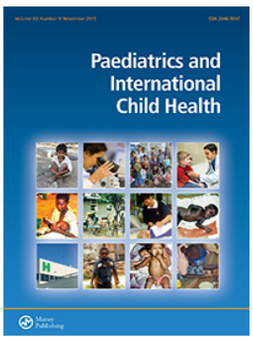

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Gastro-intestinal basidiobolomycosis in a 2-year-old boy: dramatic response to potassium iodide

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Gastro-intestinal basidiobolomycosis (GIB) is a rare fungal infection caused by *Basidiobolus ranarum*. Treatment includes surgical resection and long-term antifungal therapy. A 2.5-year-old boy presented with a 10-day history of abdominal pain, fever and diarrhoea, and a palpable abdominal mass was detected. Resection was undertaken and histology confirmed basidiobolomycosis. Treatment with amphotericin B and itraconazole was commenced, but the infection progressed and spread to involve the intestines, liver, ribs and lung, and also the abdominal wall after 6 months, requiring four operative procedures. Because of unresponsiveness to amphotericin and itraconazole, oral potassium iodide was added which resulted in complete resolution of the infection. Potassium iodide is an essential component of the treatment of systemic *B. ranarum*.

Keywords: Gastro-intestinal basidiobolomycosis, Potassium iodide, Fungal infection, Amphotericin B, Itraconazole

Introduction

Gastro-intestinal basidiobolomycosis (GIB) is a rare fungal infection caused by *Basidiobolus ranarum* which is generally associated with subcutaneous infections.[1,2] *B. ranarum* belongs to the entomophthorales order, although it was formerly categorised under the zygomycota class.[2] *B. ranarum* is an environmental saprophyte found worldwide; however, most reports of multi-organ involvement have come from sub-Saharan Africa and the tropical and sub-tropical areas of Asia, as well as from South-east Asia, Australia and North and South America.[1–3,4] Fewer than 50 cases of GIB were reported worldwide between 1964 and 2012.[5] The severity and progression of infection determines the treatment protocol, which often involves surgical resection along with long-term antifungal therapy (usually with itraconazole).[2]

A boy with *B. ranarum* infection is presented who had multi-organ involvement and responded to potassium iodide (KT).

Case Report

A previously healthy 2.5-year-old boy from the Lar area of Fars province (southern Iran) presented with a 10-day history of fever, abdominal pain, diarrhoea and vomiting. Axillary temperature was 37.6°C and a tender mass was palpable in the abdomen (epigastric region). The remainder of the examination was normal.

Investigations. Haemoglobin was 7.9 g/dl, white cell count 24.7×10^9/L [neutrophils 0.64 (0.15–0.45), lymphocytes 0.22 (0.44–0.74) and eosinophils 8% (1–4)], MCV 74.6 fl (72–88), MCH 24.0 pg/cell (25–31), platelet count 510×10^9/L (150–400), ESR 99 mm/h and serum IgE 2.16 mg/L (<0.14); kidney and liver function tests were normal. Computerised tomography (CT) of the abdomen demonstrated a large lesion with a diameter of 6 cm in the sub-hepatic area with connection to the transverse colon (Fig. 1). At laparotomy there was a large mass on the transverse colon which was attached to the lower border of the stomach. The mass was removed which required resection of the transverse colon.

Histopathological examination demonstrated transmural granulomatous inflammation, tissue eosinophilia and the presence of giant cells along with fungal hyphae. Broad, thin-walled septated hyphae surrounded by a dense eosinophilic sheath demonstrated Splendore–Hoeppli phenomenon (S-HP) (Fig. 2).

Amphotericin B was administered alone (1 mg/kg/day) for 3 weeks and the patient was discharged on

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75 mg/kg x 70 kg = 5250 mg!!

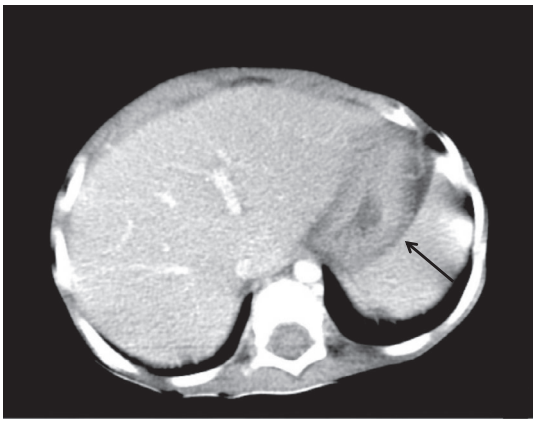

Figure 1 CT of the abdomen demonstrating a subdiaphragmatic collection between the right hepatic lobe and abdominal wall (arrow) 78×16 mm owing to extension of the fungus

amphotericin to be administered in a local hospital along with oral itraconazole (50 mg/12 h). After 1 month, a follow-up ultrasound demonstrated a soft tissue mass inferior to the liver which involved the abdominal wall and had close contact with bowel loops.

