

## Gastrointestinal basidiobolomycosis: mimicking Crohn's disease case report and review of the literature

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Ann Saudi Med 2013; 33(5): 500-504

DOI: 10.5144/0256-4947.2013.500

Gastrointestinal basidiobolomycosis (GIB) is an unusual fungal infection that manifests in the skin and rarely involves other systems. All of the few cases of GIB reported so far were diagnosed with difficulty, necessitating laparotomy and resection of the inflamed part of the bowel. We report a child with GIB who was successfully diagnosed endoscopically without surgical intervention.

**G**astrointestinal basidiobolomycosis (GIB) is a rare fungal infection with a few cases reported all over the world. However, all the cases were diagnosed with difficulty, necessitating laparotomy and resection of the inflamed part of the bowel.

### CASE

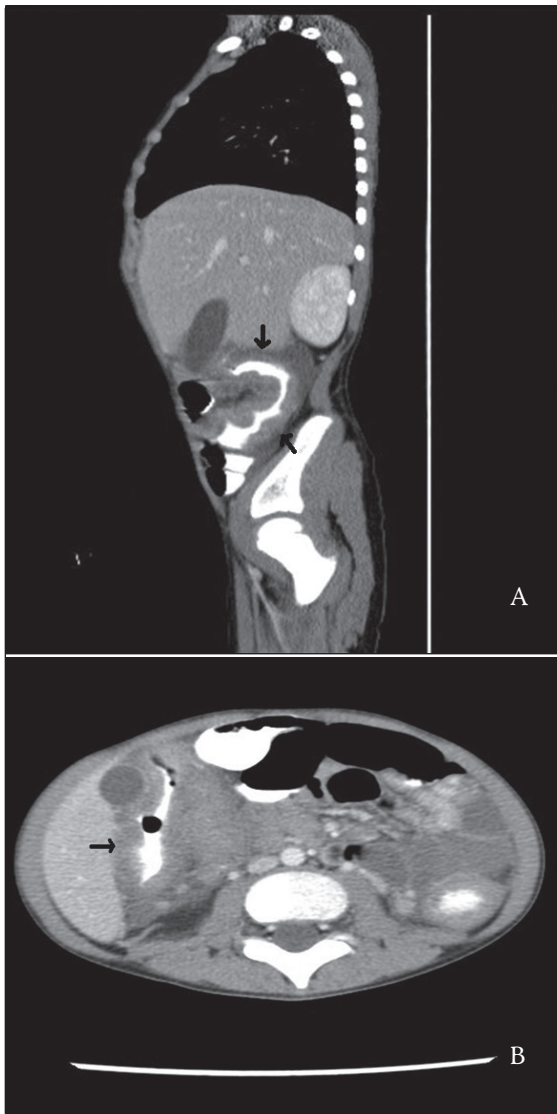
A 5-year-old Saudi boy was referred from Jizan (a city in the southern province of Saudi Arabia) with a 1-month history of abdominal pain, which was described as recurrent colicky pain, limiting the child's activity and waking him from sleep. The pain was associated with bloody mucoid stool 5 times per day, fever, decreased appetite, and weight loss. There was no history of vomiting, recurrent infections, or contact with sick patients or animals. The patient was examined at the beginning of his illness at a local dispensary and was diagnosed as gastroenteritis. However, the child did not respond to the conventional treatment, so he was referred to the local hospital. The initial investigation included a computed tomographic (CT) scan of abdomen that showed right colonic wall thickening and adjacent mildly enhancing lymph nodes. The medical history was unremarkable. No family history of immunodeficiency diseases was reported. His paternal cousin was diagnosed with Crohn disease at the age of 23 years.

On physical examination, the child looked ill, he was in pain, his vital signs were normal, his growth param-

eters were within normal for age and no lymphadenopathy or oral ulcer was observed.

