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Case report

Colonic basidiobolomycosis presenting with intestinal obstruction and a normal eosinophil count

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ABSTRACT

Gastrointestinal basidiobolomycosis (GIB), caused by *Basidiobolus ranrum*, is a rare fungal infection with a limited geographic distribution. The majority of the cases are reported from the warm areas of Arizona in USA, Saudi Arabia and Iran.

We report a middle aged patient who was admitted to hospital with suspected metastatic colonic carcinoma. He presented with constipation, anorexia and weight loss. Computed tomography scan disclosed a mass involving the mid and distal sigmoid colon and hypodense lesion in hepatic segment IV. Excised tissue during a Hartmann's surgery showed an extensive eosinophil-rich transmural inflammation with mural necrotizing granulomas and several broad septated fungal hyphae. He was commenced on voriconazole following surgery. The diagnosis of basidiobolomycosis was established by histopathological examination. Since the diagnosis was not suspected preoperatively tissue culture for fungi was not collected. However molecular testing confirmed the diagnosis of GIB. Therapy involved a combination of surgical resection of the mass and prolonged voriconazole treatment. Increased awareness among physicians is needed for early diagnosis and treatment of GIB.

Introduction

Gastrointestinal basidiobolomycosis (GIB), caused by *Basidiobolus ranrum*, is a rare fungal infection that is described mostly in immunocompetent patients [1]. A recent literature search revealed only 44 published reports in adults [2]. The colon is the most commonly involved organ (82%), followed by the small bowel (36%). On the other hand, liver and biliary disease are reported in less than 30% of GIB cases [3,4].

B. ranarum was first described by Eidam in 1886 following its isolation from frogs' dung and intestinal products [5]. Theorganism can be found in decaying vegetation, foodstuffs, fruits, and soil. It is also excreted from the gastrointestinal tracts of reptiles, amphibians, fish, and insectivorous bats [6]. While *B. ranarum* is of worldwide distribution, GIB is most commonly reported in the tropical and subtropical areas of the world [7]. The first presumed case of GIB, described in 1964, was that of a 6-year-old Nigerian boy [8]. Overall, the majority of the reported cases have been from the desert region of the USA (mainly Arizona) and from Middle Eastern countries [1,9]. In Saudi Arabia, the largest number of the cases has been detected in Tohama, in the southern area. Both Tohama and Arizona share a warm and humid climate that boosts the growth of *B. ranarum*.

GIB is a great mimicker. A number of patients have initially been suspected to have malignancy, inflammatory bowel disease (IBD), or chronic infections like tuberculosis [10,11]. For this reason and due to the unfamiliarity of the physicians with the disease, basidioblomycosis is usually either accidently discovered during surgery or misdiagnosed as tuberculosis or IBD. Hence, and due to the rarity of the disease, a high index of suspicion is required for accurate diagnosis [1]. Serological tests and histopathological findings can help in diagnosing the condition; however, the most definitive diagnostic test is fungal culture [12].

Case report

A 70-year-old diabetic man was admitted to the hospital with constipation, diffuse abdominal pain, anorexia and weight loss for one month. He denied fever, melena, or rectal bleeding.

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He lived in Aseer, in the southern part of Saudi Arabia. Examination was essentially normal apart from tenderness in the lower abdomen. No palpable masses could be felt. The rectum was empty on rectal examination.

Investigation revealed a white cell count of 11,900 /μl, hemoglobin of 12.9 g/dL, and platelets of 337,000/μl. The eosinophil count was normal 0.4 (NR 0.0–0.6 × 10^9/l). Carcinoembryonic antigen (CEA) and cancer antigen 125 (CA-125) were 3.3 (range 0.0–3.4 ug/L) and 54 (range 0–35 U/mL), respectively. The C-reactive protein (CRP) was normal, while the erythrocyte sedimentation rate (ESR) was 32 mm/hr. Colonoscopy disclosed an ulcerated rectosigmoid mass 20 cm from anal verge, obstructing the bowel lumen. An abdominal computerized tomography (CT) scan (Fig. 1A & B) confirmed a large irregular circumferential mass (10 cm length X4.5 cm transverse diameter) involving the mid and distal sigmoid colon. Furthermore, regional lymphadenopathy, mild ascites, and diffuse peritoneal fat stranding were noted. A subcentrimetric (8 mm) hypodense lesion was detected in hepatic segment IV, likely representing metastatic deposits. (Fig. 1C) A sigmoid mass invading through the small bowel mesentery was seen during emergency exploratory laparotomy, so a Hartmann's procedure, involving resection of the rectosigmoid colon with closure of the anorectal stump and formation of an end colostomy, was performed. The postoperative course was uneventful.