A second laparotomy 6 weeks after the first operation demonstrated involvement of the liver. Segmental hepatectomy, resection of the abdominal mass and segmental resection of the involved part of the ileum were undertaken. Amphotericin B (1 mg/kg/day) and itraconazole were continued and he was discharged after 4 weeks on itraconazole.

The patient was admitted for the third time 3 weeks later with an abdominal fluid collection and subcutaneous fungal infiltration. An ultrasound demonstrated a heterogeneous mass anterior to the liver involving the abdominal wall. At laparotomy, there was a hard mass in the abdominal wall anterior to the liver which involved the ipsilateral costal margins. The mass was resected and the two antifungal drugs were continued. After 4 months, the patient developed rib (6th rib, largely posterior part) and pulmonary involvement with a pleural effusion (Fig. 3) and a heterogeneous soft tissue mass in the right lateral abdominal wall.

The involved rib was resected and the pleural effusion was drained. Owing to unresponsiveness to amphotericin B and itraconazole, oral KI (75 mg/kg/day) was added. After 1 week the patient became afebrile. The amphotericin B, itraconazole and KI were continued after discharge to a local hospital. In total, the patient received these three drugs for 3 months. At follow-up, his general condition had improved and there was complete resolution of the abdominal, chest and subcutaneous lesions. Twenty-four months after completion of treatment, he was well with no relapse.

Discussion

Basidiobolomycosis is a rare fungal infection caused by *B. ranarum*, a filamentous fungi belonging to the basidiobolacea family, of the Entomophthorales order.[3,5] Basidiobolomycosis is mostly known as one of the chronic subcutaneous fungal infections; gastro-intestinal involvement is a rare form of the disease.[3,6] It mostly affects young males and is transmitted through traumatic inoculation of the skin.[7] In the absence of specific clinical symptoms, the manifestations of GIB are abdominal pain or mass, constipation, abdominal distention and fever.[4] Weight loss, diarrhoea, vomiting, lower gastro-intestinal bleeding and hepatomegaly may occur. The colon, rectum, small bowel, stomach, liver and gallbladder are the organs most likely to be involved.[4]

Diagnosis is based on imaging such as sonography, radiography, CT and endoscopy.[8] Thickening of the intestinal wall as well as the presence of a mass in the colon, especially the sigmoid flexure, terminal ileum and stomach, are the most common radiological findings.[2,6,9,10] The mass is likely to spread to surrounding organs with a polypoid shape or cobblestone appearance.[8] These symptoms can lead to misdiagnoses (e.g. Crohn disease, cancer of the colon).[2,6,9,10] Histopathological findings in basidiobolomycosis include: (i) suppurative and granulomatous inflammation, (ii) thin-walled broad hyphae surrounded by eosinophilic amorphous material (S-H combination), (iii) the presence of zygospores, and (iv) the presence of multinucleated giant cells.[11] The S-HP is a morphological structure in which fungal hyphae are surrounded by eosinophilic materials and histiocytes[11,12] and are visible in sections stained with haematoxylin and eosin.[11] In almost all of the previous cases, histological examination was the most common diagnostic method,[5] while fungus culture

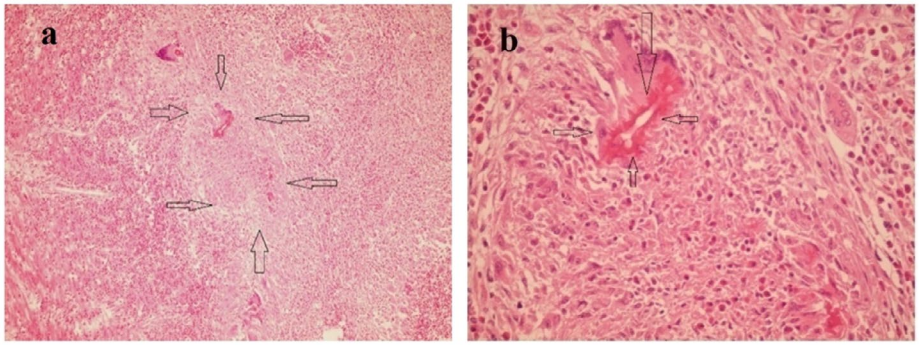

Figure 2 (a) A large granuloma (arrows) with Splendore–Hoeppli phenomenon (S-HP) rich in eosinophils containing a large hypha in the centre (H&E×100); (b) High-power view of S-HP (arrows) (H&E×400)

