disease, suggesting that GIB should be kept in the differential diagnosis of inflammatory bowel diseases of the GI tract [3,17,22,23]. Although it is supposed that traumatic implantation with contaminated vegetable matter plays an important role in initiating the infection, fungal spores can also

be transmitted by insect bites in sub-cutaneous basidiobolomycosis [17].

Microbiologic cultivation of the fungus is the gold standard for diagnosis; however most reported cases are diagnosed based on histopathology of the removed tissues showing the Splendore–Hoepli phenomenon. This phenomenon refers to radiating or annular amorphous eosinophilic deposits of host-derived materials and possibly of fungal antigens. The Splendore–Hoepli phenomenon has also been reported in association with cases of botryomycosis, actinomycosis, aspergillosis, and sporotrichosis [3]. Abdominal masses associated with colon or liver and focal bowel wall thickening are most commonly reported abdominal imaging findings in GIB worldwide. Most reports confuse GIB with inflammatory bowel disease or malignancy. [65].

Although, molecular approaches, i.e., sequencing of ITS rDNA and 18S small-subunit rDNA are powerful tools to identify entomophthorean fungi in infected tissues of putative cases of conidiobolomycosis or basidiobolomycosis, confirmation relies currently on histological examination and cultural methods (considered as the “gold-standard”). El-Shabrawi et al. used taxon-specific primer pairs Ba1–Ba2, specific for the genus *Basidiobolus*. In addition, Rose et al. amplified and sequenced the ITS-4 region of the ribosomal RNA gene of *B. ranarum* in infected tissues of their patients. Therefore, molecular approaches along with histopathology features of infected tissue may be useful to diagnose patients in endemic areas [4,17,23,66].

Geramizadeh et al. [19] reported 14 cases of GIB in Iran over a period of 10 years and all were diagnosed by histopathology (Splendore-Hoeppli phenomenon) similar to our case and most of the previous reports in the world. Neutrophilic infiltration is a rare phenomenon but eosinophilic inflammation assists in the differentiation between basidiobolomycosis and mucormycosis, the latter being generally characterized by vascular invasion with thrombosis and neutrophilic infiltration.

The optimal choice of antifungal agent for this uncommon fungal infection is not clear, but resection of the affected bowel, followed by prolonged systemic antifungal therapy, i.e., amphotericin B, itraconazole and voriconazole were successfully in many reports [22,23,41].

4. Summary

There are no prominent risk factors for GIB although climatic conditions and life style are related to this infection in arid and semi arid regions. Interestingly, most of the previous Iranian case reports of GIB came from the South, which has a warm and humid climate. This suggests that weather conditions may influence infection rates. GIB has also been commonly reported in the Middle East especially in Saudi Arabia, which has similar climate conditions as found in Southern Iran. Understanding the factors that contribute to disease in various local climatic conditions may aid in identifying sources of infection and epidemiology. We highlight the importance of consciousness and early recognition of a rare fungal infection to prevent unnecessary surgical intervention, chemotherapy, and probably less morbidity.

Disclosure of interest

The authors declare that they have no competing interest.

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