

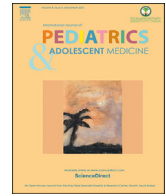
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## Gastrointestinal Basidiobolomycosis in pediatric patients: A diagnostic dilemma and management challenge

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## ABSTRACT

**Introduction:** Basidiobolomycosis is a rare fungal disease, lately appearing in the gastrointestinal system of pediatric patients. Their clinical presentation resembles that of lymphoma or granulomatous inflammations. This non-specific presentation makes Gastrointestinal Basidiobolomycosis (GIB) a diagnostic challenge.

**Methods:** We are reporting the largest series of pediatric GIB, from Saudi Arabia. 12 patients were diagnosed between January 2012 and December 2019, between the ages of 16 months and 8 years.

**Results:** The most common symptoms were fever and abdominal pain. Further examination revealed an abdominal mass. Biopsy of the mass was the mainstay of diagnosis, with histological findings of typical filamentous fungal hyphae and zygospores, surrounded by eosinophils.

**Conclusion:** Role of surgery was limited to establishing the diagnosis and dealing with complications. Antifungal medication was the cornerstone of treatment in all our patients. Three of our patients were exceptional with complications such as entero-cutaneous fistula, entero-enteric fistula and short bowel syndrome. These complications have not been previously reported. We have discussed the challenges related to their management.

The diagnosis of GIB in pediatric patients with abdominal mass, needs a high index of suspicion. We believe outcome depends on the severity of disease, involvement of surrounding tissues and presence of complications at the time of diagnosis.

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## 1. Introduction

Basidiobolomycosis in humans is a rare fungal disease caused by an organism called *Basidiobolus Ranarum*. They are classified under

the Entomophthorales, which are categorized as Zygomycetes [1,2]. It is known to inflict the subcutaneous tissue, in immune competent patients, although the Entomophthorales infections usually occur in immune-compromised patients [1–3].

This fungus was described in frogs more than 100 years ago. In 1955, it was first isolated in United States from decaying plants [1,2]. The first cutaneous disease in humans was detected in Indonesia in 1956, which was transmitted through traumatic inoculation [1,2]. But the first Gastrointestinal Basidiobolomycosis (GIB) reported was in 1964 from Nigeria in a postmortem study of a six-year-old child [4]. GIB is transmitted through the ingestion of food contaminated with excreta from frogs, lizards, decayed animals, and plants [2,3].

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In this review, we present a series of 12 pediatric patients in a tertiary center in Saudi Arabia. Their presentation, demographics, investigation, imaging, course of disease, management, and outcome are summarized in Tables 1–3.

Our patients were between the ages of 16 months and 8 years at the time of presentation, with a median of 4 years, and a male to female ratio of 5:1. All patients were from the western part of the kingdom. Nine out of 12 patients were originally from the southern region (either living there or travelling frequently for family gatherings). Travel history was negative for three patients (patient number 4, 5, and 6). None of the patients were immune compromised. Of these 12 patients, three in particular stand out due to complications and extensive surgical involvement in their management. These three patients are presented below in detail.

## 2. Patient no. 2 (Tables 1–3)

A 5-year-old boy with a one-month history of occasional fever, abdominal pain, weight loss, anorexia, and diarrhea, was received in our hospital.

At presentation he looked cachectic and pale. His weight was below the 5th percentile. The abdomen was distended with dilated superficial veins. Palpation revealed a rigid abdomen with generalized tenderness. Liver and spleen could not be appreciated but an abdominal mass could be felt in the left lower quadrant. His blood pressure and pulse were within normal limits. Investigations upon admission revealed white blood count (WBC) of  $29.9 \times 10^9/L$ , neutrophils of  $22.1 \times 10^9/L$ , hemoglobin 5.6 mg/dl, platelets  $1014 \times 10^9/L$ , ESR 140 mm/h, and CRP 269 mg/L (Table 2).

CT scan (Fig. 1) showed a huge mesenteric, hypo dense, solid mass with retroperitoneal extension infiltrating the pancreas and the duodenal wall. There was a finding of portal vein thrombosis with poor visualization of distal branches of mesenteric vessels. The mass was infiltrating the transverse colon, hepatic flexure, descending colon, cecum, and the terminal ileum. Abnormal dilatation of the proximal small bowel loops was present with suspicious pneumatosis intestinalis changes in few bowel segments. Abnormal peritoneal nodular thickening, intraperitoneal fat stranding, and ascites were identified. With the provisional diagnosis of gastrointestinal lymphoma, the plan was to proceed for a biopsy confirmation.

The patient had to be shifted to the pediatric intensive care unit (PICU) for the management of electrolyte imbalance and the initiation of enoxaparin therapy for portal vein thrombosis. A nasogastric tube was inserted to decompress the bowel, and it drained bile.

After the stabilization and correction of electrolytes, we proceeded for incisional biopsy. At laparotomy the abdomen contained a very foul-smelling fluid, which was sampled and sent for microbiology and cytology. With further exploration, the small bowel did not look healthy; there were patchy areas of compromised vascularity. Although the stomach appeared viable, the gastrocolic ligament was infiltrated by tumor from the posterior side. The transverse colon was fixed to the tumor and the bowel mesentery was extensively involved. The ileum was dusky but still viable. The proximal 40 cm of the jejunum was clearly gangrenous and had to be resected, the ends were clipped and dropped. Lymph nodes from the mesentery were sampled. The mass was biopsied and the frozen section showed fibrosis infiltrated tissue with no clear evidence of malignancy. Temporary closure of the abdomen was done, as we planned for a second look laparotomy.

At the second look laparotomy, there was an increase in areas of patchy discoloration of the small bowel. The large bowel was still viable with infiltration of the mass posteriorly including the whole mesentery of the bowel. Another biopsy was obtained from the mass near the gastrocolic ligament. The abdomen was closed to give further time for recovery and clear demarcation before any further resection of the bowel.

Intravenous (IV) Voriconazole was started with the suspicion of fungal infection. The patient was kept ventilated in the PICU until the next surgery. A third look laparotomy was done 48 h later. A leak was found from the proximal jejunal stump. Distally, the remaining small bowel appeared to be more promising with patchy areas of dusky segments. The proximal jejunal stump was excised, and a jejunal tube stoma created with a distal tube mucous fistula.

