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Gastrointestinal basidiobolomycosis: Beware of the great masquerade a case report

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ABSTRACT

Basidiobolomycosis is rare infection caused by the saprophytic fungus *Basidiobolus ranarum*. Gastrointestinal basidiobolomycosis is an infrequent, albeit, increasingly reported, emerging form of the disease and typically affects immunocompetent individuals with potentially grave sequelae if unrecognized. Acquaintance with this exceptionally rare fungus and its potential for presenting as gastrointestinal mass masquerading as colonic malignancy is critical for timely diagnosis, appropriate treatment and successful clinical outcome.

We report a case of gastrointestinal basidiobolomycosis masquerading as colonic malignancy in a 29-year-old Omani patient successfully treated with combination of surgery and prolonged azole antifungal therapy.

Introduction

Basidiobolomycosis is a rare infection caused by the saprophytic fungus *Basidiobolus ranarum* of the Zygomycetes family [1]. The disease typically affects the skin and subcutaneous tissue [2]. Gastrointestinal basidiobolomycosis (GIB) is a newly recognized emerging and rare form of the disease with 122 cases reported worldwide as of 2018 [3] of which 46 cases reported in adults [4,5]. GIB is most commonly reported in the tropical and subtropical areas despite the worldwide distribution of *Basidiobolus ranarum* [6] with most of the reported cases occurring in men [7] from the arid regions of the United States (mainly Arizona) and from Middle East [8]. It is unclear how *Basidiobolus ranarum* gains access to the host's gastrointestinal tract. It is hypothesized that ingestion of food contaminated by the fungus from soil or animal excreta is the most likely route of infection in GIB [9].

In a recent review of 102 cases of GIB, abdominal pain (86.3%) was the most common presenting symptom followed by weight loss (33.3%), abdominal distension (16.7%), vomiting (15.7%) and diarrhea (13.7%) with fever reported in 40.2% of patients and an abdominal mass was palpable in 30.4% of cases [10]. GIB most commonly involves the right colon [11] and frequently presents as abdominal mass mimicking colonic malignancy and inflammatory bowel disease [6]. Common laboratory findings in patients with GIB are neutrophilic leucocytosis, eosinophilia and a high ESR [8].

Diagnosis of basidiobolomycosis requires culture of *Basidiobolus ranarum* from tissue. When culture is not available, a plausible diagnosis can be made based on characteristic histopathology [12].

In most cases of GIB, the diagnosis is only established postoperatively with characteristic histopathological findings including mixed suppurative and granulomatous inflammation, prominent eosinophilic infiltrates, presence of degenerate thin-walled broad hyphae surrounded by eosinophilic amorphous material referred to as Splendore–Hoeppli phenomena [13]. Optimum management of GIB comprises combination of early and aggressive surgery with appropriate antifungal therapy [10]. Mortality from GIB is unacceptably high with rates reaching 16% if untreated [3].

We describe a case of gastrointestinal basidiobolomycosis masquerading as colonic malignancy in a previously healthy young Omani patient. A diagnosis of GIB was made five weeks postoperatively as part of the evaluation of recurrence of abdominal mass and review of the histopathology at the referral hospital. He was then successfully treated with prolonged azole antifungal therapy resulting in clinical cure.

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Case presentation

A 29-year-old previously healthy Omani truck driver in a road construction business presented to a local hospital with a two-month history of a painful right lower abdominal mass, fever, anorexia, constipation, and 10 kg weight loss. A complex "malignant looking" obstructing mass encasing the terminal ileum and the cecum was demonstrated on a computed tomography (CT) of the abdomen. He underwent an exploratory laparotomy which revealed an obstructive, ulcerative inflammatory mass enclosing the terminal ileum, the cecum, and the appendix. A cecectomy and appendectomy with end-end anastomosis was performed resulting in rapid and complete resolution of patient symptoms. Subsequently, microscopic examination of excised surgical tissues was interpreted as consistent with inflammatory bowel disease and possibly eosinophilic colitis with no evidence of malignancy. Five weeks later, patient symptoms recurred with reappearance of a painful right lower abdominal mass, diarrhea, nausea and vomiting. He was then referred to this hospital for further management.

Physical examination showed a conscious, emaciated and ill-looking patient with pallor and signs of dehydration. He was afebrile but tachycardic (pulse rate: 113/min) and mildly tachypneic (respiratory rate: 19/min) with oxygen saturation of 100% (room air). Blood pressure was 123/60 mmHg. Examination of the abdomen revealed a non-distended abdomen with midline laparotomy scar and a tender 8 cm × 5 cm hard mass in the right iliac fossa with no peritoneal irritation signs. Bowel sounds were present and digital rectal examination was normal. Rest of the examination was normal.

Initial laboratory investigations showed a hemoglobin of 10.3 g/dL, a total white cell count of 18,000 cells/μL with an eosinophil count of 32,000 cells/μL. Erythrocyte sedimentation rate (ESR) was 129 mm/h. Biochemistry panel was normal.

