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CASE REPORT

Gastrointestinal Basidiobolomycosis

First case report from Oman and literature review

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الفطريات الدعامية (باسيديومايكوسيس) في الجهاز الهضمي

أول حالة يتم تشخيصها في سلطنة عمان مع مراجعة للأدبيات

أمل المعنية، جورج بول، أمينة الجردانية، مدافن ناير، فاطمه اللواتية، شيخه البلوشية، إبراهيم حسين

ABSTRACT: Gastrointestinal basidiobolomycosis (GIB) is a rare fungal infection with few reported cases worldwide. We report here the first case diagnosed in Oman in a previously healthy 5-year-old Omani female child who had been thought initially to have an abdominal malignancy. The case was referred to the Royal Hospital, Muscat, Oman, in July 2012. She was treated successfully with surgical resection and prolonged antifungal therapy (voriconazole). Physicians, including clinicians, radiologists and pathologists, should have a high index of suspicion for GIB when a patient presents with an abdominal mass and fever.

Keywords: Mycoses; Zygomycosis; Entomophthorales; Gastrointestinal Diseases; Child; Case Report; Oman.

الملخص: تعتبر عدوى فطر باسيديومايكوسيس في الجهاز الهضمي من الحالات النادرة على مستوى العالم. ندرج هنا الحالة الأولى من نوعها في سلطنة عمان أصابت طفلة كانت بصحة جيدة في السابق، وشخصت مبدئيا على إنها ورم خبيث في البطن. وحولت الحالة إلى المستشفي السلطاني بمسقط في يوليو من عام 2012م. عولجت الحالة بنجاح عن طريق التدخل الجراحي ومضاد الفطريات فوريكونازول. يجب على الأطباء بما فيهم الممارسون وأخصائيو الأشعة وعلم الأمراض والجراحون وأطباء الجهاز الهضمي أن يكونوا على درجة عالية من الشك في عدوى الفطريات الدعامية (باسيديومايكوسيس) كتشخيص محتمل للمرضى المصابين بحمى وورم في الجهاز الهضمي.

مفتاح الكلمات: فطار؛ فطار عفني؛ الحاشوراوات؛ الجهاز الهضمي؛ طفل؛ تقرير حالة؛ عمان.

Basidiobolomycosis is a known fungal infection of the skin and soft tissue in otherwise healthy individuals. Gastrointestinal basidiobolomycosis (GIB) is an uncommon infection in childhood. Few cases have been reported in the literature.[1,2] The disease commonly manifests with fever, nausea, vomiting, abdominal pain, diarrhoea and/or an abdominal mass. Its non-specific presentation and unknown risk factors make it difficult to diagnose. In most reported cases the initial diagnosis is malignant neoplasm, tuberculosis or inflammatory bowel disease.[3–5]

A definite diagnosis of basidiobolomycosis requires a microbial culture of *Basidiobolus ranarum* from fresh aspiration or surgical specimens. Histopathological examinations reveal a characteristic appearance of the culture.[6] A favourable outcome depends on early diagnosis, the institution of appropriate antifungal therapy and surgical debulking.[1]

In the Middle East, the largest series of paediatric GIB cases was seen in Saudi Arabia, with 11 reported in 2012.[1,7,8] This paper reports the first case of laboratory-confirmed abdominal basidiobolomycosis in a child from Oman.

Case Report

A 5-year-old Omani female was referred to the Royal Hospital, Muscat, Oman, in July 2012 with a two-week history of nausea, vomiting, abdominal pain and low-grade fever. The child had been diagnosed with acute appendicitis in a regional hospital and had had an appendectomy. The intraoperative findings suggested a normal appendix with a paracaecal mass. The subsequent histopathological examination also showed that the appendix and regional lymph nodes had no significant morphological abnormalities. The postoperative course was eventful with high fever and the slow return of bowel functions. An ultrasound of the abdomen revealed a hypoechoic circumferential mural thickening involving the *caecum* and ascending colon with luminal effacement suggestive of colitis or typhilitis. A computed tomography (CT) scan of the abdomen showed a large mass of heterogeneous

