Fungal infection of the colon

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Abstract: Fungi are pathogens that commonly infect immunocompromised patients and can affect any organs of the body, including the colon. However, the literature provides limited details on colonic infections caused by fungi. This article is an intensive review of information available on the fungi that can cause colon infections. It uses a comparative style so that its conclusions may be accessible for clinical application.

Keywords: fungus, colitis, large bowel, large intestine

Introduction
Fungi are pathogens that commonly infect immunocompromised patients. At present, the incidence of these pathogens in disease causation is gradually increasing as a result of increased use of immunosuppressive drugs, chemotherapy, and transplantation as well as infections with the human immunodeficiency virus. Fungal infections can affect any organ, including the colon. Nevertheless, only limited details of colonic infection caused by fungi are available in the literature. This article aims to provide an intensive review of research on fungal infection of the colon in a concise, comparative style for easy clinical application.

Methods
The author initiated the review by researching fungi that can cause colonic infection on MEDLINE, in major textbooks, and existing research literature that review fungal infections of the colon. In MEDLINE, the author used keywords from two groups. The first group consisted of names of the fungi or infections related to the fungi, including “aspergillosis”, “Aspergillus”, “Blastomycoses”, “blastomycosis”, “Candida”, “candidiasis”, “chromoblastomycosis”, “Cladosiphialophora”, “Coccidioides”, “coccidioidomycosis”, “cryptococcosis”, “Cryptococcus”, “dermatophyte”, “dermatophytosis”, “Epidermophyton”, “eumycetoma”, “Fonsecaea”, “fusariosis”, “Fusarium”, “Histoplasma”, “histoplasmosis”, “Madurella”, “Microsporum”, “mucormycosis”, “Paracoccidioides”, “paracoccidioidomycosis”, “penicilliosis”, “Penicillium”, “phaeohyphomycosis”, “Pneumocystis”, “pneumocystis”, “scedosporiosis”, “Scedosporium”, “Sporothrix”, “sporotrichosis”, “Trichophyton”, “Trichosporon”, “trichosporonosis”, “Zygomycetes”, and “zygomycosis”. The second group of keywords consisted of words related to locations of the disease under our focus, including “colitis”, “colon”, “colonic”, “enterocolitis”, “large bowel”, “large intestinal”, and “large intestine”. Finally, it was determined that infections of the colon that have been reported to be caused by fungi were aspergillosis, candidiasis, cryptococcosis,
histoplasmosis, paracoccidioidomycosis, penicilliosis, pneumocystosis, scedosporiosis, and zygomycosis. Details of each fungus were further reviewed from articles retrieved on MEDLINE using the keywords as described above, citations to these articles, and references in major textbooks. In MEDLINE, all types of articles, including reviews, case series, case reports, editorials, and letters, up to June 30, 2014 were included. Initially, 124 articles were found. Only articles which were in English or had an English-language abstract with complete necessary detail that had a definite diagnosis of fungal infection of the colon, including direct visualization of typical fungus or positive fungal culture in colonic specimens, were selected. Cases of candidiasis, which is considered a normal commensal of the human gastrointestinal tract, also needed to have one of the following criteria as per the accepted case reports and revised European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and National Institute of Allergy and Infectious Diseases Mycoses Study Group criteria: deep tissue invasion in the colon, or positive Candida spp. in superficial mucosa with positive blood culture, or positive Candida spp. in superficial mucosa with evidence in response to treatment.4–14 Candida spp. in only superficial mucosa without positive blood culture or evidence in response to treatment were excluded. Dissemination was defined as involvement of two or more noncontiguous organs.15–19

At present, histoplasmosis,20,21 candidiasis,13 and zygomycosis22–25 have already been reviewed. In cases of other fungal infections, including cryptococcosis,26–35 penicilliosis,36–38 aspergillosis,9,39–44 and paracoccidioidomycosis,45–50 the author summarized case reports, as shown in Tables 1–4. Only one case report was published for each of pneumocystosis51 and scedosporiosis.52

**Epidemiology**

Candida spp. are normal commensals of the gastrointestinal tract,53,54 whereas Aspergillus spp. and Pneumocystis spp. are ubiquitous in nature55–58 and are the cause of fungal infections worldwide. Cryptococcus spp. and Scedosporium spp. are endemic mycoses that also have worldwide distribution. Cryptococcus spp. have been isolated from pigeon droppings,39 while Scedosporium spp. have been found in tidal flats, swamps, ponds, manure, and soil.60,61 Aspergillus spp. and Cryptococcus spp. can also be found as a component of human colonic mycobiota.62