Axial contrast-enhanced computed tomography (CECT) of the abdomen revealed a complex mass in the right iliac fossa involving the ileal loops and measuring8 cm × 8.4 cm × 6.3 cm (Fig. 1). An esophagogastroduodenoscopy and colonoscopy revealed multiple small/superficial duodenal ulcers and multiple ulcerations at end-end anastomosis respectively. Tissue blocks and slides of the excised surgical specimens (ileum, cecum, and appendix) were obtained from the referring hospital and were re-examined (Fig. 2).

The histopathological conclusions were characteristic of and consistent with gastrointestinal basidiobolomycosis. Due to inability to take orally and unavailability of intravenous formulation of itraconazole, treatment with intravenous voriconazole was initiated (two loading doses of 6 mg/kg every 12 h followed by 4 mg/kg every 12 h) and continued for a week prior to switch to oral itraconazole (capsules) 400 mg daily. A month later, the patient experienced marked symptomatic improvement with noticeable reduction in the size of the right iliac fossa mass. By four months of antifungal therapy, the patient was asymptomatic, the right iliac fossa mass has resolved, the eosinophilia and the ESR had normalized (eosinophil count: 300 cells/μL, ESR: 10 mm/hr). Meanwhile itraconazole was switched to oral voriconazole (4 mg/kg every 12 h) due to intolerance. Two months later, he presented with small bowel obstruction attributed to extensive adhesions from previous surgery necessitating resection of 30 cm segment of diseased small bowel with ileo-ileal and ileocolic anastomoses. Histopathological examination of the resected small bowel showed no evidence of basidiobolomycosis. The patient was discharged two weeks later after he made a full recovery. He was continued on oral voriconazole for an additional four months thus completing a total of ten months of antifungal therapy (four months of itraconazole and six months of voriconazole). He remained symptom-free three years later with no clinical or radiological evidence of disease recurrence.

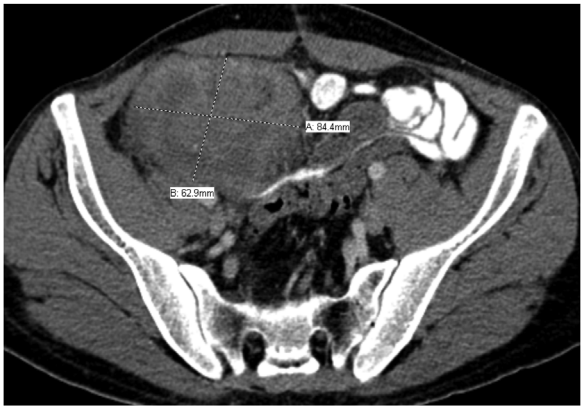

Fig. 1. Contrast-enhanced computed tomography (CECT) of the abdomen.
A complex mass in the right iliac fossa involving the ileal loops and looks separate from the ascending colon. It measures 8 cm × 8.4 cm × 6.3 cm.

Discussion

To best of our knowledge, this is the second reported case of GIB from Oman [14] and the first in an adult patient suggesting that the disease is possibly under-recognized.

Diagnosis of GIB is challenging owing to its non-specific clinical presentation and rarity. A recent review of 102 cases of GIB found that initial misdiagnosis as neoplasm and inflammatory bowel disease was made in two thirds of patients [10]. Similarly, this patient was initially assumed to have a malignant neoplasm of the colon based on clinical and radiological findings and was later thought to have inflammatory bowel disease or eosinophilic colitis based on initial histopathological interpretations of the surgical specimens. Both presumptions proved to be incorrect.

Peripheral eosinophilia [10], neutrophilic leukocytosis [8], extremely elevated ESR [8], and abdominal mass-albeit nonspecific- [6] are common findings in patients with GIB and should raise suspicion for the disease in this young individual on presentation. However, due to extreme scarcity of this condition and unfamiliarity among clinicians, the diagnosis was not considered preoperatively. This is a no not an exception from the literature where most of the diagnoses are typically made postoperatively [13]. In this patient, postoperative histopathological findings were erroneously interpreted likely due to unfamiliarity of many pathologists with this clinical entity. In our case, it takes an astute and experienced pathologist who is familiar with histopathological findings in GIB to correctly identify the pathology, hence establishing the diagnosis.

This patient did not have a tissue culture (gold standard for confirming the diagnosis of GIB). However, the histopathology was distinctive enough with demonstration of broad and thin walled hyphae consistent with *basidiobolus* on a background of dense eosinophilic infiltrate with the characteristic-albeit non pathognomonic- Splendore-hoeppli phenomenon [15]. This in accordance with most of the previous case reports of GIB where the diagnosis was made based on histopathological findings alone [8].