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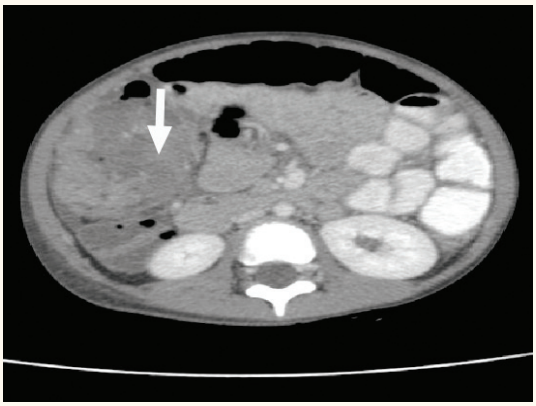

Figure 1: A large mass of heterogeneous density (arrow) in the right iliac fossa inseparable from the bowel loops with a markedly thickened irregular bowel wall involving the *caecum*, ascending colon and, to a lesser extent, the terminal ilium.

density in the right iliac fossa inseparable from the bowel loops, with a markedly thickened irregular bowel wall involving the *caecum* and ascending colon and, to a lesser extent, the terminal ileum, probably suggestive of non-Hodgkins lymphoma, typhilitis or adenocarcinoma [Figure 1].

The parents noticed that the child had lost a significant amount of weight (2.5 Kg) in a month even though she had previously been healthy and had had no blood-stained stools, constipation or *pica*. She had no history of recent travel abroad or contact with sick people. The child attended school regularly and had no history of previous hospital admissions. The family, who lived in the Al-Dakhiliyah region of Oman, an area with many arable farms surrounded by large areas of desert, used the government water supply for drinking. Her past medical and family histories were insignificant and she was fully immunised for her age.

The physical examination on admission revealed a sick, febrile child with a few palpable discrete and non-tender lymph nodes in the neck. No skin rashes or oral thrush was noted. The abdomen was soft with a tender large mass in the right iliac fossa. The liver and spleen were not palpable.

At this stage, the differential diagnoses were abdominal malignancy, lymphoma, inflammatory bowel disease, tuberculosis or infected fluid collection. Hence, an urgent ultrasound-guided aspiration and biopsy of the abdominal mass were done. The aspiration showed purulent fluid which was sent for both culture and cytological examinations. In addition, a true-cut biopsy specimen was sent for histological examination. The child was then started on piperacillin-tazobactam, gentamicin and metronidazole.

The complete blood count (CBC) highlighted a remarkable increase in eosinophils (6.2 x 10^9/L) with a total white blood count (WBC) of 14.2 x 10^9/L.

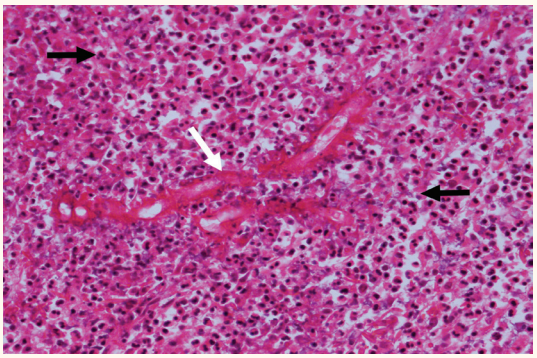

Figure 2: Fungal *hyphae* surrounded by the Splendore-Hoeppli phenomenon (white arrow) and dense eosinophil infiltrates (black arrows) at x 40 magnification with haematoxylin and eosin stain.

The peripheral blood film showed no significant morphological abnormalities other than eosinophilia. Her erythrocyte sedimentation rate, lactate dehydrogenase amounts, uric acid levels and chest X-ray were all normal.

On the third day of admission, the cytology report of the mass aspirate showed fungal filaments resembling mucormycosis. Liposomal amphotericin B was added to the existing course of antibiotics. She continued with intermittent high-grade fevers up to 39 °C. She also had nausea and colicky abdominal pain which were suggestive of a partial obstruction.

