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SHORT REPORT

Gastrointestinal basidiobolomycosis in a child; an unusual fungal infection mimicking fistulising Crohn's disease

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Abstract

Background: Gastrointestinal basidiobolomycosis is a rare disease caused by the fungus *Basidiobolus ranarum*. It has been reported in both children and adults. The disease mainly affects the colon and the small bowel; however, cases of the stomach, liver, pancreas, and renal system being affected have been reported.
Case report: A 2 year old boy presented with the following symptoms; abdominal pain, vomiting, diarrhea, fever and palpable right iliac fossa mass. Laboratory investigations revealed elevated inflammatory markers and peripheral eosinophilia. Colonoscopy showed severely inflamed mucosa of the terminal ileum, cecum and ascending colon. CT scan of the abdomen demonstrated an inflammatory mass with wall thickening of the terminal ileum and the colon. Surgical exploration demonstrated retroperitoneal mass and inflamed terminal ileum, cecum and ascending colon. Upon laparotomy, multiple internal fistulas involving the bowel loops, the urinary bladder, the right ureter and the gallbladder were observed. Further investigations using histopathology of the resected diseased bowel showed extensive necrosis, multinucleated giant cells and numerous eosinophils and large fungal hyphae surrounded by strongly eosinophilic material were seen in the tissue suggestive of *B. ranarum* infection. The patient responded well to treatment with voriconazole.

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Conclusion: Gastrointestinal basidiobolomycosis should be considered in the differential diagnosis of every child presenting with abdominal pain, fever and palpable abdominal mass with peripheral eosinophilia. The presence of bowel inflammation and fistulas should not preclude such diagnosis.
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1. Introduction

Basidiobolomycosis is a rare disease caused by the fungus *Basidiobolus ranarum*. It was first described as an isolate from frogs in 1886.[1] It is commonly found in soil, decaying vegetable and the gastrointestinal tracts of amphibians, reptiles, insects, bats, horses and dogs.[2] Basidiobolus is endemic in tropical and subtropical regions of Africa, Latin America, and Asia.[3] Patients with *B. ranarum* infection may present with subcutaneous, gastrointestinal, retroperitoneal or systemic lesions.[2] Gastrointestinal basidiobolomycosis (GIB) has been reported in the medical literature in 14 adults and 13 pediatric cases.[4–11] Nine of the 12 pediatric cases were reported from Saudi Arabia.[4,8,10,11]

Herein, we report an additional case of childhood GIB from Saudi Arabia with a unique acute behavior that mimics fistulising Crohn's disease.

2. Case report

A 2 year old Sudanese boy living in the city of Jeddah presented in April 2010 with a history of right iliac fossa pain, vomiting, diarrhea, and fever of up to 3 weeks. He had history of weight loss over the last few weeks prior to his presentation. Socially, he belongs to a family of low socioeconomic status with no history of recent travel or contact with a patient with tuberculosis (TB). However, on physical examination, he was pale with no lymphadenopathy. And a large right iliac fossa mass was palpable in the abdomen that was firm and tender. Examination of other systems showed no abnormality. His vital signs were normal apart from a temperature of 38.8 °C.

Laboratory investigations indicated the followings; leukocyte count of 14×10^3/ml with 19% eosinophils, hemoglobin 11 g/dl, platelets 495×10^9/l, elevated erythrocyte sedimentation rate (ESR) 55 mm/h, elevated C-Reactive protein (CRP) 150 mg/l, low albumin 22 g/l (normal, 36–40 g/l), negative serology for anti-*Saccharomyces cerevisiae* antibodies (ASCA) of both IgG and IgA types and peri-nucleolar antineutrophil cytoplasmic antibodies (p-ANCA) and positive stool examination for occult blood. Also liver function tests were normal.

Further investigations using colonoscopy revealed inflamed mucosa at the terminal ileum, cecum and ascending colon with cobble stoning and inflammatory pseudopolyps with deep ulcerations covered with thick inflammatory exudates overlying a hard mucosa (Fig. 1). Histopathologic examination of colonic mucosal biopsy obtained during colonoscopy demonstrated chronic active colitis with inflammatory infiltrate with eosinophils and plasma cells.