The final diagnosis of GIB was confirmed by histopathology. The patient continued to receive aggressive, supportive care in the PICU, but he deteriorated clinically with signs of sepsis and was therefore taken for re-exploration. This time the small intestine was frankly gangrenous, with multiple areas of perforation except for 10 cm from the proximal jejunum and 15 cm from the terminal ileum. Resection of the gangrenous bowel was done, proximal and distal stomas were created, and the abdomen was closed. Shortly after, he was stable enough to be sent to the general ward.

A long-term 12-month treatment plan was formulated with pediatric infectious disease service. The patient was to start combination therapy with IV Itraconazole and Voriconazole due to the severity of the disease, then to continue with oral Voriconazole alone once oral intake is tolerated.

The patient continued to be total parenteral nutrition (TPN) dependent with a high-output proximal stoma. Gradual feeding was started orally with a hydrolyzed formula. The output of the

**Table 1**

Patient details and duration of symptoms prior to presentation.

Case	Age	Sex	Clinical presentation	Duration of symptoms	Region of Origin/Travel
1	8y	M	Fever, and abdominal pain	6 weeks	Baha
2 <sup>a</sup>	4y	M	Fever, abdominal pain and mass, weight loss, and diarrhea	8 weeks	Jeddah/visits south frequently to visit grandparents
3	2y	M	Fever, abdominal mass, weight loss, diarrhea, and oral thrush	4 weeks	Gunfuda
4	22m	M	Fever, abdominal pain, weight loss, vomiting, and diarrhea.	8 weeks	Jeddah/no travel history
5	19m	M	Fever, and abdominal mass	2 weeks	Makkah/no travel history
6	6y	M	Fever, abdominal pain, distension, and signs of intestinal obstruction for two days	5 weeks	Yanbu
7	5y	F	Fever, abdominal distension, vomiting, anorexia, and night sweat.	16 weeks	Baha
8 <sup>a</sup>	7y	M	Fever, abdominal pain, and weight loss	4 weeks	Baha
9	6y	M	Fever, abdominal pain, and weight loss.	4 weeks	Al Ardiyat
10	16m	M	Fever, abdominal distension, vomiting, and diarrhea.	8 weeks	Gunfuda
11	4y	F	Fever, abdominal pain, weight loss, and night sweating.	2 weeks	Baha
12 <sup>a</sup>	3y	M	Fever, abdominal pain, and abdominal distension.	3 weeks	Al Leith

<sup>a</sup> patient is detailed in the text.

**Table 2**  
Patient investigations and imaging results.

Case	Laboratory				Radiology	Culture	Frozen section histology
	WBC X 10 <sup>9</sup> /L	Hgb g/dl	Eosinophilia (yes/no)(%)	CRP mg/L			
1	36.6	7.2	No (0.87)	106	CT scan: large lower abdominal mass measuring 10 × 5.4 × 7.6 cm	–	–
2 <sup>a</sup>	29.9	5.6	Yes (18)	269	CT scan: Large midline retroperitoneal mass measuring 7.9 × 8.2 cm, portal vein thrombosis	Negative	Inflammatory changes
3	38.3	6.5	Yes (9.8)	385.8	CT scan: large abdominal mass involving the descending and splenic flexure of colon and small bowel 11 × 7.1 × 7.2 cm	–	–
4	39.8	7.9	Yes (9.6)	297	CT scan: Mass associated with small intestine in the right lower quadrant 9.7 × 6.5 × 7.5 cm and the cecum ascending colon	Negative	Fungal hyphae
5	24.1	9	Yes (6.8)	119	CT scan: Mass involving splenic flexure and descending colon 8 × 9.5 × 10.5 cm	–	Inflammatory changes
6	20	9	Yes (12.2)	191.9	CT scan: Right sided pelvic mass, measuring 5.1 × 5.6 × 8.4 cm, signs of partial intestinal obstruction.	Negative	Fungal hyphae
7	22.2	7.4	Yes (16.4)	210.9	CT scan: Right sided abdominal mass measuring 6.2 × 8.9 × 6 cm, with involvement of mesentery.	Negative	Inflammatory changes
8 <sup>a</sup>	17.6	9.8	Yes (6.9)	195.2	CT scan: Thickening of the wall of the cecum, ileal loops and the sigmoid colon forming an amalgamated mass measuring 8.5 × 8.1 cm	–	Fungal hyphae
9	12.8	8.6	Yes (26)	184.4	CT scan: Right sided retroperitoneal mass measuring 10 × 10 × 7.5 cm	–	–
10	30.2	9.9	Yes (22.6)	192.4	CT scan: Left sided abdominal mass measuring 7 × 5.5 cm	Positive in tissue	Fungal hyphae
11	23.2	9.2	Yes (18.4)	311.8	CT scan: Circumferential mass on wall of ascending colon and hepatic flexure, measuring 6.3 × 5.2 × 5.8 cm	Negative	Fungal hyphae
12 <sup>a</sup>	19	7.2	Yes (5.64)	360	CT scan: Right sided abdominal mass 8.5 × 7.5 cm involving ascending colon, hepatic flexure and cecum, infiltration of the inferior border of the pancreas.	Candida Galbrata & Aspergillus in peritoneal fluid	Fungal hyphae in cytology of peritoneal fluid

<sup>a</sup> Patient is detailed in the text.

**Table 3**  
Patient interventions, tissue histopathology, and complications.

Case	Intervention	Histopathology	Complication
1	Tru-Cut biopsy by interventional radiology	Necrotizing granuloma, Splendore-Hoeppli phenomenon with eosinophilic necrosis	–
2 *	Multiple laparotomies, bowel resection, and secondary procedures for short bowel syndrome ( <i>see text</i> )		Short bowel syndrome
3	Laparotomy and biopsy		Wound infection
4	Laparotomy and biopsy		–
5	1st laparotomy, biopsy, and ileostomy creation; 2nd laparotomy, and closure of ileostomy		Bowel obstruction and ileostomy
6	Laparotomy and biopsy		Hydronephrosis that resolved with the resolution of the infection
7	Laparotomy and biopsy.		Wound infection
8 *	Laparotomy and biopsy ( <i>see text</i> )		Enterocutaneous fistula
9	Laparotomy and biopsy		–
10	Laparotomy and biopsy		–
11	Laparotomy and biopsy		–
12 *	1st Laparotomy wash and biopsy, 2nd laparotomy roux-en-Y duodeno-jejunostomy ( <i>see text</i> )		Duodeno-colic fistula Colocutaneous fistula and acquired atresia

