

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.¹⁻³ Nevertheless, only limited details of colonic infection caused by fungi are available in the literature.^{4,5} 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.⁴⁻⁷ 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*”, “*Blastomyces*”, “blastomycosis”, “*Candida*”, “candidiasis”, “chromoblastomycosis”, “*Cladophialophora*”, “*Coccidioides*”, “coccidioidomycosis”, “cryptococcosis”, “*Cryptococcus*”, “dermatophyte”, “dermatophytosis”, “*Epidermophyton*”, “eumycetoma”, “*Fonsecaea*”, “fusariosis”, “*Fusarium*”, “*Histoplasma*”, “histoplasmosis”, “*Madurella*”, “*Microsporium*”, “mucormycosis”, “*Paracoccidioides*”, “paracoccidioidomycosis”, “penicilliosis”, “*Penicillium*”, “phaeohyphomycosis”, “*Pneumocystis*”, “pneumocystosis”, “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,

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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.^{8–14} *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 zygomycosis^{22–25} 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 nature^{55–58} 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,⁵⁹ 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 microbiota.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.^{64,65} 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%²² 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, ^{2,6} 1951	25/male	USA	CML, chemotherapy	Not mentioned	Not mentioned	Yes	Not mentioned	Ulcer	None → died
Unat et al, ²⁷ 1960	16/male	Turkey	None	Diarrhea, abdominal pain, LGIB	8 years	No	Descending colon	Mass	Surgery and amphotericin B → improved
Hutto et al, ²⁸ 1988	29/female	USA	Job's syndrome	Rectal abscess	1 year	No	Perirectum, ascending colon	Stricture at ascending colon and perirectal abscess	Surgery and amphotericin B → improved
Van Calck et al, ²⁹ 1988	47/male	Belgium	AIDS	Hematochezia, fever	Not mentioned	Yes	Perirectum	Perirectal abscess	Surgery, amphotericin B and flucytosine → improved
Daly et al, ³⁰ 1990	63/male	USA	Cirrhosis, splenectomy, corticosteroids	Fever, chills, malaise	7 days	Yes	Transverse colon	Mass	Amphotericin B and flucytosine → died
Bonacini et al, ³¹ 1990	31/male	USA	AIDS	Hemiplegia, seizure	Not mentioned	Yes	Not mentioned	Not mentioned	Amphotericin B and flucytosine → died
Washington et al, ³² 1991	38/male	USA	AIDS	Epigastric pain, odynophagia	3 months	Yes	Cecum	Not mentioned	Antifungal therapy → died
Washington et al, ³² 1991	24/male	USA	Hodgkin's disease	Not mentioned	Not mentioned	Yes	Not mentioned	Not mentioned	None → died
Washington et al, ³² 1991	31/female	USA	AIDS	Not mentioned	Not mentioned	Yes	Not mentioned	Not mentioned	None → died
Washington et al, ³² 1991	51/male	USA	Corticosteroids	Not mentioned	Not mentioned	Yes	Not mentioned	Not mentioned	None → died
Melato and Gorji, ³³ 1998	84/female	Italy	None	Rectal bleeding	Acute	No	Sigmoid colon	Polyp	Polypectomy → improved
Law et al, ³⁴ 2007	40/male	Canada	AIDS	Abdominal pain, diarrhea, dysphagia, fever	6 weeks	Yes	Left colon	Multiple erythematous, raised, patchy lesions	Amphotericin B and flucytosine → improved
Song et al, ³⁵ 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 of report	Underlying disease/medication	Clinical presentations	Duration of onset	Dissemination	Colonic distribution	Endoscopic finding	Treatment and outcome
Tsang et al, ³⁶ 1988	58/male	Hong Kong	Corticosteroids	Fever, anemia, hepatosplenomegaly	Acute	Yes	Descending colon	Ulcer	Amphotericin B → died
Leung et al, ³⁷ 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, ³⁸ 1999	52/male	Taiwan	AIDS	Fever, diarrhea, anemia, abdominal pain	3 weeks	Yes	Cecum	Ulcer	Amphotericin B and itraconazole → improved
Ko et al, ³⁸ 1999	30/male	Taiwan	AIDS	Dyspepsia, diarrhea, fever, abdominal pain, LGIB, weight loss	2 months	No	Cecum, ascending and transverse colons	Ulcer	Amphotericin B and itraconazole → improved

