

Intra-abdominal Cryptococcosis by *Cryptococcus gattii*: Case Report and Review

Bruno S. Araújo · Monica Bay ·
Roberta Reichert · Luciano Z. Goldani

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Abstract Although abdominal cryptococcomas and visceral cryptococcal lymphadenitis as part of disseminated fungal infection have been reported mostly in HIV-infected patients, localized intra-abdominal involvement due to *Cryptococcus gattii* has not been previously described in non-HIV-infected patients. In general, a smaller proportion of cryptococcosis is caused by *C. gattii*. We report here on a type II diabetic HIV-negative patient who presented with a localized intra-abdominal cryptococcal mass due to *C. gattii*. In addition, we review the general aspects of intra-abdominal and gastrointestinal involvement by *Cryptococcus neoformans* in the literature and discuss the importance of identifying the *C. neoformans* varieties and *C. gattii* in routine laboratories.

Keywords *Cryptococcus gattii* · Cryptococcosis · Intra-abdominal · Gastrointestinal

Introduction

The proportion of non-AIDS-associated infections caused by *Cryptococcus gattii* did not change after the advent of the AIDS pandemic, whereas the number of

AIDS-associated *Cryptococcus grubii* and *Cryptococcus neoformans* infections increased significantly [1]. A smaller proportion of disease is caused by *C. gattii*, which occupies a more restricted habitat. AIDS-associated cryptococcosis is caused primarily by *C. neoformans* var. *grubii* or *C. neoformans* var. *neoformans*, even in areas where *C. gattii* is endemic [2]. Among persons not infected with HIV, *C. gattii* infection frequently presents as lesions localized in the lung (as pulmonary nodules), CNS (as localized CNS lesions) and occasionally skin, whereas in HIV-infected individuals, infection presents largely as meningitis, with or without fungemia [3–8]. Although abdominal cryptococcomas and visceral cryptococcal lymphadenitis as part of disseminated fungal infection have been reported mostly in HIV-infected patients, localized intra-abdominal involvement due to *C. gattii* has not been previously described in non-HIV-infected patients.

We report here on a type II diabetic HIV-negative patient who presented with a localized intra-abdominal cryptococcal mass due to *C. gattii*. In addition, we review the general aspects of intra-abdominal and gastrointestinal cryptococcosis in the literature and discuss the importance of identifying the *C. neoformans* varieties and *C. gattii* in routine laboratories.

Case Report

A 51-year-old male Brazilian truck driver was admitted for investigation of an abdominal mass.

B. S. Araújo · M. Bay · R. Reichert · L. Z. Goldani (✉)
Section of Infectious Diseases, Hospital de Clínicas de
Porto Alegre, Universidade Federal do Rio Grande do Sul,
Ramiro Barcelos 2350, Porto Alegre, RS 90640-002,
Brazil
e-mail: lgoldani@ufrgs.br

Approximately 2 months ago, he noted a palpable painless mass in his abdomen associated with constipation and abdominal distension. The patient denied fever, headache, nausea, vomiting and weight loss. Past medical history was significant for controlled type II diabetes mellitus. On physical examination, the patient was in no acute distress, his blood pressure was 110/70 mm Hg, oral temperature 36.8°C, heart rate 78/min, and respiratory rate 18/min. Abdominal examination revealed a palpable mass in the epigastrium. Neurological examination did not disclose any focal signs. CT scan identified a large intra-abdominal lesion measuring 9.5×5 cm (Fig. 1). Upon initial work-up, the patient was found to have negative HIV test. Chest X-ray was normal. Blood cultures were negative, and latex agglutination test revealed a serum cryptococcal antigen titer of 1:100. After incisional biopsy, histopathology of the lesion revealed a granulomatous lesion with mucicarmine stain showing the presence of numerous yeast compatible with *Cryptococcus* (Fig. 2). Culture of the biopsy material grew *C. gattii*. L-canavanine glycine bromothymol blue medium was used to identify *C. gattii*. The patient was initially treated with amphotericin B deoxycholate (1 mg/kg/day for 21 days) followed by oral fluconazole (800 mg/day), with progressive improvement of