Zygomycetes can be divided into two orders, Mucorales and Entomophthorales. Mucorales are endemic fungi found worldwide in organic substrates, including bread, fruits, vegetable matter, soil, compost, and animal excreta.63 Histoplasma spp., Entomophthorales, Paracoccidioides spp., and Penicillium spp. are endemic mycoses that have been isolated from soil in a number of regions of the world.63–71 Histoplasma spp. are found in soil enriched with bat, chicken, and blackbird droppings.6,65 Entomophthorales can be divided into Conidiobolus spp. and Basidiobolus spp. and are found in the soil of some tropical regions, especially Africa, South America, Central America, and Asia.63 Paracoccidioides spp. are limited to soil in Central and South American countries between 23° north (southern Mexico) and 34.5° north (Argentina and Uruguay). These areas have unique ecologic features, being tropical and subtropical forests with mild temperatures and high humidity.66,67 Penicillium spp. are also isolated from soil in specific areas including Southeast Asia, southern China (Guangxi), Hong Kong, and India.68–71 The epidemiologic data is summarized in Table 5.

**Prevalence of colonic involvement**

The degree of colonic involvement of fungal infections varies according to fungal type, as detailed in Table 6. Paracoccidioidomycosis and histoplasmosis are the most common colonic infections caused by fungi, with a prevalence of 29%72 and 28%,20 respectively. In contrast, penicilliosis, zygomycosis, pneumocystosis, and scedosporiosis rarely infiltrate the colon, with penicilliosis and zygomycosis occurring in 1.9%68 and 0.85% of colonic infections,25 respectively. Both pneumocystosis and scedosporiosis are known only from one case report.51,52 Excluding oropharyngeal candidiasis, the colon is the third most common gastrointestinal organ to be involved in candidiasis following the esophagus and stomach. The colon is involved in 20% of gastrointestinal candidiasis.73 Colonic cryptococcosis is the most common gastrointestinal manifestation of disseminated or pulmonary cryptococcosis, with a prevalence of about 17%32.

**Risk factors**

Colonic cryptococcosis and zygomycosis often occur in immunocompromised hosts, occurring in 77%,26–35 and 67%,27 of infections respectively, while colonic candidiasis,13 penicilliosis,36–38 and aspergillosis,9,39–44 exclusively occur in immunocompromised hosts. Risk factors for these infections are malignancy, taking immunosuppressive agents, chemotherapy, neutropenia, AIDS, renal failure, splenectomy, Job’s syndrome, cirrhosis, malnutrition, and diabetes mellitus; however, most colonic penicilliosis patients usually have AIDS.37,38 There have also been case reports of colonic pneumocystosis and scedosporiosis in immunocompromised patients with AIDS and post-liver transplantation, respectively.51,52 In colonic paracoccidioidomycosis
### Table 1 Summary data of reported cases of colonic cryptococcosis

| Source, year | Age (years)/sex | Origin of report | Underlying disease/medication | Clinical presentations | Duration of onset | Dissemination | Colonic distribution | Endoscopic finding | Treatment and outcome |
|--------------|-----------------|------------------|--------------------------------|------------------------|------------------|--------------|---------------------|-------------------|----------------------|
| Zelman et al., 1951 | 25/male | USA | CML, chemotherapy | Not mentioned | Not mentioned | Yes | Not mentioned | Ulcer | None → died |
| Unat et al., 1960 | 16/male | Turkey | None | Diarrhea, abdominal pain, LGIB | 8 years | No | Descending colon | Mass | Surgery and amphotericin B → improved |
| Hutto et al., 1988 | 29/female | USA | Job's syndrome | Rectal abscess | 1 year | No | Perirectum, ascending colon | Stricture at ascending colon and perirectal abscess | Perirectal abscess | Surgery and amphotericin B and fluconazole → improved |
| Van Calck et al., 1988 | 47/male | Belgium | AIDS | Hematochezia, fever | Not mentioned | Yes | Perirectum | Mass | None |
| Daly et al., 1990 | 63/male | USA | Cirrhosis, splenectomy, corticosteroids | Fever, chills, malaise | 7 days | Yes | Transverse colon | Mass | Amphotericin B and fluconazole → died |
| Bonacini et al., 1990 | 31/male | USA | AIDS | Hemiplegia, seizure | Not mentioned | Yes | Not mentioned | Not mentioned | Amphotericin B and fluconazole → died |
| Washington et al., 1991 | 38/male | USA | AIDS | Epigastric pain, odynophagia | 3 months | Yes | Cecum | Not mentioned | Antifungal therapy → died |
| Washington et al., 1991 | 24/male | USA | Hodgkin’s disease | Not mentioned | Not mentioned | Yes | Not mentioned | Not mentioned | None → died |
| Washington et al., 1991 | 31/female | USA | AIDS | Not mentioned | Not mentioned | Yes | Not mentioned | Not mentioned | None → died |
| Washington et al., 1991 | 51/male | USA | Corticosteroids | Not mentioned | Not mentioned | Yes | Not mentioned | Not mentioned | None → died |
| Melato and Gorji, 1998 | 84/female | Italy | None | Rectal bleeding | Acute | No | Sigmoid colon | Polyp | Polypectomy → improved |
| Law et al., 2007 | 40/male | Canada | AIDS | Abdominal pain, diarrhea, dysphagia, fever | 6 weeks | Yes | Left colon | Multiple erythematous, raised, patchy lesions | Amphotericin B and fluconazole → improved |
| Song et al., 2008 | 27/female | Korea | None | Melena | Not mentioned | No | Proximal ascending colon | Mass | Amphotericin B and fluconazole → improved |

