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Case Report

CASE REPORT

An Infant with Acute Bloody Diarrhea and Gastrointestinal Basidiobolomycosis: An Unusual Presentation of a Rare Disease

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ABSTRACT

Basidiobolomycosis is a fungal infection caused mainly by *Basidiobolus ranarum*, a filamentous fungus of the order Entomophthorales and the family Basidiobolaceae. This infection typically involves the skin and soft tissue; however, visceral organ involvement has also been reported. Here, we report a case of gastrointestinal basidiobolomycosis in a young child who presented with acute bloody diarrhea which was initially misdiagnosed as intussusception.

KEYWORDS: entomophthorales/isolation and purification, zygomycosis/microbiology, zygomycosis/diagnosis, gastrointestinal tract/microbiology

INTRODUCTION

Basidiobolomycosis is a fungal infection caused mainly by *Basidiobolus ranarum*, a filamentous fungus of the order Entomophthorales and the family Basidiobolaceae [1]. This infection typically involves the skin and soft tissue [2]; the other presentation seen is visceral organ involvement, although this latter is rarely reported in the literature [3]. The gastrointestinal (GI) type is a visceral form of basidiobolomycosis in which the fungus can invade any region of the alimentary tract including the stomach, ileum and different segments of the colon [4].

The clinical presentation of GI basidiobolomycosis (GIB) is protean. This rare disease is often misdiagnosed as other conditions such as chronic granulomatous disease, malignancy, intussusception, inflammatory bowel disease or appendicitis [5]. Most patients are from tropical and subtropical areas [6]. A high index of suspicion is the key to an early

diagnosis of GIB in an immunocompetent patient with a compatible clinical presentation in these areas. Definitive diagnosis and treatment may not be possible before microscopic examination of specimens from the lesion; therefore, diagnosis may be postponed until after surgery [7]. In this study, we report a 16-month-old infant with GIB who lived in the subtropical region of southern Iran and presented with acute bloody diarrhea.

CASE PRESENTATION

A 16-month-old male infant living in Bandar Ganaveh, Bushehr Province, southern Iran, presented with bloody diarrhea, irritability and low-grade fever of 3 days' duration. He was treated for shigella-like diarrhea with cefixime for 5 days. However, he remained febrile and his irritability was increased both in severity and duration, and the patient had several episodes of projectile vomiting. He was referred to a private hospital in Shiraz with an impression of intussusception. The boy's growth index was in the normal range. His parents did not report a history of any previous medical diseases. Laboratory studies revealed leukocytosis (15 600 cells/ml) with 55% lymphocytes, 40% neutrophils and 5% monocytes, and low levels of red blood cells (RBCs; 3.92×10^6 cells/ml), hemoglobin (10.5 g/dl) and sodium (130 Meq/l) (normal values in our center are as follows: white blood cell (WBC): 5000–10 000 cells/ml, RBC: 4.5×10^6 -6×10^6 cells/ml, hemoglobin : 11.5–14 g/dl, sodium: 135–145 Meq/l). Abdominopelvic ultrasonography revealed a mass-like lesion measuring about $4.3 \times 3.5 \times 2.8$ cm in the pelvic cavity anterior to upper part of the rectum and above the urinary bladder, with a heterogeneous internal texture. Subsequent abdominopelvic magnetic resonance imaging (MRI) confirmed the presence of a mass attached posteriorly to the sigmoid colon and involving the rectum, and anteriorly to the upper surface of the bladder. Based on a preoperative impression of malignancy, the pediatric surgeon at this center removed the mass with a laparoscopic Hartmann's procedure. The mass had invaded the sigmoid colon lumen, leading to partial obstruction, and was completely resected. Partial sigmoidectomy (10 cm), excision of the proximal part of the rectum and appendectomy were carried out with clear margins, and a biopsy specimen was obtained from the urinary bladder dome. A colostomy was also done.

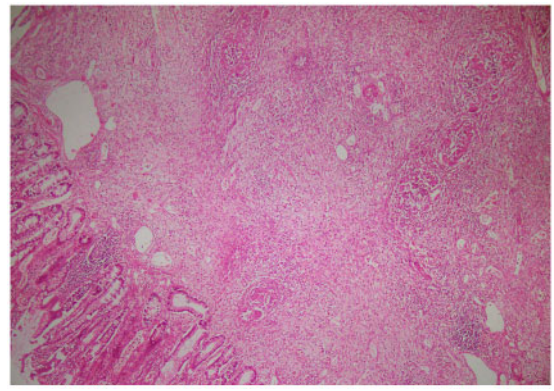

Fig. 1. Microscopic section shows low power view of colonic mucosa and submucosa with extensive acute and chronic inflammation and granuloma formation (Hematoxylin and Eosin, ×40).