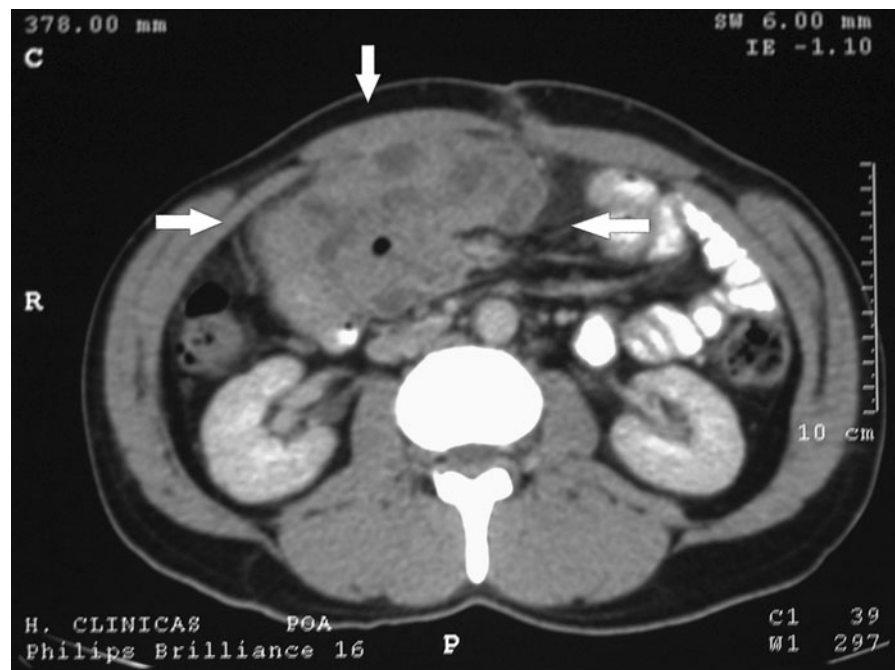
his symptoms and an approximately 70% reduction of the mass after 1 year of therapy.

Discussion

Among non-HIV-infected persons in a more restricted habitat, *C. gattii* infection frequently presents as a lesion localized in the lung, CNS or skin and rarely as an intra-abdominal mass, whereas in HIV-infected individuals, disease presents largely as meningitis. Although most cases of *C. gattii* infection do occur in otherwise healthy persons, infection is occasionally associated with immunosuppressive states.

Localized abdominal cryptococcomas and visceral cryptococcal lymphadenitis have been reported in immunocompetent and immunocompromised hosts and, as in our patient, may initially be confused with lymphoreticular disorders, such as non-Hodgkin's lymphoma. Unfortunately, *C. neoformans* varieties and *C. gattii* were not identified in those cases. As shown in Table 1, most of the patients were HIV-infected and presented with intra-abdominal cryptococcosis, most likely due to *C. neoformans* var. *grubii* or var. *neoformans*, as part of disseminated fungal infection. Immunocompetent hosts presenting with a

Fig. 1 Abdominal CT scan showing a large localized intra-abdominal cryptococcoma measuring 9.5×5 cm (arrowheads)