**Abbreviations:** AIDS, acquired immunodeficiency syndrome; CML, chronic myeloid leukemia; LGIB, lower gastrointestinal bleeding.
Table 2 Summary data of reported cases of colonic penicilliosis

| Source | Year | Age (years)/sex | Origin | Underlying disease/medication | Clinical presentations | Duration of onset | Dissemination | Colonic distribution | Endoscopic finding | Treatment and outcome |
|--------|------|-----------------|--------|------------------------------|------------------------|-------------------|---------------|---------------------|-------------------|----------------------|
| Tsang et al | 1988 | 58/male | Hong Kong | Corticosteroids | Fever, anemia, hepatosplenomegaly | Acute | Yes | Descending colon | Ulcer | Amphotericin B → died |
| Leung et al | 1996 | 32/male | Hong Kong | AIDS | Fever, diarrhea, night sweats, dry cough | Acute | No | Cecum, transverse and descending colons | Ulcer | Amphotericin B and itraconazole → improved |
| Ko et al | 1999 | 30/male | Taiwan | AIDS | Dyspepsia, abdominal pain, LGI | 3 weeks | Yes | Cecum | Ulcer | Amphotericin B and itraconazole → improved |
| Ko et al | 1999 | 52/male | Taiwan | AIDS | Abdominal pain | 2 months | No | Cecum, ascending and transverse colons | Ulcer | Amphotericin B and itraconazole → improved |

Abbreviations: AIDS, acquired immunodeficiency syndrome; LGI, lower gastrointestinal bleeding.

As shown in Table 7, males predominate in nearly all fungal infections, except for colonic candidiasis, aspergillosis, and paracoccidioidomycosis. The higher frequency of fungal infections in men may be attributed to their more intense exposure to the endemic fungi habitats through work. There is no sex preference in colonic candidiasis, since Candida spp. are normal commensals of the human gut. Aspergillus spp. are ubiquitous, thus sex is also not a risk factor for infection. Although Paracoccidioidomycosis usually occur in men, females predominate are found in colonic paracoccidioidomycosis. The author suggests that it may be caused by reporting bias.

**Immunity and colonic infection caused by fungi**

Host immune response to fungi may play an important role in the pathogenesis of colonic infection caused by fungi, especially organisms that are part of the microbiota. Normally, innate immune cells have membrane-bound and soluble receptors to eliminate fungi. Membrane-bound receptors such as lectin, a toll-like scavenger, and complement receptors can detect fungi or fungal products and then activate phagocytosis and respiratory burst. Transcription factors which can induce proinflammatory cytokines and chemokines are also activated by membrane-bound receptors. Soluble receptors can further activate complements and opsonize fungi to complement receptors. Finally, T helper (Th) 1 and 17 are triggered and produce other cytokines including interleukin (IL)-17A, IL-17F, and IL-22 for adaptive immunity. Both innate and adaptive immune systems defend the host against fungi.