The patient underwent an exploratory laparotomy which revealed a large, inflamed, necrotic mass arising from the *caecum* and ascending colon. The mesentery adjacent to the mass was found to be thickened. A small ulceration was seen in the colonic *mucosa* close to the resection margin. A few slightly enlarged mesenteric lymph nodes were present. The liver and spleen appeared normal. A right hemicolectomy was performed and the bowel continuity was restored by an ileocolic anastomosis.

Posaconazole was added to the antifungal regimen and after two days the patient's temperature started to lower and her abdominal pain improved significantly. The surgical wound still showed redness and induration despite the child being on liposomal amphotericin B and posaconazole. Therefore, she underwent extensive debridement of the abdominal wall and swabs were sent for bacterial and fungal cultures.

The histopathological examination of the resected mass showed numerous scattered broad pauciseptate fungal *hyphae* embedded in eosinophilic material rich in eosinophils and some neutrophils representing the Splendore-Hoeppli phenomenon [Figure 2]. The special stains showed no acid fast *bacilli* and there was no evidence of malignancy.

A subculture on Sabouraud's dextrose agar yielded *Basidiobolus spp*. On the third day of inoculation, the

colonies were initially white and radially-folded with short aerial *hyphae*. With age, the colonies turned cream to yellow-brown in colour. The microscopic examination revealed pauciseptated *hyphae* measuring 5–20 µm wide. Some of the *hyphae* fragmented into short hyphal bodies. Zygospores with two beak-shaped remnants of the copulation tube established this organism as *Basidiobolus spp.* [Figures 3 A and B]. Another sample from the infected surgical wound also grew the *Basidiobolus* species.

The antifungal therapy was modified after isolating the *Basidiobolus spp*. Liposomal amphotericin B and posaconazole were discontinued and intravenous voriconazole was started at a dose of 8–15 mg/Kg/day, divided into two 12-hourly doses. The abdominal wound was closed when repeated cultures showed no fungal growth. On the 28th day, the patient was discharged with a three-month course of oral voriconazole (15 mg/Kg/day, divided into two 12-hourly doses).

When she visited the outpatient clinic a month later, the patient showed a dramatic improvement in her general condition. She had started gaining weight and the wound was healing well. Her CBC showed a normal eosinophil count and the abdominal ultrasound showed no masses or thickening of the bowel. It was decided to keep her on antifungal treatment for a year with follow-up visits at three-month intervals. It was also decided to perform abdominal CT/magnetic resonance imaging scans a week prior to the end of therapy, or sooner if she became symptomatic again.

Discussion

Zygomycosis is caused by the *Mucorales* and *Entomophthorales* orders of fungi. Entomophthoromycosis consists of both basidiobolomycosis and conidiobolomycosis. *Basidiobolus ranarum*, as a causative species of basidiobolomycosis, was first isolated in 1955 in the USA from decaying plants and was later found in soil and vegetation worldwide.[9] It can be found in the faeces of amphibians, reptiles and insectivorous bats and is known to cause skin and soft tissue infections in otherwise healthy individuals. Recently, basidiobolomycosis has emerged primarily as a systemic infection of the alimentary tract; however, as it generally does not invade the blood vessels, it rarely disseminates.[10]

Vikram *et al*. reported the worldwide occurrence of GIB between 1964 and 2010 as 44 cases.[1] Of those, a total of 19 cases were reported from the USA, of which 17 were from Arizona alone. A probable environmental link to the desert climate was suggested. Saudi Arabia had the second highest prevalence with a total of 11 cases. The youngest patient was 2 years old and the oldest 81 years old. The majority of patients presented with abdominal pain, an abdominal mass, fever, weight loss, constipation and/or diarrhoea. Most of the patients had peripheral eosinophilia (76%) and the culture was positive in 71% of the cases. The colon and rectum were the most commonly involved organs, but it can also infect the small bowel, liver and stomach.[1,8]

Predicting potential risk factors that predispose a person to GIB is limited in these different case series by the small number of patients, incomplete patient information and variations in the follow-up period. A six-patient case-control study from 2001 suggested that male gender, a history of diabetes mellitus, peptic ulcer disease and *pica* could be risk factors, but these were hard to confirm in a later larger cohort.[1,11]