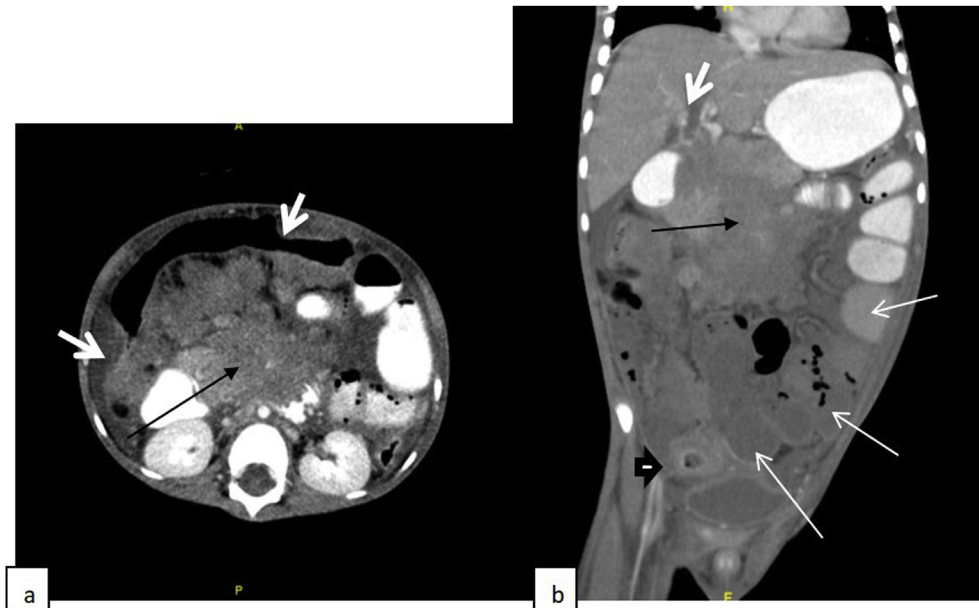
stoma was re-fed into the distal mucous fistula (bowel re-feeding). TPN could not be weaned at this stage. The stomas were closed and the bowel continuity was reestablished to facilitate weaning. At the time of stoma closure, the bowel showed signs of elongation and adaptation. The contrast study demonstrates the remaining small bowel, which was nearly 60 cm (Fig. 2). Although the ileocecal junction was preserved, the patient continued to behave like he had short bowel syndrome. Gradual weaning of the TPN and increasing the oral feeding using fully hydrolyzed milk formula was achieved. After a total of 12 months, we succeeded in stopping the TPN completely.

Follow up CT scan of the abdomen, 10 months after the last surgery, showed a small residual retroperitoneal mass (Fig. 3). The patient was discharged from the hospital, after just more than a year from his initial presentation. He was lost to follow-up after discharge. Later, we were informed that the patient passed away quietly at home, maybe due to fluid and electrolyte disturbances.

### 3. Patient no. 8 (Tables 1–3)

A 7-year-old boy, also from the western region, presented to another hospital with abdominal pain and fever for a month prior to admission. Pain was continuous in nature and was associated with frequent loose stools, and occasional non-bilious vomiting. Parents noticed that there was a decrease in appetite and loss of weight. He was operated with a suspicion of appendicitis. At surgery, an abdominal mass was found, therefore the procedure was terminated and the abdomen was closed. The patient was thought to have Crohn's disease and was referred to our center for further management.

The gastroenterologist performed colonoscopy and endoscopy, and biopsies were taken, but did not yield any pathology. A CT scan of the abdomen and pelvis was performed. It showed a large hypodense heterogeneous pelvic mass involving the wall of the rectosigmoid and sigmoid colon as well as the distal ileum with severe dilatation (Fig. 4). This mass was fungating into the bowel



**Fig. 1.** Patient 2 – Selected coronal and axial images from the contrast enhanced CT scan of the abdomen. (a) The image demonstrates the huge mesenteric mass (black arrow) encasing mesenteric vessels with retroperitoneal extension involving the duodenum wall. Also noted the thickening of the transverse colon and hepatic flexure walls (short white arrows). (b) The coronal image shows the extension of the intra-abdominal mass with the portal vein thrombosis (short white arrow). Also identified the thickening of the terminal ileum (arrow head) and the dilated small bowel loops (thin white arrows).

lumen in multiple areas without any radiological signs of obstruction. Associated large mesenteric lymph nodes were noted together with ascites and peritoneal thickening. These changes raised the suspicion of lymphoma. Consequently, a laparotomy for incisional biopsy was performed.

At laparotomy, a firm avascular mass, extremely adherent to the peritoneal surface, was found. It involved the bowel wall almost circumferentially. Incisional biopsy was taken from a firm area of the mass, avoiding injury to the bowel wall, and a part of that biopsy was sent for frozen section histology, which revealed fungal hyphae. A drain was left in the abdomen.

The patient had an uneventful course postoperatively. The drain was removed the following day. The patient regained his bowel functions and tolerated his diet. Final histopathology of the biopsy showed typical necrotizing granuloma, Splendore-Hoeppli phenomenon with eosinophilic necrosis, which confirmed Basidiobolomycosis. The pediatric infectious disease service started him on IV Voriconazole.

One week later, some bile-stained fluid was observed to come from the site of the peritoneal drain and from the corner of the surgical wound. CT scan was repeated and confirmed the presence of an enterocutaneous fistula originating from the cecum, but without intra-abdominal contamination.

Conservative management of the fistulae was started in the form of bowel rest and TPN. As they were low output fistulae, possibility of spontaneous closure of the enterocutaneous fistulae was thought to be high.

The patient was afebrile and continued to receive IV antibiotics and Voriconazole. He had normal bowel function with a small amount of discharge from both fistulae. One fistula closed within 2 weeks, but the other fistula formed a tract. After two weeks of bowel rest, the patient was gradually started on oral diet and TPN was discontinued. The patient had normal feces per rectum, while the fistula had only little discharge. Three weeks later, the patient was sent home on oral Voriconazole, to be continued for at least 18 months.