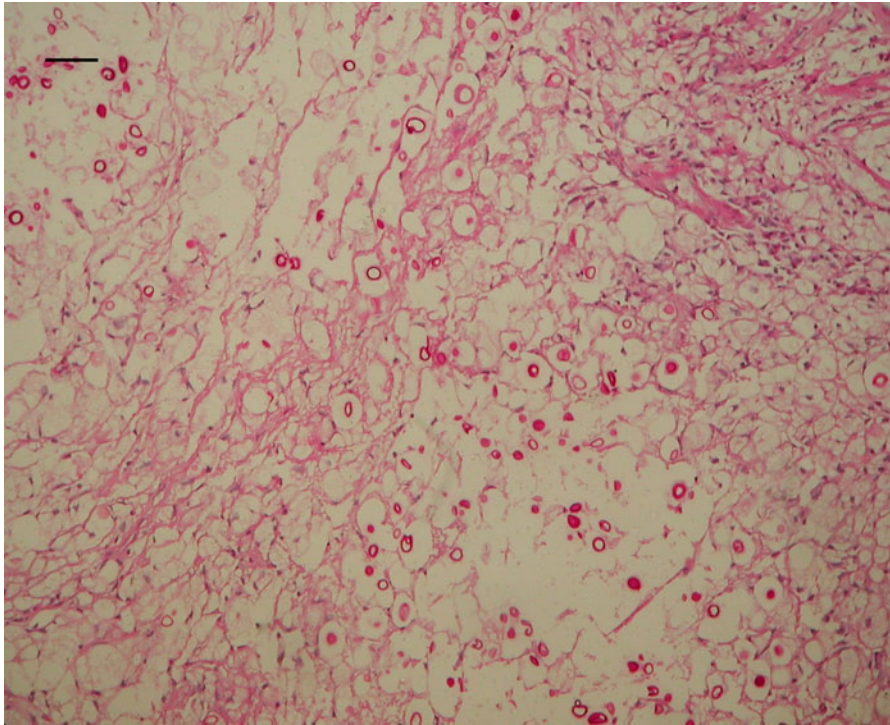


Fig. 2 Biopsy of intra-abdominal mass stained with mucicarmine showing the presence of numerous yeasts compatible with *Cryptococcus* (magnification $\times 400$)

localized intra-abdominal mass due to *C. neoformans* have also been reported in the literature [9–26]. In fact, both inhibition of polymorphonuclear leukocyte migration to the site of infection and inhibition of neutrophil function by products of *Cryptococcus* may promote survival of extracellular organisms and local multiplication to form cryptococcomas [27].

Although our patient had type II diabetes mellitus under control, the localized intra-abdominal cryptococcal mass by *C. gattii* occurred in the absence of a known immunocompromised state, such as HIV infection or immunosuppressive treatment. Moreover, *C. gattii* infections have been described in tropical and subtropical areas, such as occurred in our patient who lived and worked as a truck driver in rural areas in Brazil [2]. An ongoing outbreak in western Canada strengthens the case that the range of the pathogen has expanded [28]. Although most cases of *C. gattii* infection do occur in otherwise healthy persons, infection is occasionally associated with immunosuppressive states. Additional immunological tests were not done to exclude any immunosuppressive condition

in our patient. The lack of prominent gastrointestinal and constitutional symptoms of our patient, such as fever, malaise, weight loss and anorexia, is important features of localized infection in a patient with apparently normal cellular-mediated immunity. Although the localized intra-abdominal cryptococcosis of our patient had a favorable response to antifungal therapy, previous reports have shown that, when compared with *C. neoformans* var. *grubii* and var. *neoformans*, intracranial *C. gattii* infection is associated with a greater number of neurological sequelae and delayed responses to therapy, primarily because of a higher proportion of cerebral mass lesions (cryptococcomas) and late presentations [3]. In addition, previous studies suggest that *C. gattii* isolates have higher MICs than do non-*C. gattii* isolates, raising concerns that *C. gattii*-infected patients might demonstrate slower responses to antifungal therapy [29].

Physicians should be aware that the clinical spectrum of cryptococcosis varies from localized to disseminated forms of the disease according to the

Table 1 Characteristics of the reported patients with intra-abdominal cryptococcosis