On histopathological examination, the fungal *hyphae* are irregularly branched, thin-walled and occasionally septate. In most reported cases, the fungal *hyphae* were surrounded by a thick eosinophilic cuff—the Splendore-Hoeppli phenomenon.[12] This

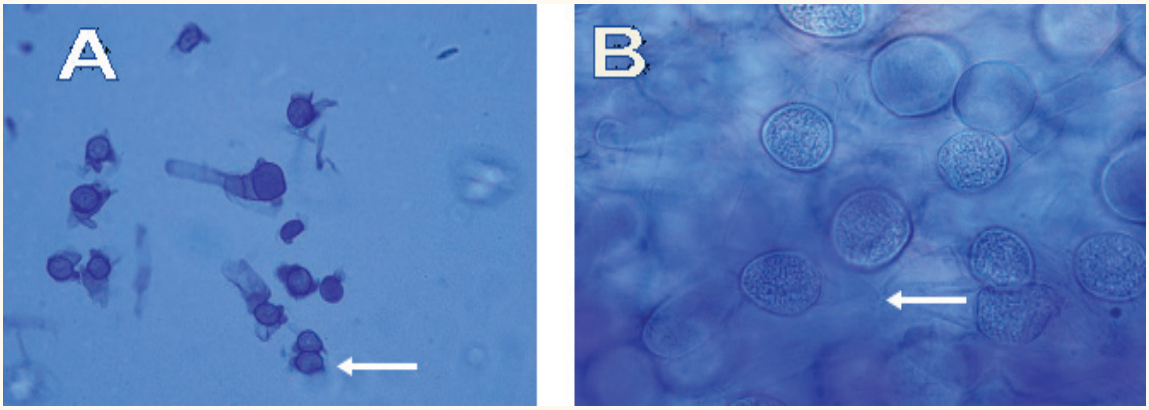

Figure 3 A & B: Microscopic morphology of Basidiobolus spp showing globose one-celled conidia that are forcibly discharged from a sporophore (arrow) at x 100 magnification with lactophenol blue stain (**A**). Microscopic morphology of Basidiobolus spp showing numerous round smooth thick-walled zygospores (arrow) at x 100 magnification (**B**).

phenomenon is not specific to GIB and can also be seen around other fungi, helminths or their *ova*, bacterial colonies or, rarely, around suture material in tissues.[3]

The treatment for GIB combines both surgical resection and appropriate antifungal therapy. The possibility of eradicating the infection using only antifungal therapy without surgical resection remains theoretical as there have not been many opportunities to follow this treatment method. The importance of early surgical intervention for paediatric GIB was emphasised in a retrospective review of nine paediatric cases managed at the King Faisal Specialist Hospital & Research Centre, Riyad, Saudi Arabia.[13] The azole antifungal group is considered the best for treating GIB, including ketoconazole, itraconazole and voriconazole. There is concern about the resistance of *B. ranarum* to amphotericin B products and some reported mortality in patients treated with them.[10,14]

Almost all previously reported cases were initially misdiagnosed as inflammatory bowel disease, malignancy, diverticulitis, appendicitis and gastrointestinal tuberculosis, among others.[1,3–5,9,15] In the current case, the patient was initially thought to have appendicitis and then was referred to the Royal Hospital in order to rule out lymphoma. Limited awareness about the histopathological findings in such an infection led to a misleading report that suggested mucormycosis in the patient. This resulted in the delay in instituting the proper antifungal course of treatment earlier in the course of the illness.

The previously healthy child reported in this report presented with abdominal pain, abdominal mass, fever and weight loss. She had *caecal* and colonic involvement. Her CBC showed peripheral eosinophilia. The histopathology of the biopsy showed typical fungal *hyphae* surrounded by the Splendore-Hoeppli phenomenon, which together with the clinical input met the definition of probable GIB. The fungal culture later confirmed the diagnosis. This case highlights the crucial importance of performing appropriate cultures to confirm the diagnosis of GIB. She had a successful outcome with surgical resection and prolonged antifungal treatment. This is the first reported and diagnosed case of GIB in Oman; however, some cases may have been missed previously, especially those with atypical presentations and/or no request for microbial cultures.