The patient was regularly seen in the outpatient clinic. He was

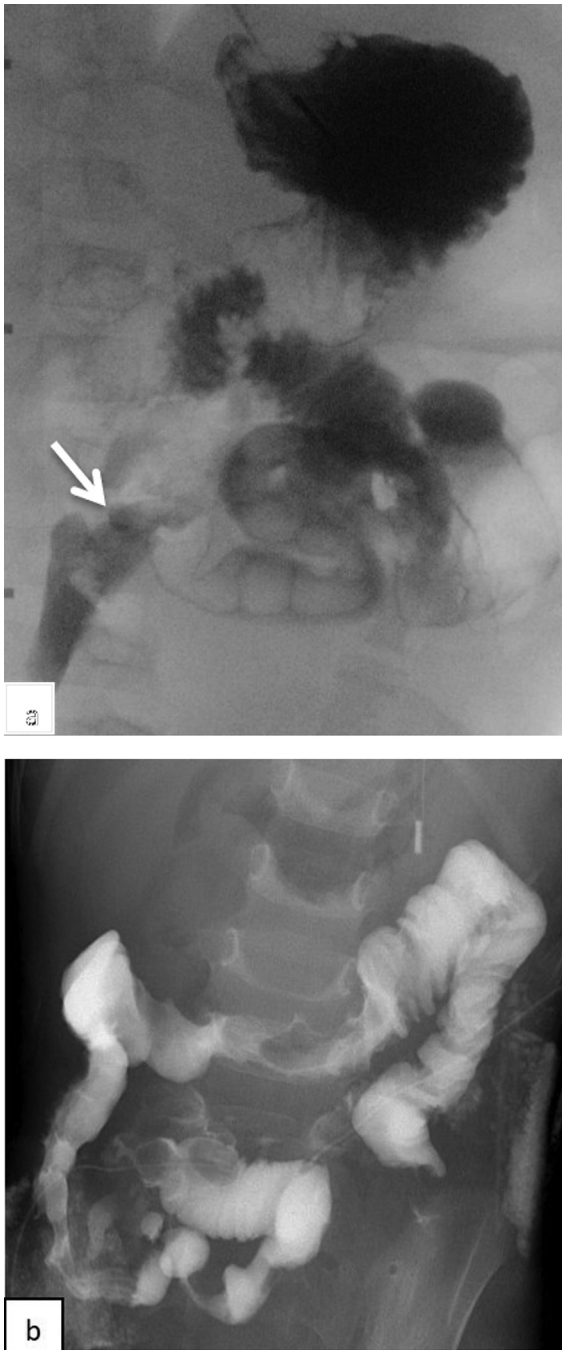
living a normal life with all activities, but continued to have some staining from the fistula. Three months later, the fistula closed spontaneously. The patient completed 18 months of Voriconazole therapy, follow up CT scan at 19 months showed no residual mass, and was therefore discharged from our clinics.

#### 4. Patient no. 12 (Tables 1–3)

A 3-year-old previously healthy boy presented to our hospital with a history of abdominal pain, fever, and abdominal distension. His symptoms started three weeks prior to presentation and progressed over time. His family sought medical advice elsewhere and he was managed for gastroenteritis. Eventually, imaging in the other facility demonstrated an abdominal mass and he was referred as possible lymphoma for further management. CT scan images were reviewed in our facility and they demonstrated a large intraperitoneal mass measuring  $8.5 \times 7.5$  cm with heterogeneous enhancement with a necrotic, liquefied center extending from the right hypochondrium till the right iliac region (Fig. 5). The mass involved the colon starting from the cecum up to the hepatic flexure and was causing aneurysmal dilatation of the colonic lumen. Loss of the continuity of bowel-enhancing mucosa was noted, which was associated with fistulous communication with the necrotic center of the mass. Whereas the superior and posterior extension of the mass was infiltrating the pancreas and the right perirenal fascia with the involvement of the right kidney. Multiple enlarged mesenteric lymph nodes, ascites, and thickened peritoneal reflection were also noted.

In our hospital, the patient looked sick but alert. His vital signs were as follows: pulse 121 beats per min, blood pressure was 120/94 mmHg, and the temperature was  $38.4^\circ$  Celsius. His abdomen was moderately distended with tenderness on the right side. His initial investigations showed elevated WBC count  $19 \times 10^9$  per liter, hemoglobin of 7.2 g/dl, and platelet count of  $770 \times 10^9$  per liter. His CRP was 360 mg/L.

The patient was deteriorating rapidly, necessitating PICU admission, and ventilator support. A CT scan was repeated, which

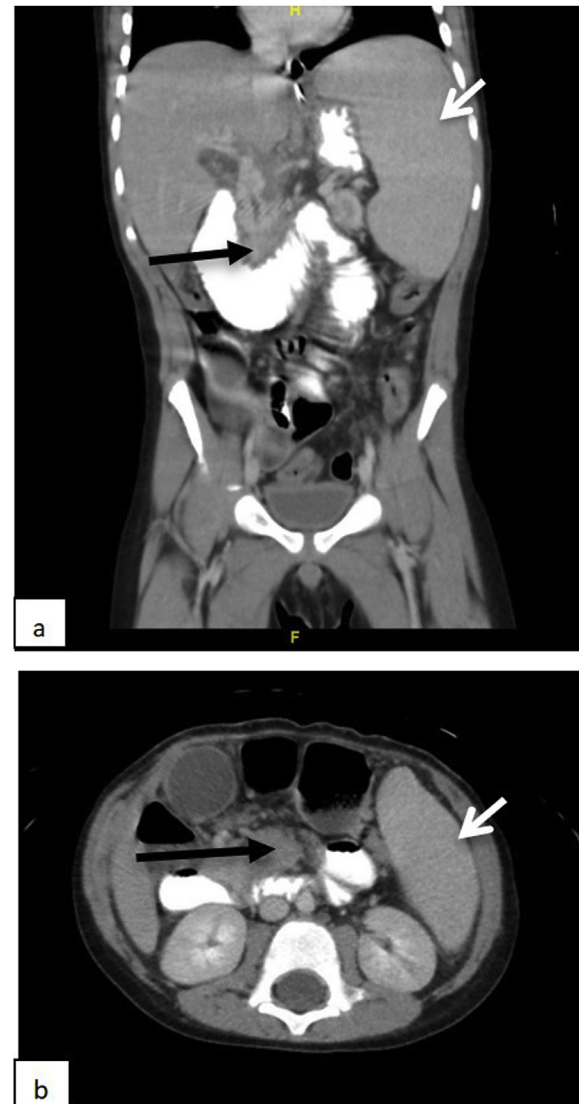


**Fig. 2.** Patient 2 – Selected images from upper (a) and lower (b) GI contrast studies show the abnormally short remaining small bowel. The arrow is at the cecum.

showed an increase in the mass size and invasion.