References	Age/sex	<i>C. neoformans</i> variety	Immune status	Clinical presentation	Outcome
Scalfano et al. [9]	38/male	Unknown	HIV+	Abdominal pain; massive retroperitoneal and mesenteric adenopathy	Death
Chong et al. [10]	29/male	Unknown	No evidence of immunodeficiency	Abdominal discomfort; localized 8 cm lesion in the omentum	Alive
Gordon et al. [11]	36/male	Unknown	No evidence of immunodeficiency	Small bowel obstruction; multiple pinhead-sized granulomas studded the visceral peritoneum	Alive
Campins et al. [12]	34/female	Unknown	No evidence of immunodeficiency	Abdominal mass due to mesenteric lymphadenitis	Alive
Pittarelli et al. [13]	35/female	Unknown	HIV+	Abdominal pain; nausea; increasing abdominal girth portahepatic mass	Alive
Karagüzel et al. [14]	3/female	Unknown	No evidence of immunodeficiency	Acute abdomen; abdominal mass due to mesenteric lymphadenitis	Alive
Kim et al. [15]	42/female	Unknown	SLECorticosteroids Cyclophosphamide	Fever, abdominal pain; mesenteric and retroperitoneal cryptococcal lymphadenitis; obstruction of the stomach and proximal duodenum	Alive
Zou et al. [16]	5/male 9/female	Unknown	No evidence of immunodeficiency	Fever, abdominal pain, vomiting; severe intra-abdominal lymphadenopathy	Alive
Sing et al. [17]	25/female	Unknown	HIV+	Pseudocystic ovarian mass measuring 140 × 80 × 60 mm	Alive
Sundar et al. [18]	48/male	Unknown	HIV+	Odynophagia, vomiting, gastric involvement	Alive
Girardin et al. [19]	26/female	Unknown	HIV+	Abdominal pain; vomiting; thickened third part of the duodenum with an infiltrated mesentery	Alive
Saha et al. [20]	30/female	Unknown	HIV+	Jejunal perforation; peritonitis, acute abdomen	Alive
Law et al. [21]	40/male	Unknown	HIV+	Abdominal pain, dysphagia, diarrhea; large bowel	Alive
Nawabi et al. [22]	39/female	Unknown	HIV+	Abdominal pain, vomiting; a 3 cm stricture of the distal ileum	Alive
Chaitowitz et al. [23]	50/male	Unknown	No evidence of immunodeficiency	Acute abdomen, jejunal perforation	Death
Daly et al. [24]	63/male	Unknown	Chronic cortisteroid use; cirrhosis	Peritonitis, colitis, and skin lesions	Death
Bonacini et al. [25]	31/male 30/male 31/male	Unknown	HIV+	Stomach, duodenum, colon, pancreas and liver involvement	2 deaths 1 alive
Markowitz et al. [26]	?	Unknown	HIV+	Abdominal pain and cholestasis; lymphadenitis; biliary tract obstruction;	Alive

host and *Cryptococcus* species. As more routine laboratories are identifying the *C. neoformans* varieties and *C. gattii*, further clinical experience will be important to better assess the spectrum of clinical manifestations and antifungal therapy response for unusual clinical forms of cryptococcosis.