There is some evidence that impaired immunity can increase colonic infection. IL-22, which is produced by innate cells and regulated by IL-23, has been demonstrated to activate inflammatory cells and thus control initial fungal growth. Defective IL-23 and IL-22 pathways increase the fungal burden in the gastrointestinal tract; nevertheless, Th1 cells prevent dissemination of fungi. Th17 cells play a major role in adaptive immune responses, though their impairment results in decreased resistance to late fungal infection. IL-17 receptor A deficiency reduces Th1 activation, thus decreasing fungal resistance. Therefore, immunosuppressive status is one of the major predisposing factors for colonic infection caused by fungi.

**Clinical manifestations**

Colonic infections caused by fungi have varied clinical manifestations, as detailed in Table 8. Excluding zygomycosis and histoplasmosis, there are no necessary risk factors present. As shown in Table 7, males predominate in nearly all fungal infections, except for colonic candidiasis, aspergillosis, and paracoccidioidomycosis. The higher frequency of fungal infections in men may be attributed to their more intense exposure to the endemic fungi habitats through work. There is no sex preference in colonic candidiasis, since Candida spp. are normal commensals of the human gut. Aspergillus spp. are ubiquitous, thus sex is also not a risk factor for infection. Although Paracoccidioidomycosis usually occur in men, females predominate are found in colonic paracoccidioidomycosis. The author suggests that it may be caused by reporting bias.
### Table 3 Summary data of reported cases of colonic aspergillosis

| Source, year | Age (years)/sex | Origin of report | Underlying disease/medication | Clinical presentations | Duration of onset | Dissemination | Colonic distribution | Endoscopic finding | Treatment and outcome | Diagnosed from |
|--------------|-----------------|------------------|-------------------------------|------------------------|-----------------|---------------|---------------------|-------------------|----------------------|------------------|
| Kinder and Jourdan, 1985 | 37/female | UK | Post-renal transplant, immunosuppressive agents | LGIB | Acute | Yes | Cecum and sigmoid colon | Ulcer | Amphotericin B and surgery → died | Deep tissue involvement in surgical specimen |
| Prescott et al, 1992 | 62/female | UK | AML, chemotherapy, neutropenia | Fever, abdominal pain, diarrhea, and vomiting | Acute | No | Not mentioned | Ulcer | Not mentioned → died | Deep tissue involvement in autopsy |
| Prescott et al, 1992 | 43/male | UK | CML, chemotherapy, neutropenia | Fever | Acute | Yes | Transverse colon | Pseudomembrane | Not mentioned → died | No deep tissue involvement in colon but definite other organ involvement |
| Prescott et al, 1992 | 66/female | UK | CA stomach, chemotherapy, neutropenia | Fever | Acute | Yes | Transverse colon | Necrosis | Not mentioned → died | Deep tissue involvement in autopsy |
| Sousa et al, 2002 | 21/female | Portugal | Aplastic anemia | Fever, abdominal pain | Subacute | No | Cecum | Mass | Surgery → died | Deep tissue involvement in surgical specimen |
| Finn et al, 2006 | 75/female | Ireland | Aplastic anemia, immunosuppressive agents | Fever, abdominal pain | Acute | No | Cecum | Ulcer with necrosis | Amphotericin B and surgery → died | Deep tissue involvement in surgical specimen |
| Andres et al, 2007 | 42/female | USA | Burn | Abdominal pain, distension, LGIB | Acute | No | Whole colon | Necrosis | None | Deep tissue involvement in surgical specimen |
| Mohite et al, 2007 | 42/male | UK | AML, chemotherapy, neutropenia | Fever, diarrhea, abdominal pain, abdominal distension | Acute | No | Whole colon | Ulcer with necrosis | Caspofungin and surgery → improved | Deep tissue involvement in surgical specimen and responded to treatment |
| Choi et al, 2010 | 72/male | Korea | DM, steroid, CA colon | LGIB | Acute | No | Sigmoid colon and descending colon | Ulcer | Amphotericin B → improved | Responded to treatment |

**Abbreviations:** AML, acute myeloid leukemia; CA, cancer; CML, chronic myeloid leukemia; DM, diabetes mellitus; LGIB, lower gastrointestinal bleeding.
and aspergillosis, more than one-half of patients with colonic fungal infections have disseminated disease. Abdominal pain is the most common presentation in colonic zygomycosis and aspergillosis.9,22,24,39–44 Deep tissue involvement and angioinvasion, which are common pathological findings in both aspergillosis and zygomycosis, may explain these manifestations.22,25,74 Diarrhea is a symptom that is often found in paracoccidioidomycosis and candidiasis.13,45–50 Cases of colonic histoplasmosis and penicilliosis include diarrhea and abdominal pain as predominant symptoms.20,21,36–38 Perirectal abscess is a specific feature that is only found in colonic cryptococcosis.28,29 Fever is a usual finding in fungal infection of the colon, especially in cases of colonic penicilliosis patients, all of whom experience fever.36–38 For example, a case of colonic pneumocystosis presented with fever and diarrhea,51 while one with colonic scedosporiosis presented with diarrhea and abdominal pain.52