The patient was planned for laparotomy and biopsy, but his general condition did not allow it. A percutaneous biopsy from the mass was taken under ultrasound guidance at the bedside. The frozen section histology showed fungal hyphae. Later, the final histopathology report confirmed the diagnosis of Basidiobolomyces, with findings of necrotizing granulomas and fungal hyphae with Splendore-Hoeppli phenomenon.

The patient was started on an IV Voriconazole. Unfortunately, he developed an enterocutaneous fistula from the site of biopsy. The patient continued to deteriorate despite maximal medical therapy with increasing abdominal distension and respiratory

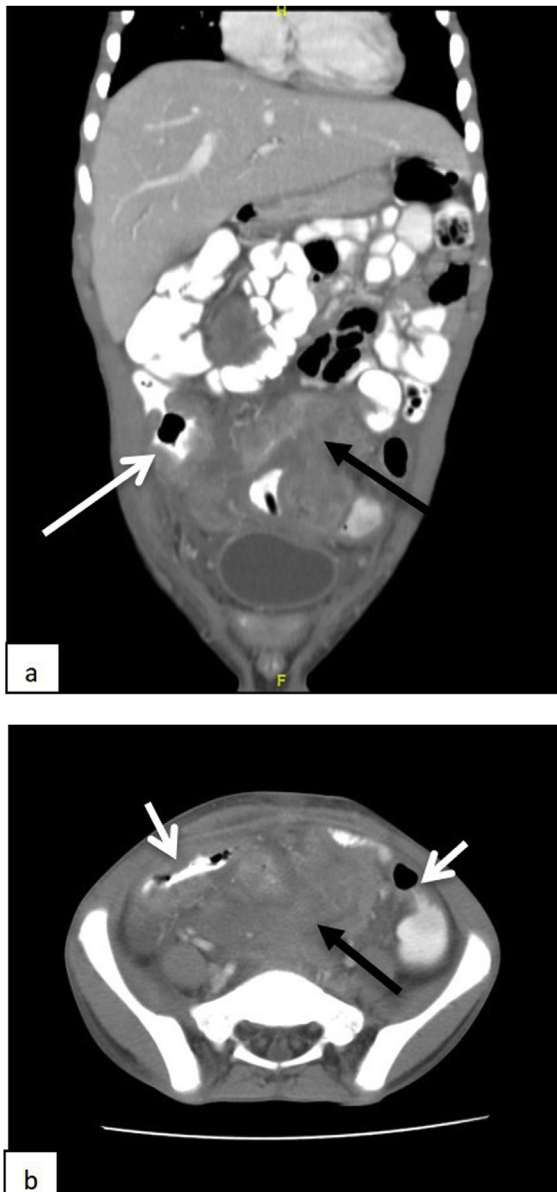


**Fig. 3.** Patient 2 – The last CT scan of the abdomen with oral and IV contrast. Coronal and axial images demonstrate the small residual mass (black arrow). Also noted the persistent thrombosis of the portal vein with consequences of the venous collaterals at the porta hepatis and the splenomegaly (white arrow).

embarrassment.

An abdominal CT scan was repeated. It showed the same large right lower abdomen mass with extensive necrotic changes and no appreciable outline to differentiate the involved right colonic segments from the retroperitoneal component (Fig. 6). The imaging demonstrated a cecocutaneous fistula from the right lower quadrant to the anterior abdominal wall. Oral contrast was noticed flowing into the right side of the colon raising the possibility of duodeno-colic fistula as well. There was massive abdominopelvic ascites with peritoneal enhancement and poor visualization of superior mesenteric artery.

Because of the respiratory compromise and new findings on imaging, operative exploration was undertaken in the hope to decompress the abdomen. At laparotomy, an amalgamated mass was found involving the bowel, the visible bowel loops were completely engulfed by the mass. Dissection of the mass was not considered to be feasible because of the high risk of organ injury versus benefit. An abdominal wash was done and a drain was placed.



**Fig. 4.** Patient 8 – CT scan of the chest and abdomen with IV and oral contrast. (a) Selected coronal image demonstrates the large heterogeneous hypo dense pelvic mass (black arrow) with infiltration of the distal ileum. Fungating mass and the aneurysmal dilatation (long white arrow). (b) Axial image shows the pelvic mass and the bowel involvement (short white arrows).

The patient stayed in PICU for three weeks on respiratory support, and Voriconazole and TPN. During this time, his abdominal wall wound dehiscid and bowel could be seen within the gaping wound. Also, succus entericus was freely coming through the wound. Daily dressing was applied initially until the defect contracted and the enterocutaneous fistula became like a stoma. A stoma bag was applied, and the fistula continued to have a high output of bowel contents.