Microscopic examination of biopsies of both the sigmoid specimen and urinary bladder dome revealed highly vascularized tissue with signs of transmural acute and chronic necrotizing inflammation with marked eosinophil infiltration and foreign body-type giant cell granulomatous reaction (Fig. 1). There were also congested areas with broad, thick-walled hyphae and the Splendore–Hoeppli phenomenon (Fig. 2). In addition, two resected lymph nodes showed fungal involvement. There was no evidence of dysplasia or malignancy in the embedded tissues. The pathologist made a presumptive diagnosis of intestinal basidiobolomycosis, the most common cause of intestinal zygomycosis in immunocompetent individuals.

The patient was referred to the pediatric infectious diseases ward for further evaluation and management. In the ward, laboratory analyses yielded the following values: WBCs: 17 300 cells/ml, RBC: 4.25×10^6 cells/ml, hemoglobin: 11.3 g/dl, platelets: 592 000 cells/ml, erythrocyte sedimentation rate (ESR): 62 mm/h and C-reactive protein: (CRP) 45 mg/l (normal values in our center are as follows: platelet: 150 000–450 000 cells/ml, ESR: 0–20 mm/h, CRP: 0–6 mg/l). Immune system tests were done, including human immunodeficiency virus antibody, complement and immunoglobulins

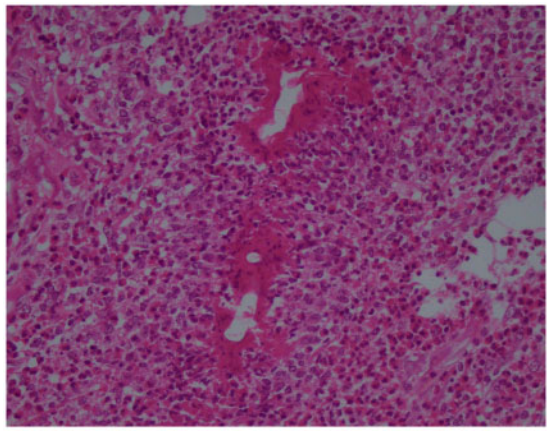

Fig. 2. Microscopic section shows broad and thick hyphae with Splendore-Hoeppli phenomenon surrounded by many eosinophils (Hematoxylin and Eosin, ×400).

levels, dihydrorhodamine and flow-cytometric assessment of lymphocyte subpopulations; however, none of them were suggestive of an immunodeficiency disorder. Material from the colostomy drainage was sent for Gram staining and culture, which disclosed a few puss cells and traces of occult blood. In the stool culture, neither salmonella nor shigella was isolated. Confirmation of the diagnosis was obtained with polymerase chain reaction (PCR), which showed 99% sequence identity for basidiobolomycosis [8].

Following the initial presumptive diagnosis of intestinal Zygomycosis, patient was treated with liposomal amphotericin B (1 mg/kg intravenously per day), potassium iodide (KI; 325 mg per 5 ml oral solution, 2 ml every 8 h) and co-trimoxazole (trimethoprim/sulfamethoxazole) (40 mg/200 mg per 5 ml oral solution, 5 ml twice per day) for 4 weeks. During his 1-month hospital stay, the patient became afebrile after 4 days. Leukocyte count, ESR and CRP decreased to 10 800 cells/ml, 38 mm/h, and 26 mg/l, respectively. Abdominopelvic sonography revealed no mass before discharge. The patient was discharged with KI and co-trimoxazole planned to continue for 6 months. At 6-month follow-up, he was well and KI and co-trimoxazole were discontinued. At the end of his treatment course, ESR and CRP were both normal, and abdominopelvic sonography and MRI revealed no mass.

DISCUSSION

GIB is considered an emerging fungal infection involving the alimentary tract, most commonly the colon and rectum (84.2%), and presenting with non-specific symptoms [7]. These symptoms can make prompt diagnosis and treatment difficult.