### Pathological findings and distribution

Colonic ulcer is the most common pathological finding in patients with fungal infection of the colon, as shown in Table 9. All cases of colonic aspergillosis, and penicilliosis have ulcers.36–38,74 Ulcer is also usually found in colonic histoplasmosis, paracoccidioidomycosis, and candidiasis.21,45–50,73 Colonic scedosporiosis, likewise, presents with ulcer.52 On the contrary, colonic cryptococcosis presents with a mass or polyp as the most common pathologic finding, while colonic cryptococcosis may also present with atypical pathologic findings, including rectal abscess or stricture.26–35 Another colonic infection that can present with a mass or polyp is histoplasmosis.21 In one case of colonic pneumocystosis, the patient presented with bowel edema.51

Distributions of colonic infection caused by fungi differ according to fungus type, as shown in Table 10. Colonic histoplasmosis, zygomycosis, and penicilliosis tend to occur

### Table 4 Summary data of reported cases of colonic paracoccidioidomycosis

| Source, year | Age(years)/sex | Origin of report | Underlying disease/medication | Clinical presentations | Duration of onset | Dissemination | Colonic distribution | Endoscopic finding | Treatment and outcome |
|--------------|----------------|-----------------|-------------------------------|-----------------------|-----------------|--------------|---------------------|---------------------|---------------------|
| Penna,45 1979 | 8/female | Brazil | None | Diarrhea, abdominal pain, abdominal distension, fever, failure to thrive | 4 years | No | Whole colon | Stricture, ulcer | Co-trimoxazole → improved |
| Chojniak et al,46 2000 | 57/not mentioned | Brazil | None | Abdominal pain, diarrhea, weight loss | 2 years | No | Cecum | Mass | Ketoconazole → not mentioned |
| Costa Vieira et al,47 2001 | 60/male | Brazil | None | Fever, perianal nodule, dysphonia, cough, dyspnea weight loss | 2 years | Yes | Transverse | Ulcer | Sulfadiazine → improved |
| Bravo et al,48 2010 | 39/female | Peru | None | Diarrhea, abdominal pain, fever, weight loss | 2 months | Yes | Whole colon | Ulcer | Amphotericin B → died |
| Leon et al,49 2010 | 34/male | Peru | None | Diarrhea, oral ulcers, odynophagia, weight loss, cough | 18 months | Yes | Whole colon | Ulcer | Amphotericin B and itraconazole → improved |
| Leon et al,49 2010 | 40/female | Peru | None | Diarrhea, weight loss, hepatomegaly | 1 year | Yes | Not mentioned | Not mentioned | Amphotericin B → died |
| Benard et al,50 2013 | 56/female | Brazil | None | None (colonoscopy for check up) | Unknown | No | Transverse colon | Polyp | Itraconazole → improved |
| Benard et al,50 2013 | 58/female | Brazil | None | Diarrhea, weight loss, fever | 6 months | No | Whole colon | Ulcer | Itraconazole → improved |

### Table 5 Epidemiology of fungi that can cause colonic infection

| Fungi | Epidemiology |
|-------|--------------|
| Aspergillus spp.55,56 | Worldwide |
| Candida spp.,53,54 | Tropical areas in Africa, South America, Central America, and Asia |
| Cryptococcus spp.,56 | South and Central American countries, particularly in Brazil, Colombia, Venezuela, and Argentina |
| Histoplasma spp.,64,65 | Southeast Asia, southern China (Guangxi), Hong Kong, and India |
| Mucorales,60 | Caribbean, Africa, and South America |
| Pneumocystis spp.,67,68 | Europe, Asia, and South America |
| Scedosporium spp.,60,61 | Asia, South America, and Central America |
| Entomophthorales63 | Europe and Asia |
| Paracoccidioides spp.,64,67 | South America and Africa |
| Penicillium spp.,68,71 | Worldwide |
### Table 6 Prevalence of colonic involvement in each fungal infection