A site of perforation was noted on the gross histopathology. Microscopically, an extensive eosinophil-rich transmural inflammation was seen with mural necrotizing granulomas and abscesses. Several broad septated fungal hyphae were noted with the characteristic Splendore-Hoeppli phenomenon. (Fig. 2A,B). This is an intense amorphous esoinophilic substance with star-like appearance surrounding the micro-organism. Periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS) stains were positive in the fungal walls. These features were highly suggestive of colonic basidiobolomycosis (Fig. 3A,B). Since the disease was not suspected preoperatively, the tissue was not sent for fungal culture. However, molecular testing using PCR assay was performed with Panfungal specific primers that amplified the internal transcribed spacer 1 and 2 regions of the ribosomal DNA. Sequence analysis of the PCR products using the Basic Local Alignment Search Tool (BLAST) confirmed the fungal pathogen to be *Basidiobolus ranarum.*

Three months following combined surgery and voriconazole treatment, he remained asymptomatic and compliant with his medications. He was planned for a six-month oral voriconazole therapy.

Discussion

GIB poses diagnostic difficulties as its clinical presentation is non-specific. Abdominal pain, anorexia, and loss of weight were found in all patients with colonic basidiobolomycosis, and less common symptoms include diarrhea (9.0%) and lower gastrointestinal bleeding (13.6%) [4]. Our case presentation was suspicious for metastatic colon cancer in view of the patient's age and the presence of the colonic mass. The hepatic lesion was questionable for metastasis. In such patients the presence of eosinophilia can favor the diagnosis of GIB. Remarkably, our patient's eosinophil count remained normal before and following surgery. Peripheral eosinophilia is observed in 76–94.0% of the

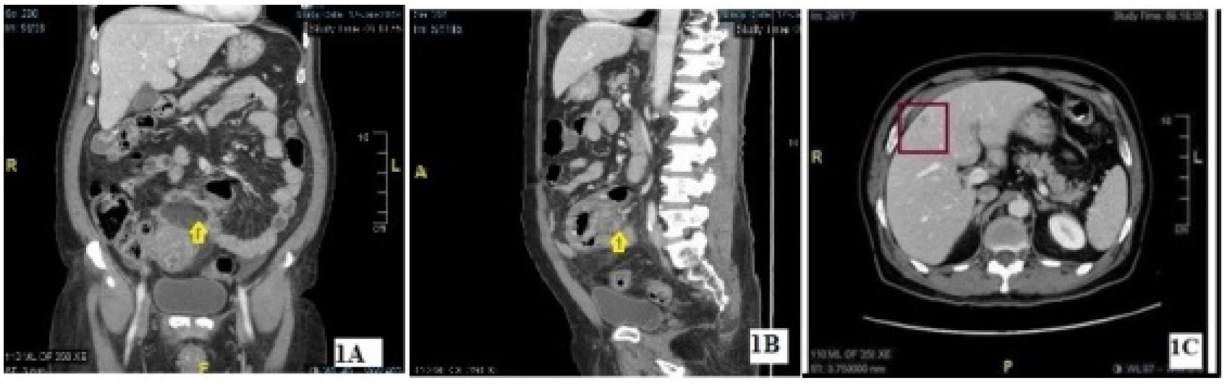

Fig. 1. CT scan of abdomen with contrast (A & B): Coronal and sagittal section showing large irregular circumferential mass involving mid and distal sigmoid colon (yellow arrows). **C:** Axial section showing a subcentrimetric (8mm) hypodense lesion in hepatic segment IV (red square).

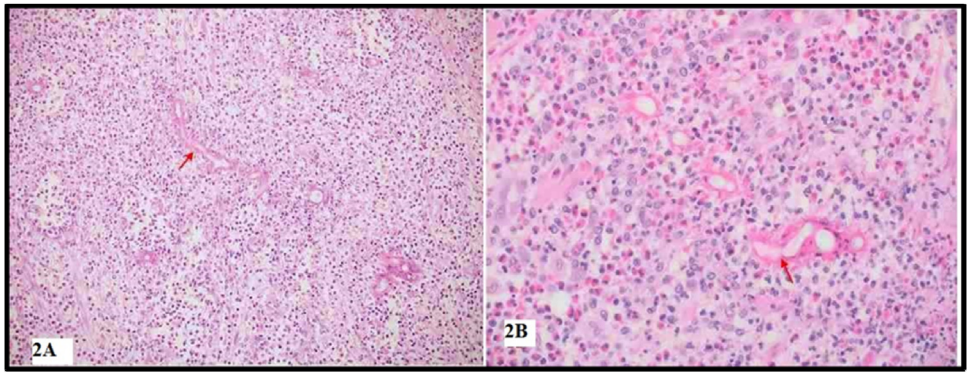

Fig. 2. A: H&E STAIN, X200 magnification showing several broad fungal hyphae within necrotizing granuloma (red arrow). B: High-power magnification showing Splendore-Hoeppli phenomenon with abundant eosinophils (red arrow).