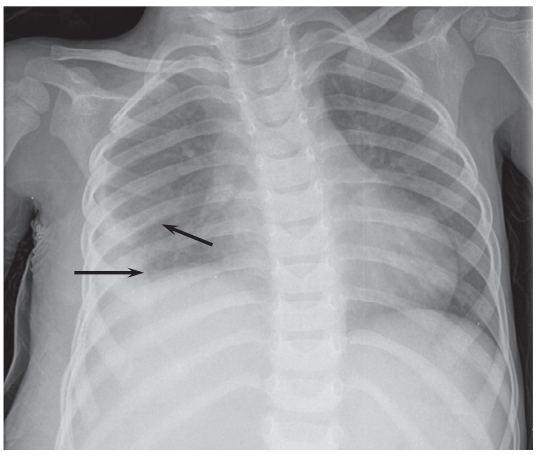

Figure 3 Radiograph demonstrating involvement (both infiltration and destruction) of the right lung and 6th rib (posterior) with a pleural effusion (arrows)

is considered to be the gold standard for a definitive diagnosis of *B. ranarum*.[1,2] Of the 46 GIB cases reported up to 2012, 41.3% were paediatric. All children showed leucocytosis and marked eosinophilia; the mean WBC count was 20.68×10^3/L and the mean eosinophil percentage was 17.1% (all had eosinophilia). Thus, a complete blood cell count is a helpful clue to basidiobolomycosis.[5]

The optimal management of infection includes resection of the mass and other involved structures along with long-term treatment with antifungal drugs.[4] There are some reports of improvement on antifungal therapy alone.[4,9,13] There is no specific choice of antifungal agent for GIB, probably because the disease is so uncommon. Itraconazole is the most commonly used agent for basidiobolomycosis (i.e. the drug of choice for 73% of the patients who received antifungal drugs until 2012), followed by amphotericin products (22%).[4,12] Amphotericin B has led to several unsatisfactory results, and resistance has been documented in isolated cases of infectious basidiobolus.[14,15] Although there are few clinical reports of antagonism between azoles and amphotericin B, there are some supportive pre-clinical studies.[16] In one study, itraconazole and amphotericin B were used against *Aspergillus fumigatus*.[17] *In vitro* results indicated that there was an antagonistic effect between the two drugs in both concomitant and sequential treatment.

Ketoconazole and voriconazole are other drugs that have rarely been used.[1,4] Posaconazole is an antifungal triazole currently used for zygomycosis. There are few clinical data on its usage in children and high-risk patients. Posaconazole is well tolerated with few adverse side-effects. Its activity is similar to that of voriconazole with greater effectiveness against zygomycosis.[18] However, its high cost and availability only as an oral suspension limit its use.[12] Voriconazole is another broad-spectrum triazole which has good results in treating many fungal infections including invasive aspergillosis and a variety of paediatric mycoses.[19] There are many interactions between voriconazole and other drugs which limit its usefulness.[20] Co-trimoxazole has also proved effective in several cases of basidiobolomycosis.[7,21,22] Potassium iodide is the drug of choice for the subcutaneous form of basidiobolomycosis although some patients do not respond.[22,23] There is one other report of a dramatic response to KI: an 8-year-old Pakistani boy with a retroperitoneal mass owing to *B. ranarum*.[15] In addition to *B. ranarum*, subcutaneous zygomycosis can be caused by *Conidiobolus coronatus* which involves the nose, paranasal tissue and upper lip.[24,25] Although some reports indicate success with KI for conidiobolus infection, some cases did not respond.[26] A Brazilian woman with *C. coronatus* infection for 6 years failed to respond to KI but treatment with ketoconazole was successful.[25] Treatment of systemic basidiobolomycosis should include a combination of two or more drugs.[27,28] Responses to the combination treatment of itraconazole and KI were evaluated in a case series of ten patients with rhino-facial conidiobolomycosis; the combination treatment was effective in seven (70%). Potassium iodide was commenced at approximately 1 g/day and gradually increased to a maximum 3 g/day, depending on the patient's condition.[27]

Although KI is mostly used for the subcutaneous form of basidiobolomycosis, in this case, a systemic form of the disease, complete resolution was achieved after combination therapy with potassium iodide.

Potassium iodide is an effective antifungal drug, and, given its availability and low cost, should be considered as a therapeutic option for the treatment of systemic basidiobolomycosis.

Conflict of interest

None.

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