Additional investigations using computed tomography (CT) scan of the abdomen showed diffuse circumferential wall thickening affecting distal ileal loops, cecum and ascending colon with a large mass observed at the side of mesentery (3.6×3.2 cm) (Fig. 2).

Two weeks following his initial presentation, he had abdominal distension and vomiting. Abdominal X-ray examination showed multiple fluid levels suggesting intestinal obstruction. And laparotomy identified a large mass involving terminal ileum, right colon and extending to the hepatic flexure. Also ileostomy was carried out and multiple biopsies were taken.

Histopathology of the tissue biopsy obtained during laparotomy indicated tissue inflammation with acute and chronic

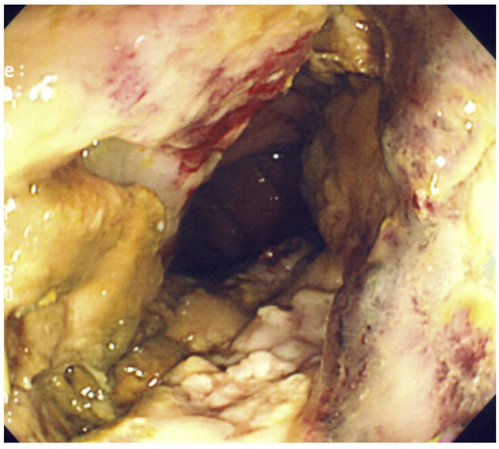

Figure 1 Severely inflamed colonic mucosa covered with exudates with cobble stoning of the mucosa and deep ulcers.

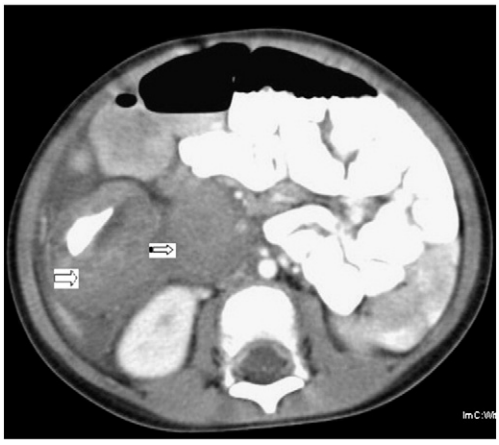

Figure 2 CT scan of the abdomen with contrast showed wall thickening of distal ileal loop (the large arrow) and large inflammatory mass (the small arrow).