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

and histoplasmosis, there are no necessary risk factors present.^{20,21,45–50} 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.⁶⁷ There is no sex preference in colonic candidiasis, since *Candida* spp. are normal commensals of the human gut.^{13,53,54} *Aspergillus* spp. are ubiquitous, thus sex is also not a risk factor for infection.^{9,39–44,55,56} Although Paracoccidioidomycosis usually occur in men,⁶⁷ females predominate are found in colonic paracoccidioidomycosis.^{45–50} 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.^{75,76} 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.⁷⁶

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.⁷⁵ 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.⁷⁵ 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

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, ³⁹ 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, ⁹ 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, ⁹ 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, ⁹ 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, ⁴⁰ 2002	21/female	Portugal	Aplastic anemia	Fever, abdominal pain	Subacute	No	Cecum	Mass	Surgery → died	Deep tissue involvement in surgical specimen
Finn et al, ⁴¹ 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, ⁴² 2007	42/female	USA	Burn	Abdominal pain, distension, LGIB	Acute	No	Whole colon	Necrosis	None	Deep tissue involvement in surgical specimen
Mohite et al, ⁴³ 2007	42/male	UK	AML, chemotherapy, neutropenia	Fever, diarrhea, abdominal pain, 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, ⁴⁴ 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.

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 and descending colons	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

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

Table 5 Epidemiology of fungi that can cause colonic infection

Fungi	Epidemiology
<i>Aspergillus</i> spp., ^{55,56} <i>Candida</i> spp., ^{53,54} <i>Cryptococcus</i> spp., ⁵⁹ <i>Histoplasma</i> spp., ^{64,65} <i>Mucorales</i> , ⁶³ <i>Pneumocystis</i> spp., ^{57,58} <i>Scedosporium</i> spp. ^{60,61}	Worldwide
Entomophthorales ⁶³ <i>Paracoccidioides</i> spp. ^{66,67}	Tropical areas in Africa, South America, Central America, and Asia South and Central American countries, particularly in Brazil, Colombia, Venezuela, and Argentina
<i>Penicillium</i> spp. ^{68–71}	Southeast Asia, southern China (Guangxi), Hong Kong, and India

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 6 Prevalence of colonic involvement in each fungal infection

Fungal infections	Prevalence of colonic involvement	Comments
Paracoccidioidomycosis ⁷²	29%	Prevalence ascertained by autopsy series
Histoplasmosis ²⁰	28%	
Candidiasis ⁷³	20% of gastrointestinal candidiasis (excluding oropharyngeal candidiasis)	Prevalence ascertained by autopsy series Only seven symptomatic cases
Cryptococcosis ³²	17% of disseminated or pulmonary cryptococcosis	
Aspergillosis ⁷⁴	9.2%	
Penicilliosis ⁶⁸	1.9%	Only four cases
Zygomycosis ²⁵	0.85%	
Pneumocystosis ⁵¹	No data	Only one case
Scedosporiosis ⁵²	No data	Only one case