| Fungal infections                | Prevalence of colonic involvement | Comments                                                                                   |
|---------------------------------|-----------------------------------|--------------------------------------------------------------------------------------------|
| Paracoccidioidomycosis<sup>34</sup> | 29%                               | Prevalence ascertained by autopsy series                                                    |
| Histoplasmosis<sup>20,21</sup>   | 28%                               | Prevalence ascertained by autopsy series                                                    |
| Candidiasis<sup>13</sup>         | 20% of gastrointestinal candidiasis (excluding oropharyngeal candidiasis) |                                             |
| Cryptococcosis<sup>26–35</sup>  | 17% of disseminated or pulmonary cryptococcosis |                                             |
| Aspergillosis<sup>9,39–44</sup> | 9.2%                              |                                             |
| Penicilliosis<sup>48</sup>       | 1.9%                              | Only four cases                                                                            |
| Zygomycosis<sup>22,24</sup>     | 0.85%                             |                                             |
| Pneumocystosis<sup>51</sup>     | No data                           | Only one case                                                                              |
| Scedosporiosis<sup>52</sup>     | No data                           | Only one case                                                                              |

### Table 7 Risk factors for fungal infections of the colon

| Fungal infections                | Immune competent | Immune compromised | Risk factors                                                                 | Male   | Comments                                                                 |
|---------------------------------|------------------|--------------------|------------------------------------------------------------------------------|--------|--------------------------------------------------------------------------|
| Paracoccidioidomycosis<sup>45–50</sup> | 100%             | 0%                 | –                                                                            | 29%    |                                                                          |
| Histoplasmosis<sup>20,21</sup>   | 81%              | 19%                | Malignancy, immunosuppressive drugs, AIDS, Job’s syndrome, DM, splenectomy   | 76%–86.5% |                                                                          |
| Candidiasis<sup>13</sup>         | 0%               | 100%               | Malignancy, immunosuppressive agents, neutropenia, AIDS, ESRD                | 43%    |                                                                          |
| Cryptococcosis<sup>26–35</sup>  | 23%              | 77%                | AIDS, immunosuppressive agents, hematologic malignancy, splenectomy, Job’s syndrome, cirrhosis | 64%    |                                                                          |
| Aspergillosis<sup>9,39–44</sup> | 0%               | 100%               | Malignancy, chemotherapy, neutropenia, immunosuppressive agents, DM, burn    | 33%    |                                                                          |
| Penicilliosis<sup>16–18</sup>   | 0%               | 100%               | AIDS (75%), immunosuppressive agents                                        | 100%   |                                                                          |
| Zygomycosis<sup>22,24</sup>     | 33%              | 67%                | Immunosuppressive agents, malnutrition, renal failure, DM, hematologic malignancy | 65%    |                                                                          |
| Pneumocystosis<sup>51</sup>     | 0%               | 100%               | AIDS                                                                          | 100%   | Only one case                                                             |
| Scedosporiosis<sup>52</sup>     | 0%               | 100%               | Post-liver transplantation, immunosuppressive agents                         | 100%   | Only one case                                                             |

**Abbreviations:** AIDS, acquired immunodeficiency syndrome; DM, diabetes mellitus; ESRD, end-stage renal disease.

### Table 8 Clinical manifestations of colonic infections caused by fungi

| Fungal infections                | Dissemination | Diarrhea | Abdominal pain | LGIB | Rectal abscess | Fever | Comments                                                                 |
|---------------------------------|---------------|----------|----------------|------|----------------|-------|--------------------------------------------------------------------------|
| Paracoccidioidomycosis<sup>45–50</sup> | 50%          | 75%      | 38%            | –    | –              | 50%   | Asymptomatic in 12.5%                                                   |
| Histoplasmosis<sup>20,21</sup>   | 83%          | 83%      | 67%            | 32%  | –              | 77%   |                                                                          |
| Candidiasis<sup>13</sup>         | 71%          | 57%      | 29%            | 29%  | –              | 71%   |                                                                          |
| Cryptococcosis<sup>26–35</sup>  | 71% (all patients immunocompromised) | 20%    | 30%            | 40%  | 20%            | 30%   | Asymptomatic in 20%                                                     |
| Aspergillosis<sup>9,39–44</sup> | 33%          | 22%      | 56%            | 33%  | –              | 67%   |                                                                          |
| Penicilliosis<sup>16–18</sup>   | 50%          | 75%      | 75%            | 25%  | –              | 100%  |                                                                          |
| Zygomycosis<sup>22,24</sup>     | 38%          | 18%      | 64%            | 18%  | –              | 55%   |                                                                          |
| Pneumocystosis<sup>51</sup>     | 100%         | 100%     | –              | –    | –              | 100%  | Only one case                                                            |
| Scedosporiosis<sup>52</sup>     | 100%         | 100%     | 100%           | –    | –              | –     | Only one case                                                            |