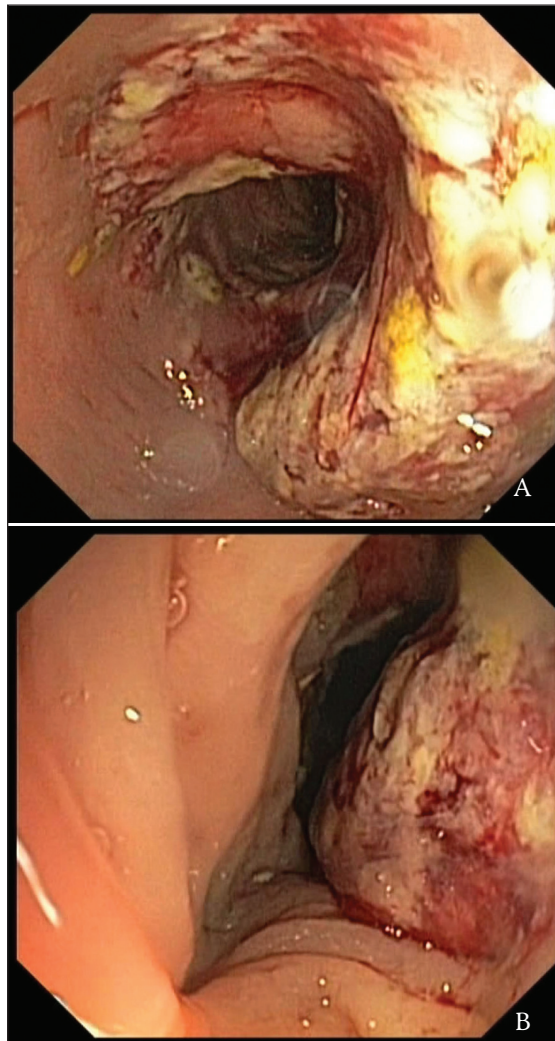
The abdominal examination revealed generalized tenderness in the right hypochondrium with guarding, organomegaly were not observed. Bowel sounds were positive. The rectal examination was normal. The systemic examination was unremarkable. The child was investigated thoroughly. Complete blood count showed mild leukocytosis with a white blood cell count of 15 600 showing marked eosinophilia (15%) absolute eosinophil count 2340/ $\mu$ L. He suffered from hypochromic microcytic anemia with a high platelet count (690 000) and high erythrocyte sedimentation rate (ESR; 69 mm/h). His renal profile, bone profile, and hepatic profile were normal. The stool for occult blood was positive, whereas the stool for ova and parasite was negative (3 times, stool cultures were negative). Immunological workups including immunoglobulin levels and nitroblue tetrazolium test were normal. The abdominal ultrasound showed enlarged mesenteric and para-aortic lymph nodes. The CT scan of abdomen (**Figure 1**) showed marked thickening of the right-sided colon and cecum up to the hepatic flexure (the thickness was around 1 cm), inflammatory fat stranding, edema, mild intraperitoneal fluid, and regional enlarged lymph node.

The patient underwent upper gastrointestinal (GI) endoscopy, which was normal. He also underwent colonoscopy (**Figure 2**), which showed 3 skip lesions



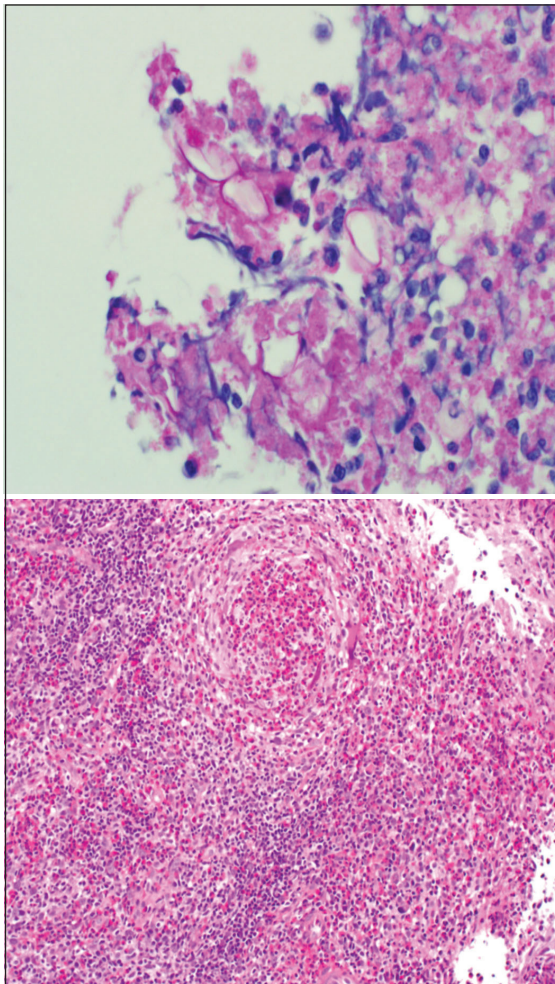
**Figure 1.** CT abdomen showed marked thickening of the right-sided colon and cecum up to the hepatic flexure; the thickness was around one cm, inflammatory fat stranding plus edema and mild intraperitoneal fluid and regional enlarged lymph node.