The clinical manifestations of this unusual fungal infection can be completely different from one patient to another, even with similar organ involvement [9]. In a recent review of 102 patients in 2019, the most common presentation of GI involvement of this infection was abdominal pain, seen in 86.3% of patients, followed by fever in 40.2%. Other symptoms include constipation, abdominal distension, weight loss and vomiting. Furthermore, in about one fifth of the cases, an abdominal mass was detected on physical examination or radiologic evaluation. Diarrhea, which was seen in our patient, has been reported in 13.7% of previous cases [7]. Because of its vague and non-specific presentation, the disease is often misdiagnosed initially, and has been confused mostly with malignancies, inflammatory bowel syndrome, or appendicitis. Our patient is the first case reported from Iran with acute bloody diarrhea; the only other patient reported to date with bloody diarrhea from Iran had a prolonged course of 1.5 months' duration [10].

Diagnosis requires a tissue biopsy of the affected organ, and histopathological examination and culture or PCR [11]. However, because the presentation of this infection closely mimics the signs and the symptoms of other diseases in many cases, specimens suitable for culture from the lesion may not be collected during the surgical procedure, and thus a presumptive diagnosis will be used instead of a definitive one [12]. This issue can result in the initiation of treatment for basidiobolomycosis without confirmation of the infection in a majority of patients, based only on microscopic diagnosis of biopsy samples with typical morphologic characteristics such as foreign body-type giant cell granulomatous reaction and the eosinophilic feature termed Splendore–Hoeppli phenomenon [13, 14]. This aspect of the diagnosis can have two significant consequences for therapy. First, the typical findings of eosinophilic material in the Splendore–Hoeppli phenomenon and the granulomatous reaction are not observed in all infections

by this filamentous fungal microorganism, and if the diagnosis is consequently not obtained, severe complications can ensue which may be life-threatening. According to one earlier study, in four cases the diagnosis was obtained only upon autopsy [7]. Therefore, as culture is the gold standard for the diagnosis of this infection, physicians in endemic regions with high numbers of GIB cases such as Saudi Arabia, Iran and the USA (Arizona state) [15] should consider the possibility of basidiobolomycosis infection in young patients with fever and abdominal pain coexisting with an abdominal or pelvic mass, especially those with a high rate of eosinophil infiltration and elevated ESR, and should request cultures and other assessments. Our center in Shiraz, a referral hospital in southern Iran, sees many cases with this clinical picture. Each year approximately two or three cases of basidiobolomycosis infection are diagnosed, with most patients from provinces in subtropical areas of Iran such as Bushehr and Hormozgan. At our center, when the histopathological examination is suggestive of this fungal infection, specimens are sent to the laboratory for PCR and the definitive diagnosis is based mainly on the results of this analysis. Second, these typical findings are not pathognomonic for basidiobolomycosis infection; the Splendore–Hoeppli phenomenon, including reactions surrounding the hyphae, can also be found in different fungal infections such as sporotrichosis, candidiasis, aspergillosis and blastomycosis [16]. The pathologic features of foreign body-type giant cell granulomatous reaction are observed in an even wider range of different etiologies associated with underlying infectious and non-infectious agents [17, 18]. However, the presence of these two typical morphologic features narrows the spectrum of likely diagnoses.

The therapeutic approach for basiobolomycosis depends on the patient's age, severity of symptoms, the organ(s) involved and the extent of involvement [15]. For GI involvement of this infection, a combination of surgical and medical approaches is usually used. During surgery, the infected tissues should be resected as completely as possible, and if GIB is subsequently diagnosed, medical regimens should be initiated. However, since GIB is uncommon, there are no comprehensive studies designed to assess the effect of different antifungal regimens, and consequently there is no standard antifungal regimen for treatment [19]. The antifungal agent used most commonly is itraconazole (53.8% of cases reported between 1964 and 2017), followed by amphotericin B (33.3%) [7]. However, due to the rather high cost of azole derivatives and high rate of resistance to amphotericin B (50%), their use is restricted, and there is growing interest in other antifungal therapies for GIB, such as KI, a more widely available and affordable alternative. Traditionally, KI has been used mainly to treat cutaneous and subcutaneous symptoms of basidiobolomycosis; however, it has also been used successfully for several patients at other centers, where complete resolution was achieved. This antifungal agent was also used to treat the young patient reported here.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was obtained from the patient's parents.

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