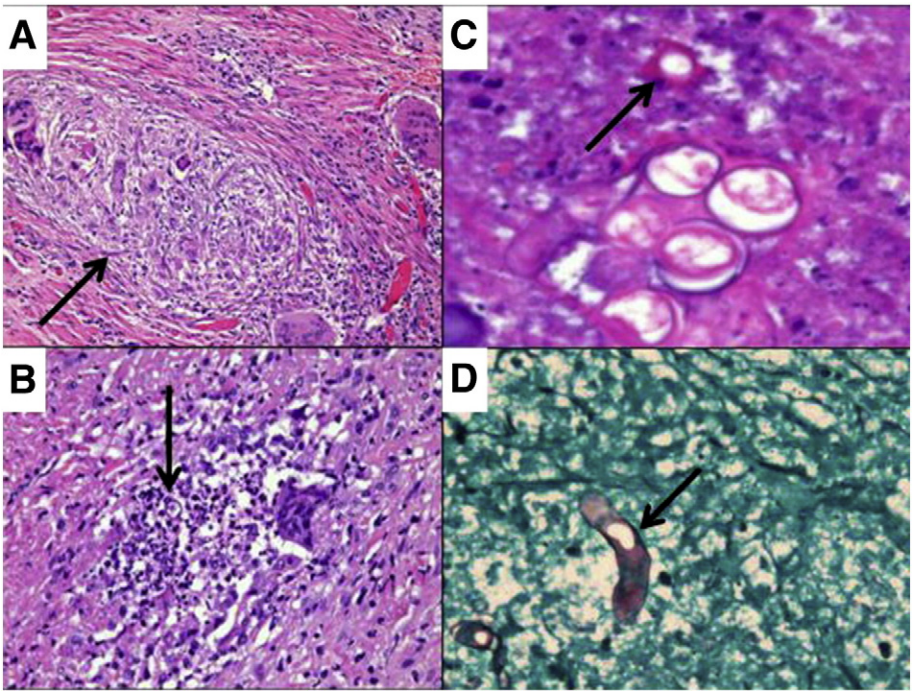

Figure 3 Histopathological features seen in this patient. A. A well defined granuloma (blue arrow) rich in foreign body giant cells in the muscle layer of the intestine close to a fistula (H&E,×10). B. Extensive necrosis of the muscle layer of the colon showing a giant cell, fungal spore (red arrow) and neutrophilic infiltrate (H&E, ×20). C. PAS positive large spores and hyphae of the fungus. Splendore-Hoeppli phenomenon (green arrow) in the form of the eosinophilic sheath around the spores of the fungus. (PAS, ×40). D. Spores and hyphae of the zygomycetes (pink arrow) positive for the fungus stain (Methenamine silver, ×40).

inflammatory cells including eosinophils and histocytes as well as multinucleated foreign body giant cells. Broad pleomorphic hyphae of fungal elements surrounded by intense eosinophilic infiltrate, characteristic of basidiobolomycosis were indentified, especially in the necrotic areas (Fig. 3).

Based upon the histopathologic findings, anti-fungal treatment was initiated with amphotericin B followed by oral voriconazole in a dose of 100 mg twice daily, aiming for 12 months therapy.

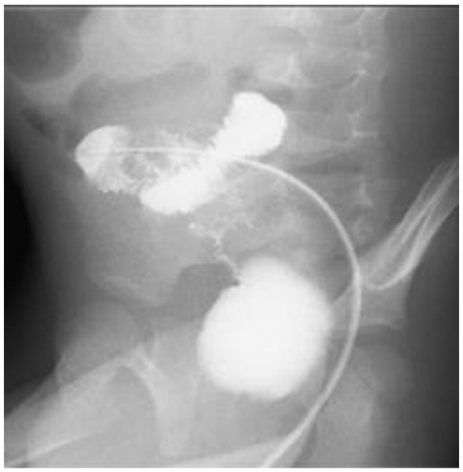

Figure 4 Contrast study with gastrograffin through ileostomy showed ileo-vesical fistula.

Moreover, shortly after the diagnosis of GIB in this patient, passage of stool was observed through the urethra suggesting the presence of entero-vesical fistula and this was established by contrast study using gastrograffin through the ileostomy that demonstrated the presence of both entero-enteric and entero-vesical fistulas (Fig. 4). Following these findings another laparotomy was conducted which identified multiple fistulas (entero-enteric, entero-vesical, colo-cholecystic, and colo-ureteric involving the right ureter) and a large inflammatory mass involving the terminal ileum and the right colon. The mass was excised together with 15 cm from the terminal ileum. Ileocolonic anastomosis was generated for the proximal colon and colostomy was created from the distal colon. All fistula connections were repaired and the patient left with nephrostomy because of the short right ureter.

The child was discharged in a good condition and placed on voriconazole treatment and trimethoprim for renal prophylaxis. Repeated evaluation by colonoscopy through the colostomy after 12 months of treatment showed normal ileocolonic anastomosis, colonic and small bowel mucosa (Fig. 5). Histopathologic examination of the mucosal biopsy was normal.

3. Discussion

Basidiobolomycosis is a rare form of zygomycosis. Subcutaneous mycosis was the usual infection reported in relation to *B. ranarum*.[12–14] Gastrointestinal basidiobolomycosis (GIB) is an

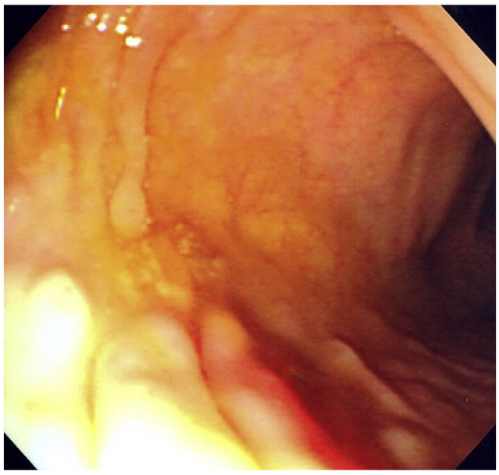

Figure 5 Normal colonic mucosa following 12 months of antifungal therapy.