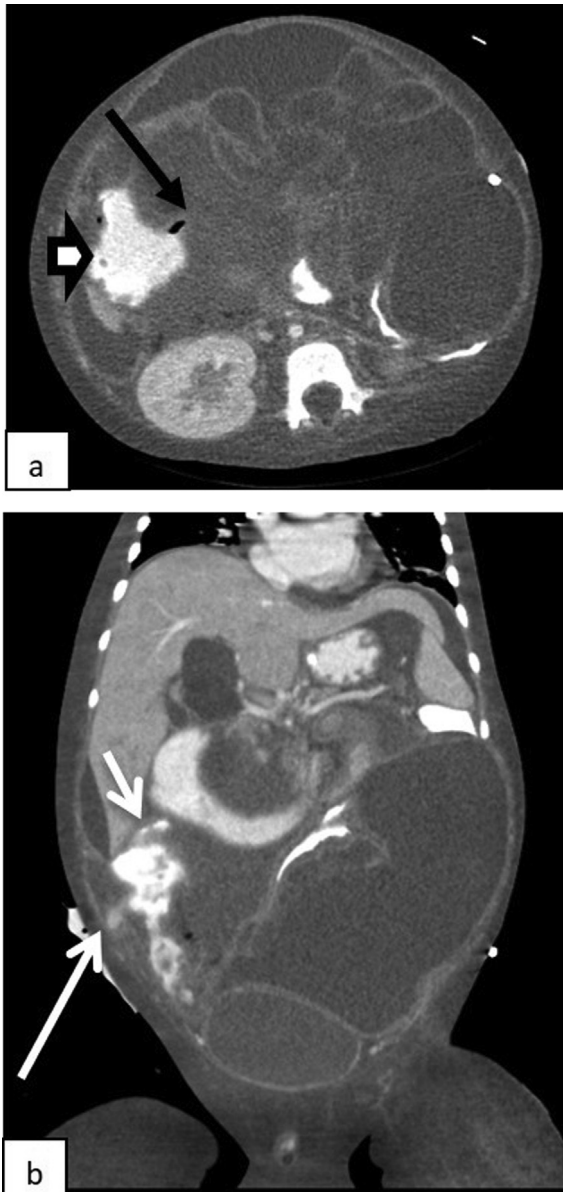
After a stormy three-week period, the patient's general condition improved enough for him to be transferred to the surgical floor. An upper gastrointestinal contrast study (Fig. 7) was performed to study the level and size of the duodeno-colic fistula.

Enteral feeding was started but was not tolerated due to his duodeno-colic fistula. He was managed on TPN and regular wound care to his colocutaneous fistula site. Periodic evaluations were



**Fig. 5.** Patient 12 - The first CT scan of the abdomen with IV and oral contrast. (a) Selected axial image demonstrates the large right hypochondrium necrotic mass (short black arrow) involving the ascending colon causing aneurysmal dilatation of the bowel lumen (short white arrow). There is fistulous communication between the lumen and the necrotic center of the mass (long black arrow). (b) Selected coronal image demonstrates the large necrotic mass infiltrating the head of the pancreas (outlined arrow head).

done by CT scan of abdomen to follow the status of the fungal mass and the surrounding tissue involvement. After seven months of start of treatment, a follow-up CT scan revealed marked interval reduction of the abdominal necrotic mass with residual amalgamated mesenteric mass involving the small bowel and duodenum. There was associated abnormal dilatation of the common bile duct (Fig. 8). There was persistence of a large fistulous tract between the colon and the skin as well as the duodeno-colic fistula. The previous infiltration in the pancreas and the right kidney was no longer appreciated. However, there was marked atrophy of the

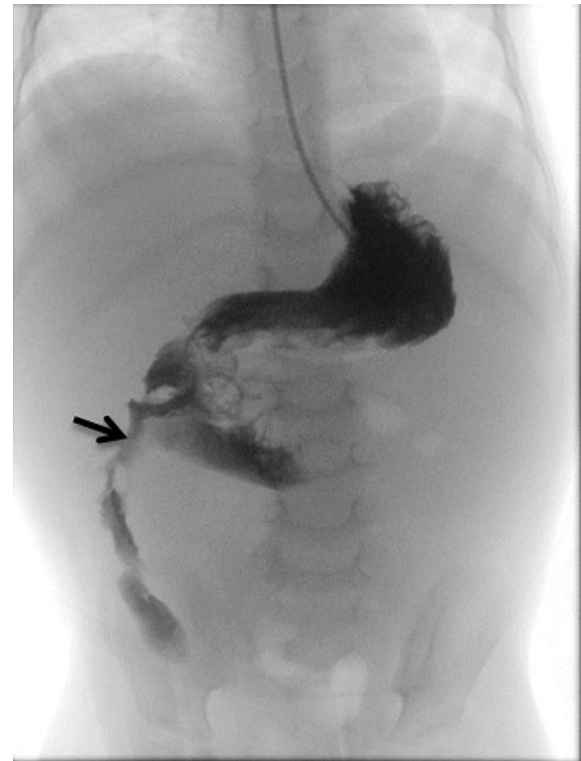


**Fig. 6.** Case 12 - Follow up CT scan of the abdomen with IV and oral contrast administration. (a) The axial image demonstrates the necrotic right abdominal mass (black arrow) with retroperitoneal extension. The oral contrast is already in the right side of the colon (outlined arrow head) with massive intraperitoneal free fluid. (b) Coronal image demonstrates the duodeno-colic fistula (short white arrow) and the colcutaneous fistula (long white arrow).

pancreatic head and neck.

After a total of 8 months, the patient was taken for laparotomy for management of the sequelae of the fungal infection. At surgery, multiple large masses composed of amalgamated bowel, several enteroenteric fistulae, a fistulous tract between the skin and transverse colon, and multiple atretic segments of small bowel with no proximal or distal connection were found.

The most challenging among the fistulae was the one between the duodenum and the hepatic flexure. After extensive adhesiolysis, a total of 85 cm of small bowel were salvaged. The duodenum was ending after the second part into the fistula and no distal duodenum could be identified. A Roux-en-Y duodenojejunal anastomosis was done with multiple enteroenteric anastomoses to re-establish bowel continuity. The last anastomosis was an entero-



**Fig. 7.** Upper GI water soluble contrast study shows the contrast flowing from the duodenum into the right colon through a fistulous tract (arrow).

transverse colon end to end anastomosis, as the terminal ileum and ascending colon were all eaten up by the infectious process.