Table 7 Risk factors for fungal infections of the colon

Fungal infections	Immunocompetent	Immunocompromised	Risk factors	Male	Comments
Paracoccidioidomycosis ⁴⁵⁻⁵⁰	100%	0%	–	29%	
Histoplasmosis ^{20,21}	81%	19%	Malignancy, immunosuppressive drugs, AIDS, Job's syndrome, DM, splenectomy	76%–86.5%	
Candidiasis ¹³	0%	100%	Malignancy, immunosuppressive agents, neutropenia, AIDS, ESRD	43%	
Cryptococcosis ²⁶⁻³⁵	23%	77%	AIDS, immunosuppressive agents, hematologic malignancy, splenectomy, Job's syndrome, cirrhosis	64%	
Aspergillosis ^{9,39-44}	0%	100%	Malignancy, chemotherapy, neutropenia, immunosuppressive agents, DM, burn	33%	
Penicilliosis ³⁶⁻³⁸	0%	100%	AIDS (75%), immunosuppressive agents	100%	
Zygomycosis ^{22,24}	33%	67%	Immunosuppressive agents, malnutrition, renal failure, DM, hematologic malignancy	65%	
Pneumocystosis ⁵¹	0%	100%	AIDS	100%	Only one case
Scedosporiosis ⁵²	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 ⁴⁵⁻⁵⁰	50%	75%	38%	–	–	50%	Asymptomatic in 12.5%
Histoplasmosis ^{20,21}	83%	83%	67%	32%	–	77%	–
Candidiasis ¹³	71%	57%	29%	29%	–	71%	–
Cryptococcosis ²⁶⁻³⁵	71% (all patients immunocompromised)	20%	30%	40%	20%	30%	Asymptomatic in 20%
Aspergillosis ^{9,39-44}	33%	22%	56%	33%	–	67%	–
Penicilliosis ³⁶⁻³⁸	50%	75%	75%	25%	–	100%	–
Zygomycosis ^{22,24}	38%	18%	64%	18%	–	55%	–
Pneumocystosis ⁵¹	100%	100%	–	–	–	100%	Only one case
Scedosporiosis ⁵²	100%	100%	100%	–	–	–	Only one case

Note: Dissemination is defined as involvement of noncontiguous organs.¹⁵⁻¹⁹

Abbreviation: LGIB, lower gastrointestinal bleeding.

Table 9 Pathological findings of colonic infections caused by fungi

Fungal infections	Ulcer	Inflamed mucosa/erosion	Pseudomembrane	Mass/polyp	Rectal abscess	Stricture	Comment
Paracoccidioidomycosis ⁴⁵⁻⁵⁰	63%	–	–	25%	–	13%	
Histoplasmosis ²¹	79%	14%	–	7%	–	–	
Candidiasis ⁷³	64%	14%	23%	–	–	–	From autopsy series
Cryptococcosis ²⁶⁻³⁵	11%	11%	–	44%	22%	11%	
Aspergillosis ⁷⁴	100% (with necrosis 55.6%)	–	–	–	–	–	From autopsy series
Penicilliosis ³⁶⁻³⁸	100%	–	–	–	–	–	
Zygomycosis ^{22,25}	–	–	–	–	–	–	Ulcer, necrosis, mass occurred, but numbers of patients not specified
Pneumocystosis ⁵¹	–	100%	–	–	–	–	Only one case
Scedosporiosis ⁵²	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 ⁴⁵⁻⁵⁰	13%	25%	13%	–	–	50%	
Histoplasmosis ²⁰	66%	–	8%	26%	–	–	
Candidiasis ¹³	20%	–	40%	20%	–	20%	
Cryptococcosis ^{27-30,32-35}	30%	10%	40%	–	20%	–	
Aspergillosis ^{9,39-44}	33%	22%	22%	–	–	22%	
Penicilliosis ³⁶⁻³⁸	50%	25%	25%	–	–	–	
Zygomycosis ²³	50%	–	18%	7%	–	25%	
Pneumocystosis ⁵¹	–	–	–	–	–	100%	Only one case
Scedosporiosis ⁵²	–	–	–	–	–	100%	Only one case

Table 11 Treatment response of fungal infections in the colon

Fungal infections	Treatment	Treatment response	Comments
Paracoccidioidomycosis ^{45,47-50}	Co-trimoxazole, sulfadiazine, amphotericin B, or itraconazole	71%	
Histoplasmosis ²¹	Amphotericin B	77%	
Candidiasis ¹³	Fluconazole or caspofungin	100%	
Cryptococcosis ²⁷⁻³⁵	Amphotericin B + flucytosine ± surgery	67%	Response to treatment in immunocompetent patients was 100%
Aspergillosis ^{39,41,43,44}	Amphotericin B or caspofungin ± surgery	50%	
Penicilliosis ³⁶⁻³⁸	Amphotericin B	75%	
Zygomycosis ²⁵	Amphotericin B + surgery	50%	Combined surgery improved treatment response
Pneumocystosis ⁵¹	Pentamidine	100%	Only one case
Scedosporiosis ⁵²	Amphotericin B	100%	Only one case