**Note:** Dissemination is defined as involvement of noncontiguous organs.<sup>15–19</sup>

**Abbreviation:** LGIB, lower gastrointestinal bleeding.
### Table 9 Pathological findings of colonic infections caused by fungi

| Fungal infections       | Ulcer (%) | Inflamed mucosa/erosion (%) | Pseudomembrane (%) | Mass/poly (% | Rectal abscess (%) | Stricture (%) | Comment |
|------------------------|-----------|----------------------------|---------------------|--------------|---------------------|--------------|---------|
| Paracoccidioidomycosis | 63%       | –                          | –                   | 25%          | –                   | 13%          |         |
| Histoplasmosis         | 79%       | 14%                        | –                   | 7%           | –                   | –            |         |
| Candidiasis            | 64%       | 14%                        | 23%                 | –            | –                   | –            |         |
| Cryptococcosis         | 11%       | 11%                        | –                   | 44%          | 22%                 | 11%          | From autopsy series |
| Aspergillosis          | 100% (with necrosis 55.6%) | –                         | –                   | –            | –                   | –            | From autopsy series |
| Penicilliosis          | 100%      | –                          | –                   | –            | –                   | –            | Ulcer, necrosis, mass occurred, but numbers of patients not specified |
| Zygomycosis            | –         | –                          | –                   | –            | –                   | –            |         |
| Pneumocystosis         | –         | 100%                       | –                   | –            | –                   | –            | Only one case |
| Scedosporiosis         | 100%      | –                          | –                   | –            | –                   | –            | Only one case |

### Table 10 Distributions of colonic infections caused by fungi

| Fungal infections       | Cecum or ascending colon or appendix (%) | Transverse colon (%) | Descending or sigmoid colon (%) | Rectum (%) | Perirectum (%) | Whole colon (%) | Comments |
|------------------------|-----------------------------------------|----------------------|---------------------------------|------------|----------------|-----------------|---------|
| Paracoccidioidomycosis | 13%                                     | 25%                  | 13%                             | –          | –              | 50%             |         |
| Histoplasmosis         | 66%                                     | –                    | 8%                              | 26%        | –              | –               |         |
| Candidiasis            | 20%                                     | –                    | 40%                             | 20%        | –              | 20%             |         |
| Cryptococcosis         | 30%                                     | 10%                  | 40%                             | –          | 20%            | –               |         |
| Aspergillosis          | 33%                                     | 22%                  | 22%                             | –          | –              | 22%             |         |
| Penicilliosis          | 50%                                     | 25%                  | 25%                             | –          | –              | –               |         |
| Zygomycosis            | 50%                                     | –                    | 18%                             | 7%         | –              | 25%             |         |
| Pneumocystosis         | –                                       | –                    | –                               | –          | –              | 100%            | Only one case |
| Scedosporiosis         | –                                       | –                    | –                               | –          | –              | 100%            | Only one case |