as follows: the first lesion was in the ascending colon and associated with the narrowing of the lumen, the second was in the transverse colon, and the third was in the descending colon. The lesions looked inflamed and red with necrotic tissue fungating into the lumen, and the mucosa in between the lesions looked normal. The histopathologic findings (Figure 3) showed marked active colitis with ulceration. The acute inflammatory cells exclusively composed of eosinophils with eosinophilic cryptitis and crypt abscesses. A single granuloma was identified. No chronic glandular destruction was observed. Rare fungal hyphae ringed by eosinophilic



**Figure 2.** A) Colonoscopy which showed three skip lesions, the 1st was in the ascending colon and associated with narrowing of the lumen, the 2nd was in the transverse colon and the 3rd was in the descending colon. The lesions looked inflamed and red, with necrotic tissue, fungating into the lumen, and the mucosa in between the lesions looked normal (127×73 mm). B) Colonoscopy which showed three skip lesions, the 1st was in the ascending colon and associated with narrowing of the lumen, the 2nd was in the transverse colon and the 3rd was in the descending colon. The lesions looked inflamed and red, with necrotic tissue, fungating into the lumen, and the mucosa in between the lesions looked normal (127×73 mm).

deposits (Splendore–Hoepli phenomenon) were seen. No acid fast bacilli or viral cytopathic changes were identified. The cultures of tissue samples for fungus, tuberculosis (TB), and bacteria were all negative. The multiple biopsies from the colon showed the same findings. There was extensive expansion of the lamina propria by chronic inflammatory cells, which mainly included lymphocytes and plasma cells and



**Figure 3.** The histopathologic findings were marked active colitis with ulceration. The acute inflammatory cells are almost exclusively composed of eosinophils with eosinophilic cryptitis and crypt abscesses. A single granuloma was identified. There was no chronic glandular destruction identified. Rare fungal hyphae ringed by eosinophilic deposits (Splendore-Hoeppli phenomenon) was identified. No acid fast bacilli or viral cytopathic changes identified. Culture of tissue samples for fungal, TB and bacteria were all negative.

also included extensive eosinophilic infiltrate. Multiple granulomas with a central sheath of eosinophilia were noticed. The eosinophilic sheath surrounded the centrally located rare fungal hyphae, a phenomenon known as the Splendore–Hoeppli phenomenon. In addition, the architecture of the colonic crypts and glands were distorted with the presence of chronic active inflammation. Periodic acid–Schiff with diastase stain treatment highlighted the fungal microorganism that was surrounded with a large number of eosinophils. No acid fast bacilli or viral cytopathic changes could be seen.

The patient was diagnosed with GIB on the basis

of histopathologic findings. He was started on oral Voriconazole with a dose of 7 mg/kg every 12 hours (100 mg PO BID) and showed excellent response. The fever subsided within 3 days and abdominal pain resolved.

During the outpatient follow-up, the child remained asymptomatic, gaining weight. Repeated abdominal ultrasound showed the resolution of abdominal masses. Four months later, colonoscopy was repeated, which showed a complete resolution of the previously noted lesions. The child was continued on Voriconazole, 100 mg PO BID, for a total of 6 months.

### DISCUSSION

Basidiobolomycosis is an unusual fungal infection that manifests in the skin and rarely involves other systems including the GI tract. Basidiobolomycosis is caused by *Basidiobolus ranarum*, an environmental saprophyte found worldwide. *B. ranarum* causes infection in immunocompromised hosts, and is an opportunistic pathogen in immunocompetent hosts.<sup>1</sup> The disease can cause significant morbidity and mortality if not early diagnosed and promptly treated. Basidiobolus infection can result in subcutaneous infections, and *B. ranarum* is a known cause of subcutaneous zygomycosis.<sup>1-3</sup> Most cases have been reported from tropical and subtropical regions.<sup>4-6</sup>

The first recognized human case of infection caused by *B. ranarum* was one of subcutaneous mycoses reported in 1956 in Indonesia,<sup>7</sup> and other cases subsequently occurred in India,<sup>8</sup> Africa,<sup>9</sup> and South America.<sup>10</sup> In 1978, the first culture proved the case of invasive basidiobolomycosis of the maxillary sinus and the palate and was reported in the United States.<sup>11</sup> In 1980, the first documented case of GIB occurred in a 4-year-old Brazilian boy.<sup>12</sup>

GIB has been reported worldwide. The number of published pediatric cases has increased (2 cases from Brazil,<sup>10,12</sup> 1 case from Nigeria,<sup>13</sup> 1 case from Iran,<sup>14</sup> and 7 cases from Saudi Arabia<sup>15,16</sup>).