Conclusion

GIB is an invasive fungal infection that should be among the differential diagnoses for children presenting with abdominal masses and fever. An awareness of this condition among paediatricians, paediatric surgeons and pathologists may lead to the discovery of more cases and help the treating physician to arrive at a diagnosis earlier and manage the case appropriately. A worldwide collection of case studies is needed to identify risk factors for GIB.

References

1. 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. doi: 10.1093/cid/cis250.
2. El-Shabrawi MH, Kamal NM. Gastrointestinal basidiobolomycosis in children: An overlooked emerging infection. J Med Microbiol 2011; 60:871–80. doi: 10.1099/jmm.0.028670-0.
3. Nemenqani D, Yaqoob N, Khoja H, Al Saif O, Amra NK, Amr SS. Gastrointestinal basidiobolomycosis: An unusual fungal infection mimicking colon cancer. Arch Pathol Lab Med 2009; 133:1938–42. doi: 10.1043/1543-2165-133.12.1938.
4. van den Berk GE, Noorduyn LA, van Ketel RJ, van Leeuwen J, Bemelman WA, Prins JM. A fatal pseudo-tumour: Disseminated basidiobolomycosis. BMC Infect Dis 2006: 6:140. doi: 10.1186/1471-2334-6-140.
5. Zavasky DM, Samowitz W, Loftus T, Segal H, Carroll K. Gastrointestinal zygomycotic infection caused by Basidiobolus ranarum: Case report and review. Clin Infect Dis 1999; 28:1244–8. doi: 10.1086/514781.
6. Yousef OM, Smilack JD, Kerr DM, Ramsey R, Rosati L, Colby TV. Gastrointestinal basidiobolomycosis. Morphologic findings in a cluster of six cases. Am J Clin Pathol 1999; 112:610–6.
7. Al Jarie A, Al-Mohsen I, Al Jumaah S, Al Hazmi M, Al Zamil F, Al Zahrani M, et al. Pediatric gastrointestinal basidiobolomycosis. Pediatr Infect Dis J 2003; 22:1007–14.
8. Khan ZU, Khoursheed M, Makar R, Al-Waheeb S, Al-Bader I, Al-Muzaini A, et al. Basidiobolus ranarum as an etiologic agent of gastrointestinal zygomycosis. J Clin Microbiol 2001; 39:2360–3. doi: 10.1128/JCM.39.6.2360-2363.2001.
9. Drechsler C. A Southern basidiobolus forming many sporangia from globose and from elongated adhesive conidia. J Wash Acad Sci 1955; 45:49–56.
10. Pasha TM, Leighton JA, Smilack JD, Heppell J, Colby TV, Kaufman L. Basidiobolomycosis: An unusual infection mimicking inflammatory bowel disease. Gastroenterology 1997; 112:250–4. doi: 10.1016/S0016-5085(97)70242-7.
11. 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; 32:1448–55. doi: 10.1086/320161.
12. Hussein MR, Musalam AO, Assiry MH, Eid RA, El Motawa AM, Gamel AM. Histological and ultrastructural features of gastrointestinal basidiobolomycosis. Mycol Res 2007; 111:926–30. doi: 10.1016/j.mycres.2007.06.009.
13. Al-Shanafey S, AlRobean F, Bin Hussain I. Surgical management of gastrointestinal basidiobolomycosis in pediatric patients. J Pediatr Surg 2012; 47:949–51. doi: 10.1016/j.jpedsurg.2012.01.053.
14. Yangco BG, Okafor JI, TeStrake D. In vitro susceptibilities of human and wild-type isolates of Basidiobolus and Conidiobolus species. Antimicrob Agents Chemother 1984; 25:413–6. doi: 10.1128/AAC.25.4.413.
15. Saadah OI, Farouq MF, Daajani NA, Kamal JS, Ghanem AT. Gastrointestinal basidiobolomycosis in a child: An unusual fungal infection mimicking fistulising Crohn's disease. J Crohns Colitis 2012; 6:368–72. doi: 10.1016/j.crohns.2011.10.008.