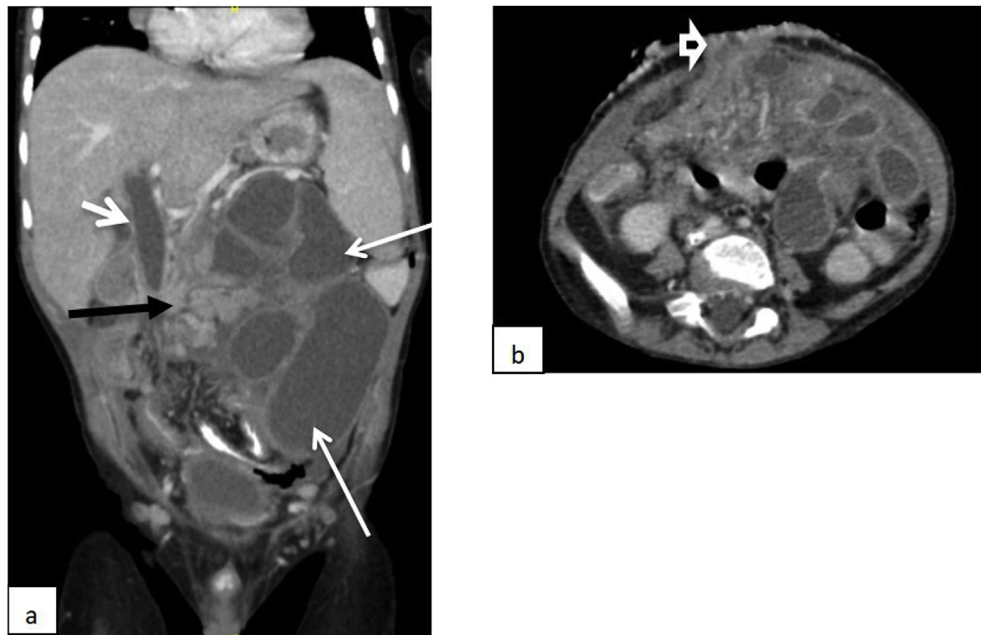
The patient did well postoperatively and continues to be on TPN and IV Voriconazole. Histopathology result of the distal ileum and omentum still shows the presence of fungal hyphae. A late upper gastrointestinal (GI) contrast study showed two segments of strictures at the proximal and distal jejunal level but no evidence of leak. He is still on antifungal therapy and awaiting surgery to deal with his strictures.

## 5. Discussion

Basidiobolomycosis has been widely reported in the form of subcutaneous infections [6]. Only recently has it been reported to affect the GI tract of children, endemic in certain tropical and subtropical regions [1–3]. The route of infection in gastrointestinal Basidiobolomycosis (GIB) is the ingestion of fungal-infested discharges from certain reptiles such as lizards (particularly the Gecko) and frogs [2,5].

On review of literature, most patients were male [1,2,5]. This was also seen in our series, where we had a 5:1 male to female ratio. They all presented to our hospital within 2–16 weeks from the onset of symptoms. Table 4 describes the frequency of symptoms found in our patients. Common among them were findings of fever and abdominal pain, which goes with symptoms reported by others [1–3,5]. Parents of six children noted weight loss. Only few had vomiting and diarrhea (Table 1). All patients had a palpable abdominal mass on physical examination.

A complete laboratory workup for malignancy including, but not limited to, complete blood count, biochemistry, and tumor markers was performed. Leukocytosis and anemia was noticed in all patients, with the highest leukocyte count of  $39 \times 10^9/L$  and lowest of  $12.8 \times 10^9/L$ , and a hemoglobin level as low as 6.5 g/dl (Table 2). The



**Fig. 8.** Patient 12 – Follow-up CT scan of the abdomen 7 months after the start of treatment (a) Coronal planes show marked reduction of the lower abdominal necrotic mass with a residual mesenteric mass (black arrow) involving the duodenum. A dilated CBD (short white arrow) and persistent dilated small bowel segments (long white arrows) are seen. (b) Axial planes show persistent colocolic fistula (arrow head).

**Table 4**  
Frequency of symptoms arranged in ascending pattern.

Symptoms	Frequency
Oral Thrush	1
Anorexia	1
Night Sweats	2
Vomiting	3
Diarrhea	4
Weight Loss	6
Mass/Distension	6
Abdominal Pain	8
Fever	12

low hemoglobin might be explained by anemia of chronic illness. They could have had the involvement of the GI tract much earlier than the actual presentation.

Eosinophilia was seen in all patients except one. Range of eosinophilia was between 5.6% and 26% of the total leukocyte count. The degree of eosinophilia did not correlate with the final outcome or response to antifungal therapy.

An abdominal ultrasound was the initial imaging modality, but CT scan of abdomen was more informative to determine the nature of mass and extent of involvement of surrounding tissues. All were found to have a mass involving a part of the large or small intestine, or both; except our second patient who had findings of a large midline retroperitoneal mass of  $7.9 \times 8.2$  cm, with multiple lymph nodes and portal vein thrombosis (Table 2). This patient already had complications of extensive bowel vascular compromise, at presentation, thus he ended up with short bowel syndrome.

All our patients are alive and well except one (patient 2 as described above). He died at home, possibly secondary to complications of short bowel syndrome. The only two other pediatric series that reported mortality are Al Shanafey et al. and Ezzedien et al. They reported a mortality of 2 out of 9 and 1 out of 6 patients, respectively [2,7].

In our series, the mass mostly involved the colon, anywhere

between the cecum and sigmoid colon. The mass was of significant sizes, (up to  $10 \times 10$  cm) at the time of diagnosis. Adherence of the mass to the anterior abdominal wall was only noticed in three patients (patient 8, 11, and 12 from Tables 1–3). None of these findings were related to the severity of the disease or their outcome.

GIB is an infiltrative disease that is not limited to the GI tract. Involvement includes the retroperitoneal structures with encasement of vessels and involvement of the kidney and pancreas (patient 12). Also, the formation of enteroenteric (patient 12) and enterocutaneous fistula has been noted in two of our patients (patients 8 and 12). No other series has reported such findings.

One of enterocutaneous fistulae patients needed surgical closure (patient 12). Mesenteric artery thrombosis leading to bowel necrosis was only seen in one patient (patient 2). There was one patient who required ileostomy at the time of biopsy due to the circumferential involvement of the ileum causing bowel obstruction (patient 5 in Table 3). That ileostomy was reversed after 12 months of Voriconazole therapy and complete disappearance of the mass.

GIB has been diagnosed when patients were investigated for abdominal mass to rule out malignancies or inflammatory bowel disease, as seen in other case series in the past [1–3,8]. This signifies how difficult it is to reach the diagnosis without a biopsy. There is no specific imaging modality or blood test to date that can diagnose GIB without tissue biopsy.