Most of the cases were reported from tropical areas where the climate was warm and humid; such a climate enhances the growth of the fungus, suggesting environmental contamination. It is unclear how the fungus is introduced into the host's GI tract; however, this probably occurs through the ingestion of contaminated soil, animal feces, or food.<sup>14</sup>

The onset of GIB is usually insidious. In one of the studies, all patients had abdominal pain and fever as presenting symptoms.<sup>15</sup> The presence of abdominal mass necessitated laparotomy, leading to GIB diagnosis. Diarrhea, tenesmus, and bloody mucoid stool were



noted in our patients. Patients had also presented the picture of bowel obstruction. GIB may present a similar picture as inflammatory bowel disease;<sup>17,18</sup> in such cases the patients do not respond to conventional treatment, necessitating the consideration of other diagnosis, such as GIB, especially in tropical areas.

The main differential diagnosis of GIB with granuloma includes inflammatory bowel disease, intestinal TB, sarcoidosis, amebiasis, and malignancy.<sup>19</sup>

The diagnosis of GIB is always confusing and requires a high index of suspicion.<sup>15</sup> So far, there is no well-identified risk factor. However, the diagnosis might be suspected in the previously healthy children, especially those living in, or near, tropical areas who develop symptoms that may suggest the diagnosis, or cases that mimic inflammatory bowel disease (IBD), especially Crohn's disease, but not typically fit the diagnosis, i.e. abdominal mass, high peripheral eosinophilia.

To our knowledge all the reported cases were diagnosed based on histologic findings of the resected masses through laparotomy. However, our case was diagnosed endoscopically, and surgical intervention was avoided. The endoscopic finding in our case was 3 skip lesions identified in the ascending, transverse, and descending colon. The gross appearance was fungating, inflamed, friable mucosa covered with necrotic tissue—which easily bleeds on touch—with totally healthy colonic mucosa in between the lesions. Leukocytosis, marked eosinophilia, and high ESR are frequently reported from GIB cases.

Ultrasound may show enlarged mesenteric, para-aortic lymph nodes. In the CT scan of the abdomen the most frequently encountered pattern is marked concentric colonic wall thickening with a polypoid mass simulating inflammatory and granulomatous diseases (**Figure 3**). Perivisceral inflammation, fistulization, perforation, and abscess formation may be present and mimic Crohn's disease.<sup>20</sup>

In the suspected cases of GIB, samples should be sent for fungal stain and culture. *B ranarum* can be isolated from surgical specimens; however, media should be inoculated soon after resection because *B ranarum* does not survive at 4°C. Sabouraud agar is an adequate medium for the growth of *B ranarum*, and a visible growth is usually present 3 to 4 days after inoculation at 25–30°C. Colonies appear white or pale gray and have

radial folds.<sup>4</sup> A silver stain of surgically resected specimens will show fungal elements that appear as broad, pleomorphic, sparsely septated hyphae, the walls of which stain faintly with fungal preparations (grocott's methenamine silver stain or periodic acid-schiff stain).<sup>4</sup>

The histological features of GIB include transmural granulomatous inflammation composed of abundant eosinophils, lymphocytes, histiocytes, and giant cells. Histochemical stains revealed broad, non-septate, hyphae-like structures surrounded by an eosinophilic sheath (Splendore–Hoepli phenomenon). This morphologically unique phenomenon of eosinophilic material found around infectious agents was first described in sporotrichosis by Splendore and in schistosomiasis by Hoepli.<sup>21</sup>

The appropriate treatment of GIB has not been outlined. In most reported cases of GIB treatment is instituted using oral itraconazole.<sup>13,14</sup> Potassium iodide has been used with success in the treatment of subcutaneous basidiobolomycosis; however Nazir et al reported a case of invasive retroperitoneal infection due to *B ranarum* with response to potassium iodide.<sup>22</sup>

From the reported cases, it was found that surgical intervention combined with prolonged medical therapy was used for the treatment of GIB;<sup>14</sup> however, in our case surgical intervention was avoided and the patient showed excellent response to oral Voriconazole. Whether surgical intervention is needed or not depends on the nature of the disease, its location, extension, and the patient's condition.

## CONCLUSION

GIB is an emerging infection and needs high index of suspicion to reach the diagnosis. It may lead to significant morbidity and mortality if not early diagnosed and promptly treated. Considering GIB in the differential diagnosis of abdominal mass with eosinophilia, or cases that mimic IBD but do not fit the diagnosis, may help reach an early diagnosis and early initiation of medical therapy. In suspected cases, an endoscopic diagnosis—obtaining specimens for fungal culture and histopathologic examination with special fungal stains—is a better less-risk procedure and may help avoid surgical intervention. GIB showed a good response to antifungal therapy; however, it needs extended courses of treatment.

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