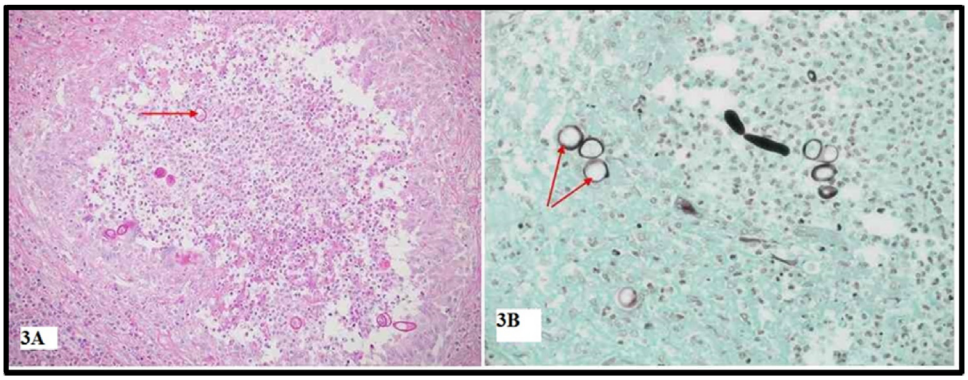

Fig. 3. A: Periodic acid-Schiff (PAS) stain highlights a thin-walled fungal hyphae (PAS stain x 200 magnification) (red arrow). B: Positive GMS stain in the fugal walls (red arrows) (GMS stain x 400 magnification).

cases [1,13,14]. Interestingly, the persistence of peripheral eosinophilia following surgery could indicate an on-going focus of infection and demand further investigation [1]. Our patient's hepatic mass was suspicious for distant infection. Unfortunately, biopsies were not possible in view of the subtle nature of the masses. Concomitant hepatic and colonic masses are extremely rare in adults [15,16].

Unlike mucormycosis, GIB is only rarely angioinvasive, with liver and pulmonary dissemination reported in a few cases [17]. On the other hand, colonic and concomitant liver lesions are more commonly reported in children. A case published in 2018 from Riyadh, Saudi Arabia, presented a 12-year-old boy with colonic basidiobolomycosis and hepatic dissemination which was mistakenly treated as intestinal tuberculosis. Subsequently, a biopsy confirmed GIB. He had a successful outcome following a course of itraconazole [18]. Another unusual feature in the case presented is the presence of bowel perforation. Although thickening of the bowel wall was seen in 25% of cases, bowel perforation, as seen in our patient, is very uncommon and occurred in only two patients [1,19]. In addition, GIB may have a similar picture to inflammatory bowel disease. A 5-year-old Saudi boy was initially identified as having Crohn's disease due to presence of three skip lesions in addition to other features observed during colonoscopy. Ultimately, the histopathology findings confirmed the diagnosis of GIB. Consequently, treatment with voriconazole led to an excellent outcome [11].

Similar to previous case reports, our patient did not have a tissue culture. The histopathology was distinctive. Although Splendore-Hoeppli phenomenon can occur in a number of infectious and eosinophilic non-infectious conditions, its presence in a male patient from an endemic area should raise suspicion of GIB [20]. The described patient was from the Aseer area, which is endemic for GIB, and had a classical pathological picture. The PCR test further confirmed the diagnosis.

Optimal treatment of GIB requires combined early aggressive surgical intervention and prolonged use of antifungals. A combination of surgery plus antifungal treatment was used in the majority (77.5%) of patients [14]. There is no current consensus on the antifungals to be used to treat this disease. Importantly, *B. ranrum* is inherently resistant to amphotericin B, with well-documented failures of up to 50% [21]. Azoles are the usual effective antifungals used. There is well-established experience with prolonged itraconazole treatment. Recently, voriconazole has been used with good success, while posaconazole is described in a number of case reports. Despite aggressive treatment, the mortality remains high at 20% within 2 years [1]. High index of suspicion, early intervention, and close follow-up are essential to improving the prognosis.

Our patient's eosinophil count and inflammatory markers, including CRP, were normal, precluding objective assessment for recurrence. Remarkably, the CA-125 level was high. Previous studies have demonstrated increased CA-125 levels in granulomatous diseases including pelvic coccidiomycosis and tuberculosis [22]. In one study, 40% of active pulmonary TB patients had a raised serum CA-125 with a mean level of 38.9 U/mL. Although of doubtful diagnostic significance, the test may be used for monitoring the response to treatment and detection of relapses in tuberculosis [23]. More work is needed before recommending the use of this test in GIB.

Conclusion

GIB is an emerging disease in southwestern Saudi Arabia. Diagnosis of GIB is always challenging because it is rare and has non-specific symptoms that mimic other more common conditions. Colonic basidiobolomycosis is a life-threatening fungal infection that can necessitate urgent surgical interventions. Persistent elevation of eosinophil counts following surgery raises suspicion of fungal dissemination. The characteristic histopathological features are the key to proper diagnosis. In cases where there is a lack of both awareness and the facilities to diagnose such a rare disease, the diagnosis can be missed, putting patients at a heightened risk of morbidity and mortality. Increased awareness and further research are needed for a better understanding of GIB.

Conflicts of interest

None.

Funding

None.

Consent

"Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Dr. FE,SA, NM and AA had looked after the patient, made the diagnosis and followed up the treatment. Dr. Ahmed Al Barrag performed the molecular testing. All authors including contributed significantly to the study conception and design, data acquisition,

analysis, and interpretation, in addition to drafting and revising the article for intellectual content. They have all agreed to be accountable for all aspects of the work related to the accuracy or integrity of any part of the work and approval of the final version of the manuscript

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