unusual form of visceral involvement caused by *B. ranarum*. GIB has been reported in both adults[15–23] and children.[4–11]

Thirteen cases of childhood GIB have been reported in the medical literature.[4–11] The current case is considered the fourteenth. The first pediatric case was reported from Nigeria in 1964 by Edington[7] after postmortem examination of a 6 year old boy with GIB that affected the ileum, transverse colon rectum and urinary bladder. This was followed by two additional reported cases of GIB from Brazil.[5,6] These included a 13 year old boy in which the stomach, duodenum, transverse colon, pancreas, liver and biliary system were affected[5] and a 4 year old boy whose stomach and transverse colon were affected and also had abdominal pain, fever and epigastric mass.[6] The disease was fatal in all early reported pediatric cases.

Most of the recent reported cases came from Saudi Arabia including the current case.[4,8,10,11] However, one case has been reported from Iran of 1.5 year old boy who presented with bowel obstruction and urinary retention due to pressure effect.[9] The patient recovered fully following treatment with bowel resection and antifungal therapy. The remaining 10 cases including the current case were either Saudis or Arabs living in Saudi Arabia. Only two patients died out of the 11 recently diagnosed pediatric patients.[4]

The improved survival of these patients may be correlated with the increased awareness of the condition, aggressive surgical approach to debulk the inflammatory tissues, and the availability of more effective and safe antifungal therapy.

The clinical manifestations of childhood GIB include abdominal pain, fever, vomiting, diarrhea and weight loss.[4–6,8–11] Unlike adults constipation was uncommon in children. The presence of abdominal mass was a common finding, either observed during abdominal examination or demonstrated by imaging or during laparotomy. Bowel obstruction has been reported in 3 patients,[5,8,9] which resulted in perforation in one.[8] Furthermore, liver damage was observed more commonly in children than in adults.[4,5] Also the presence of retroperitoneal mass involving the renal system has been reported in two pediatric patients[4] and fungal infection of the urinary bladder in one.[7] Our patient had local invasion of the right ureter as well as involvement of the urinary bladder through fistula formation.

The unique feature presented in our case is the development of multiple fistulas. The patient had fistulas developed between ileal loops (enteroenteric), ileum and urinary bladder (enterovesical), the colon and the gall bladder (colocholecystic) and the colon and the right ureter (coloureteric). The development of multiple fistulas has not been reported in the previous publications. This may support the penetrating behavior of the disease that mimics Crohn's disease or intestinal tuberculosis.

Both conditions were considered in the differential diagnoses of this patient when first presented. The absence of history for contact with tuberculosis patients, negative tuberculin test and PCR for tuberculosis conducted in the tissue obtained during colonoscopy and the absence of caseating granuloma in the histopathology examination makes tuberculosis unlikely. However because we are living in an endemic area, a trial of anti-tuberculosis medication was started with no improvement. Crohn's disease was strongly considered, however before we take the decision for treatment, the patient' condition deteriorated and required laparotomy after which the diagnosis of GIB was clear. The similarity in the clinical presentation between Crohn's disease and GIB is often reported as a reason for misdiagnosis and confusion between the two conditions.[15,19,23]

In most reported cases of GIB treatment is instituted using amphotericin B and oral itraconazole.[4,8,9,16] However, our patient was successfully treated with a new generation, triazole antifungal "voriconazole" a derivative of fluconazole. It is available in both oral and intravenous formulation. It has been approved by the European Union for use in children 2–12 years of age based on large clinical study of voricoazole in 58 children with invasive fungal infections including aspergillosis, candidimia, and scedosporiosis.[24] This is the first study that reported the use of voriconazole for treatment of GIB in children or adults.

4. Conclusion

From the findings of this study the GIB diagnosis should be considered in any child presenting with abdominal pain and fever with palpable abdominal mass in the presence of peripheral eosinophilia and eosinophilic infiltration of the colonic mucosa. Early consideration of surgery and antifungal treatment may be life saving.

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