Although surgical resection of the inflammatory mass combined with antifungal therapy is considered standard for treatment of GIB, successful outcome with antifungal treatment alone is well described [10] with azoles being the most preferred antifungals of which itraconazole is most desirable agent [5]. Recently, voriconazole has also been used with success [16]. The patient presented here had surgical resection of the inflammatory mass before recognizing it as GIB. He therefore did not receive antifungal therapy until his second presentation with recurrence five weeks

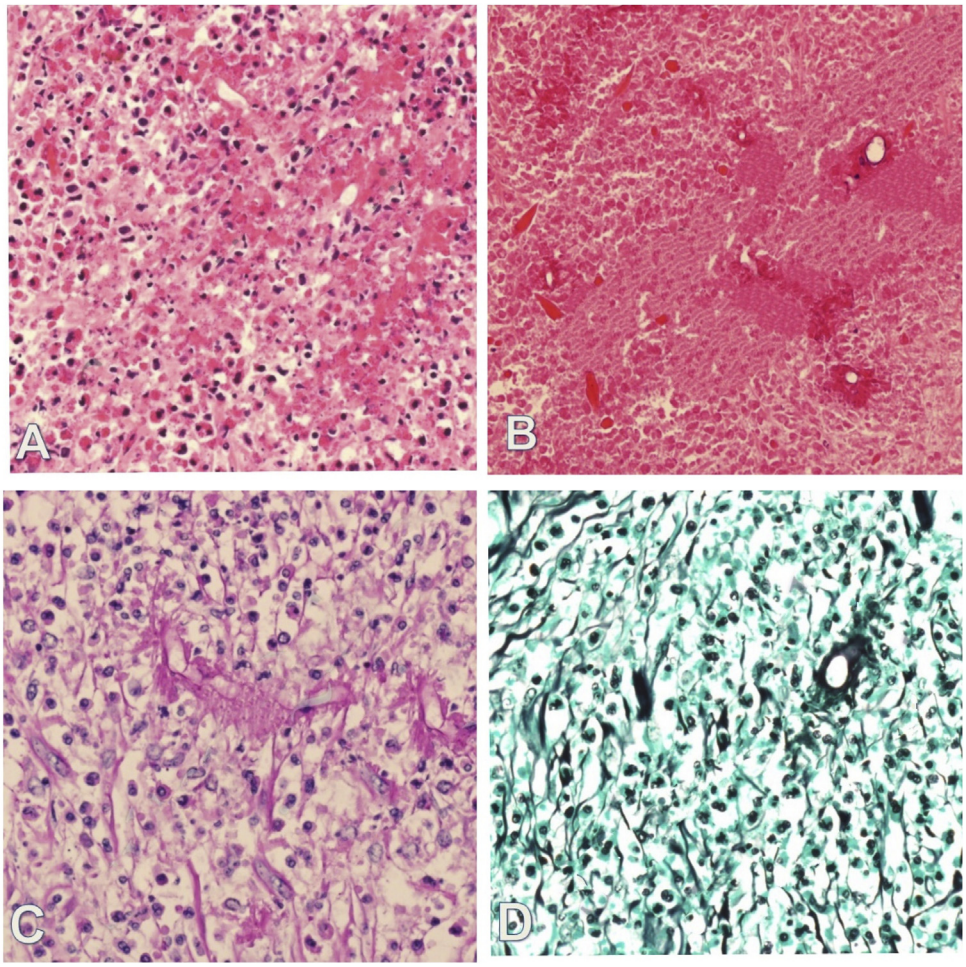

Fig. 2. (A–D): Histopathologic section of cecum.
A: Multiple areas of mucosal ulceration, transmural dense inflammatory infiltrate dominated by eosinophils with multiple micro and macro abscesses with thin walled hyphae surrounded by a bright eosinophilic hyaline material radiating out into the surrounding infiltrate creating the Splendore–Hoeppli phenomena. (H&E x600). **B:** Coagulative necrosis in the wall of the cecum with fungal hyphae of Basidiobolus with the Splendore–Hoeppli phenomena. (H&E x400). **C** and **D:** Numerous broad and thin walled hyphae with occasional septations demonstrated with Periodic Acid Schiff stain (PAS x600) and with Gomorrhi's Methenamine-Silver stain (GMS x 600).

later. He was then managed with antifungals without surgical intervention resulting in complete cure. Duration of antifungal therapy in GIB is presently unidentified with most experts recommending a minimum of six months post-surgical resection to minimize risk of relapse [7,10]. This patient received ten months of antifungal therapy (four months of itraconazole followed by six months of voriconazole due to intolerance to itraconazole). This length of therapy was guided by clinical and radiological responses.

Finally, the route of acquisition of *Basidiobolus ranarum* resulting in gastrointestinal disease in this patient remains elusive. We hypothesize that his occupation as a truck driver in a road construction company in arid areas of Oman may have exposed him inadvertently to this saprophytic fungus from soil or decaying plants resulting in this infection.

GIB rarity combined with its broad symptomatology and potential for clinical mimicry of more common clinical entities make its early recognition exceedingly challenging. Without a high index of clinical suspicion and clinician familiarity, GIB will continue to be a missed diagnosis with potentially grave consequences.

Patient consent

Patient consent was obtained for publication.

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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First/corresponding author was responsible for the writing and revising the manuscript, second author contributed to the first draft of the manuscript, and all authors contributed to the clinical care of the patient and to the revision of several drafts before submission.

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