The suspicion of GIB should be high when a pediatric patient presents with an abdominal mass, with concurrent findings of fever, anemia and leukocytosis or eosinophilia. This is consistent with other cases reported in the literature [9–14]. Adequate biopsy and histological findings on the frozen section of fungal hyphae, have played a very important role in establishing the diagnosis and early initiation of the antifungal therapy.

Seven out of twelve patients had a fungal culture done from the tissue or the peritoneal fluid. Only one of these had a positive culture for *Basidiobolus* (Table 2). One other patient had the isolation of other fungal species (*Candida* and *Aspergillus*) from the



peritoneal fluid but not Basidiobolus. This is consistent with the available literature that reports a low yield from tissue fungal cultures, as low as 50% [5,8]. Waiting for culture confirmation usually takes 4–6 weeks, which could adversely affect the outcome.

Zabolinejad et al., Al Shanefy et al., and Shreef et al. reported that surgical excision has a pivotal role in treatment [1,2,8]. From our series, we found that surgical excision at presentation was not feasible, mainly due to the amalgamated nature of the mass and involvement of multiple loops of small and large bowel. Surgical excision would have carried a considerable risk of increased morbidity due to a high chance of inadvertent bowel injury and injury to surrounding structures. In our series, surgical intervention was limited to obtaining a tissue biopsy and dealing with complications of the disease. The mass was not resected in any of our patients and resolved completely after the completion of antifungal treatment, as evidenced by follow-up imaging.

Some centers have practiced surgical excision of the infected mass in pediatric and adult patients [1,2,8,10]. In our experience, surgical excision of mass has no role in the treatment of GIB. Uncomplicated patients in our series, who received antifungal treatment without the excision of the infected mass showed full recovery, and this has been stressed in literature by Ezzedien et al. as well [7].

## 6. Conclusion

Gastrointestinal Basidiobolomycosis is a rare disease, more so in the pediatric age group. Diagnosis can be challenging because of confusion with abdominal malignancies and other inflammatory diseases. Children affected by this infection are usually healthy, immunocompetent with nothing in their past history to suggest susceptibility to infections.

In pediatric patients from rural areas with an abdominal mass, there should be a high index of suspicion of this invasive fungal disease. Early diagnosis with biopsy and histological reporting of fungal hyphae with eosinophilia, can significantly decrease morbidity and complications.

Fungal culture has poor yield and can take up to 4 weeks to be reported. Waiting for results of the fungal culture is not recommended and can delay start of therapy. Delay in therapy initiation may adversely affect the outcome.

Role of surgery is only in the management of complications. Surgical excision of the mass has no benefit in the course or outcome of the disease and might potentially increase the morbidity by injuring the bowel and surrounding structures.

Public awareness of hazards of vectors, such as lizards, and good hygiene should be practiced in areas where it is more prevalent.

## Declaration of competing interest

The Authors have no interests to declare.

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## Visual abstract

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## References

- [1] Zabolinejad N, Naseri A, Davoudi Y, Joudi M, Aelami MH. Colonic basidiobolomycosis in a child: report of a culture-proven case. *Int J Infect Dis* 2014 May 1;22:41–3.
- [2] Al-Shanafey S, AlRobean F, Hussain IB. Surgical management of gastrointestinal basidiobolomycosis in pediatric patients. *J Pediatr Surg* 2012 May 1;47(5):949–51.
- [3] Vikram HR, Smilack JD, Leighton JA, Crowell MD, De Petris G. Emergence of gastrointestinal basidiobolomycosis in the United States, with a review of worldwide cases. *Clin Infect Dis* 2012;54:1685–91.
- [4] Edington GM. Phycomycosis in ibadan, western Nigeria. *Trans R Soc Trop Med Hyg* May 1964;58(3):242–5.
- [5] Geramizadeh B, Heidari M, Shekarkhar G. Gastrointestinal basidiobolomycosis, a rare and under-diagnosed fungal infection in immunocompetent hosts: a review article. *Iran J Med Sci* 2015 Mar;40(2):90.
- [6] Joe LK, Eng NI, Pohan A, Van der Meulen H, Emmons CW. Basidiobolus ranarum as a cause of subcutaneous mycosis in Indonesia. *AMA Arch Dermatol* 1956 Oct 1;74(4):378–83.
- [7] Rabie ME, Al Qahtani AS, Jamil S, Mikhail NT, El Hakeem I, Hummadi A, et al. Gastrointestinal basidiobolomycosis: an emerging potentially lethal fungal infection. *Saudi Surg J* 2019 Jan 1;7(1):1.
- [8] Shreef K, Saleem M, Saeedd MA, Eissa M. Gastrointestinal basidiobolomycosis: an emerging, and a confusing, disease in children (a multicenter experience). *Eur J Pediatr Surg* 2018 Apr;28:194–9. 02.
- [9] El-Shabrawi MH, Kamal NM, Jouini R, Al-Harbi A, Voigt K, Al-Malki T. Gastrointestinal basidiobolomycosis: an emerging fungal infection causing bowel perforation in a child. *J Med Microbiol* 2011 Sep 1;60(9):1395–402.
- [10] Lyon GM, Smilack JD, Komatsu KK, Pasha TM, Leighton JA, Guarner J, et al. Gastrointestinal basidiobolomycosis in Arizona: clinical and epidemiological characteristics and review of the literature. *Clin Infect Dis* 2001 May 15;32(10):1448–55.
- [11] Almoosa Z, Alsuhailani M, AlDandan S, Alshahrani D. Pediatric gastrointestinal basidiobolomycosis mimicking malignancy. *Med Mycol Case Rep* 2017 Dec 1;18:31–3.
- [12] Al-Juaid A, Al-Rezqi A, Almansouri W, Maghrabi H, Satti M. Pediatric gastrointestinal basidiobolomycosis: case report and review of literature. *Saudi J Med Med Sci* 2017 May;5(2):167.
- [13] Mandhan P, Hassan KO, Samaan SM, Ali MJ. Visceral basidiobolomycosis: an overlooked infection in immunocompetent children. *Afr J Paediatr Surg: AJPS (Asian J Plant Sci)* 2015 Jul;12(3):193.
- [14] Al-Maani AS, Paul G, Jardani A, Nayar M, Al-Lawati F, Al-Balushi S, et al. Gastrointestinal basidiobolomycosis: first case report from Oman and literature review. *Sultan Qaboos Univ Med J* 2014 May;14(2):e241.