### Table 11 Treatment response of fungal infections in the colon

| Fungal infections       | Treatment                                                                 | Treatment response (%) | Comments |
|------------------------|---------------------------------------------------------------------------|-------------------------|---------|
| Paracoccidioidomycosis | Co-trimoxazole, sulfadiazine, amphotericin B, or itraconazole             | 71%                     |         |
| Histoplasmosis         | Amphotericin B                                                            | 77%                     |         |
| Candidiasis            | Fluconazole or caspofungin                                                | 100%                    |         |
| Cryptococcosis         | Amphotericin B + flucytosine ± surgery                                     | 67%                     | Response to treatment in immunocompetent patients was 100% |
| Aspergillosis          | Amphotericin B or caspofungin ± surgery                                    | 50%                     |         |
| Penicilliosis          | Amphotericin B                                                            | 75%                     | Combined surgery improved treatment response |
| Zygomycosis            | Amphotericin B + surgery                                                  | 50%                     |         |
| Pneumocystosis         | Pentamidine                                                               | 100%                    | Only one case |
| Scedosporiosis         | Amphotericin B                                                            | 100%                    | Only one case |
| Fungal infections | Prevalence of colonic involvement | Risk factors | Clinical manifestations | Dissemination | Lesions | Distribution | Initial treatment | Response |
|-------------------|----------------------------------|--------------|------------------------|---------------|---------|-------------|------------------|---------|
| Paracoccidioidomycosis | 29% | Endemic area (South America) | Diarrhea, abdominal pain, fever | 50% | Ulcer, mass, polyp, stricture | Whole colon | Co-trimoxazole, sulfadiazine, amphotericin B, or itraconazole | 71% |
| Histoplasmosis | 28% | Any host | Diarrhea, abdominal pain, LGIB, fever, weight loss | 83% | Ulcer, edema mucosa mass | Whole colon but predominantly right side of colon and rectum | Amphotericin B | 77% |
| Candidiasis | 20% of intestinal candidiasis in autopsy | Malignancy, immunosuppressive agents, neutropenia, AIDS, ESRD | Diarrhea, abdominal pain, fever | 71% | Ulcer, plaque, erosion | Whole colon | Fluconazole or caspofungin | 100% |
| Cryptococcosis | 17% of disseminated or pulmonary cryptococcosis | AIDS, immunosuppressive agents, hematologic malignancy, splenectomy, Job’s syndrome, cirrhosis, Immunocompetent patients (23%) | Symptoms: LGIB, fever, abdominal pain, diarrhea, rectal abscess, 20% asymptomatic | 71% (all patients immunocompromised) | Mass, perirectal abscess, colonic ulcer, patchy lesions, stricture, polyp | Whole colon | Amphotericin B + flucytosine ± surgery | 60% |
| Aspergillosis | 9.2% | Malignancy, chemotherapy, neutropenia, immunosuppressive agents, DM, burn | Fever, abdominal pain, LGIB, diarrhea | 86% | Ulcer, necrosis | Whole colon | Amphotericin B or caspofungin ± surgery | 50% |
| Penicilliosis | 1.9% | Endemic area (Southeast Asia, southern China, Hong Kong, and India) | Fever, diarrhea, abdominal pain, LGIB | 50% | Ulcer | Predominantly in right side of colon and spare rectum | Amphotericin B | 75% |
| Zygomycosis | 0.85% | Immunocompetent patients (33.3%) | Abdominal pain, abdominal distention, fever, LGIB, diarrhea | 38% | Ulcer, necrosis, mass | Whole colon but predominantly in the right side of the colon | Amphotericin B + surgery | 50% |

(Continued)
in the right side of the colon. The rectal area tends to be involved in cases of histoplasmosis, candidiasis, and zygomycosis. Colonic cryptococcosis is the only fungus that involves the perirectal area. Diffuse involvement of the colon is commonly found in colonic paracoccidioidomycosis. Cases of both colonic pneumocystosis and scedosporiosis also presented with diffuse lesions.

### Treatment response

Amphotericin B is the most commonly used drug to treat nearly all colonic fungal infections except candidiasis and pneumocystosis. Colonic candidiasis responds to fluconazole or caspofungin and has the best prognosis if antifungal therapy is initiated with 100% compliance. Good response was also achieved in colonic pneumocystosis and scedosporiosis. A case of colonic pneumocystosis was treated with intravenous pentamidine due to sulfamethoxazole–trimethoprim allergy. Combined antifungal therapy and surgery have been used to treat gastrointestinal zygomycosis and aspergillosis due to angioinvasion and infarction. Nevertheless, prognosis is still poor in these cases, with 50% mortality. The choices of antibiotic and treatment response of fungal infections are summarized in Table 11.

### Conclusion

This is the first study to intensively review the literature on fungal infections of the colon. The entire content is summarized in Table 12. It provides basic information on causes, manifestations, and management and can be easily applied in clinical practice. Physicians should be aware of this fungal entity when patients have colonic symptoms, especially in immunocompromised cases. Although many fungal infections have been reported to cause colonic disease, including aspergillosis, candidiasis, cryptococcosis, histoplasmosis, paracoccidioidomycosis, penicilliosis, pneumocystosis, scedosporiosis, and zygomycosis, knowing the differences in epidemiology, risk factors, clinical manifestations, and pathological findings will help physicians to better diagnosis and manage these infections. Appropriate treatment with antifungal therapy definitely improves outcomes; nevertheless, zygomycosis and aspergillosis cases still have high mortality rates.

### Disclosure

The author reports no conflicts of interest in this work.

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