Table 12 Summary of colonic infection caused by fungi

Fungal infections	Prevalence of colonic involvement	Risk factors	Clinical manifestations	Dissemination	Lesions	Distribution	Initial treatment	Response
Paracoccidioidomycosis ^{45-50,72}	29%	<ul style="list-style-type: none"> • Endemic area (South America) • Any host 	Diarrhea, abdominal pain, fever	50%	Ulcer, mass, polyp, stricture	Whole colon	Co-trimoxazole, sulfadiazine, amphotericin B, or itraconazole	71%
Histoplasmosis ^{20,21}	28%	<ul style="list-style-type: none"> • 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 ^{13,73}	20% of intestinal candidiasis in autopsy	<ul style="list-style-type: none"> • Malignancy, immunosuppressive agents, neutropenia, AIDS, ESRD • No immunocompetent patients 	Diarrhea, abdominal pain, fever	71%	Ulcer, plaque, erosion	Whole colon	Fluconazole or caspofungin	100%
Cryptococcosis ²⁶⁻³⁵	17% of disseminated or pulmonary cryptococcosis	<ul style="list-style-type: none"> • AIDS, immunosuppressive agents, hematologic malignancy, splenectomy, Job's syndrome, cirrhosis • Immunocompetent patients (23%) 	<ul style="list-style-type: none"> • 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 ^{9,39-41,74}	9.2%	<ul style="list-style-type: none"> • Malignancy, chemotherapy, neutropenia, immunosuppressive agents, DM, burn • No immunocompetent patients 	Fever, abdominal pain, LGIB, diarrhea	86%	Ulcer, necrosis	Whole colon	Amphotericin B or caspofungin ± surgery	50%
Penicilliosis ^{36-38,68}	1.9%	<ul style="list-style-type: none"> • Endemic area (Southeast Asia, southern China, Hong Kong, and India) • Mostly AIDS (75%) • No immunocompetent patients 	Fever, diarrhea, abdominal pain, LGIB	50%	Ulcer	Predominantly in right side of colon and spare rectum	Amphotericin B	75%
Zygomycosis ²²⁻²⁵	0.85%	<ul style="list-style-type: none"> • Immunosuppressive agent, malnutrition, renal failure, DM, hematologic malignancy • Immunocompetent patients (33.3%) 	Abdominal pain, abdominal distension, fever, LGIB, diarrhea	38%	Ulcer, necrosis, mass	Whole colon but predominantly in the right side of the colon	Amphotericin B + surgery	50%

(Continued)

Table 12 (Continued)

Fungal infections	Prevalence of colonic involvement	Risk factors	Clinical manifestations	Dissemination	Lesions	Distribution	Initial treatment	Response
Pneumocystosis ⁵¹	Only one case	<ul style="list-style-type: none"> • AIDS 	Fever, diarrhea	100%	Edema mucosa	Whole colon	Pentamidine	100%
Scedosporiosis ⁵²	Only one case	<ul style="list-style-type: none"> • Post-liver transplantation, immunosuppressive agents 	Diarrhea, abdominal pain	100%	Ulcer	Whole colon	Amphotericin B	100%

Abbreviations: AIDS, acquired immunodeficiency syndrome; DM, diabetes mellitus; ESRD, end-stage renal disease; LGIB, lower gastrointestinal bleeding.

in the right side of the colon.^{20,23,36–38} The rectal area tends to be involved in cases of histoplasmosis, candidiasis, and zygomycosis.^{13,20,23} Colonic cryptococcosis is the only fungus that involves the perirectal area.^{28,29} Diffuse involvement of the colon is commonly found in colonic paracoccidioidomycosis.^{45–50} Cases of both colonic pneumocystosis and scedosporiosis also presented with diffuse lesions.^{51,52}

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.¹³ Good response was also achieved in colonic pneumocystosis and scedosporiosis.^{51,52} A case of colonic pneumocystosis was treated with intravenous pentamidine due to sulfamethoxazole–trimethoprim allergy.⁵¹ 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.^{25,39,41,43,44} 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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