References

1. Kwon-Chung KJ, Bennett JE. Epidemiologic differences between the two varieties of *Cryptococcus neoformans*. Am J Epidemiol. 1984;120:123–30.
2. Sorrell TC. *Cryptococcus neoformans* variety *gattii*. Med Mycol. 2001;39:155–68.
3. Speed B, Dunt D. Clinical and host differences between infections with the two varieties of *Cryptococcus neoformans*. Clin Infect Dis. 1995;21:28–34.
4. Oliveira Fde M, Severo CB, Guazzelli LS, Severo LC. *Cryptococcus gattii* fungemia: report of a case with lung and brain lesions mimicking radiological features of malignancy. Rev Inst Med Trop Sao Paulo. 2007;49:263–5.
5. Lehmann PF, Morgan RJ, Freimer EH. Infection with *Cryptococcus neoformans* var. *gattii* leading to a pulmonary cryptococcoma and meningitis. J Infect. 1984;9:301–6.
6. Pisarevsky AA, Larriera A, Cean P, Petrucci EA. Pulmonary cryptococcoma with involvement of the chest wall in an immunocompetent patient. Medicina. 2010;70:166–8. (B Aires).
7. Bellissimo-Rodrigues F, Baciotti M, Zanatto MP, Silva JO, Martins Mdos A, Martinez R. Cutaneous cryptococcosis due to *Cryptococcus gattii* in a patient on chronic corticotherapy. Rev Soc Bras Med Trop. 2010;43:211–2.
8. Dora JM, Kelbert S, Deutschendorf C, Cunha VS, Aquino VR, Santos RP, Goldani LZ. Cutaneous cryptococcosis due to *Cryptococcus gattii* in immunocompetent hosts: case report and review. Mycopathologia. 2006;161:235–8.
9. Scalfano FP Jr, Prichard JG, Lamki N, Athey PA, Graves RC. Abdominal cryptococcoma in AIDS: a case report. J Comput Tomogr. 1988;12:237–9.
10. Chong PY, Panabokke RG, Chew KH. Omental cryptococcoma. An unusual presentation of cryptococcosis. Arch Pathol Lab Med. 1986;110:239–41.
11. Gordon SM, Gal AA, Amerson JR. Granulomatous peritoneal cryptococcomas. An unusual sequela of disseminated cryptococcosis. Arch Pathol Lab Med. 1994;118:194–5.
12. Campins H, Galavis D, Vegas H. Cryptococcosis in Venezuela. Comments on a clinical case with unusual location. Mycopathologia. 1975;55:153–7.
13. Pittarelli LA, Faris-Young SL. Photo quiz: cryptococcoma. Clin Infect Dis. 1999;29(759):917.
14. Karagüzel G, Kiliçarslan-Akkaya B, Melikoğlu M, Karpuzoğlu G. Cryptococcal mesenteric lymphadenitis: an unusual cause of acute abdomen. Pediatr Surg Int. 2004;20:633–5.
15. Kim SH, Kim SD, Kim HR, Yoon CH, Lee SH, Kim HY, Park SH. Intraabdominal cryptococcal lymphadenitis in a patient with systemic lupus erythematosus. J Korean Med Sci. 2005;20:1059–61.
16. Zou CC, Yu ZS, Tang LF, Liang L, Zhao ZY. Primary abdominal lymphonodular cryptococcosis in children: 2 case reports and a literature review. J Pediatr Sur. 2006;41:e11–5.
17. Sing Y, Ramdial PK, Ibrahim T. Cryptococcosis masquerading as a tuboovarian abscess. Int J Gynecol Pathol. 2008;27:37–40.
18. Sundar R, Rao L, Vasudevan G, Gowda PB, Radhakrishna RN. Gastric cryptococcal infection as an initial presentation of AIDS: a rare case report. Asian Pac J Trop Med. 2011;4:79–80.
19. Girardin M, Greloz V, Hadengue A. Cryptococcal gastroduodenitis: a rare location of the disease. Clin Gastroenterol Hepatol. 2010;8:e28–9.
20. Saha S, Agarwal N, Srivastava A, Kumar A. Perforation peritonitis due to gastrointestinal cryptococcosis as an initial presentation in an AIDS patient. Singap Med J. 2008;49:e305–7.
21. Law JK, Amar JN, Kirby SD, Zetler PJ, Enns RA. Colonic cryptococcus infection. Gastrointest Endosc. 2007;65:525–6.
22. Nawabi DH, Ffolkes L, O'Bichere A. Cryptococcal small-bowel obstruction in an HIV-positive patient. J R Soc Med. 2005;98:513–4.
23. Chaitowitz M, Shaw ML, Mokoena TR. Gastrointestinal cryptococcosis presenting as spontaneous jejunal perforation in a nonimmunocompromised host. Dig Dis Sci. 2003;48:1196–9.
24. Daly JS, Porter KA, Chong FK, Robillard RJ. Disseminated, nonmeningeal gastrointestinal cryptococcal infection in an HIV-negative patient. Am J Gastroenterol. 1990;85:1421–4.
25. Bonacini M, Nussbaum J, Ahluwalia C. Gastrointestinal, hepatic, and pancreatic involvement with *Cryptococcus neoformans* in AIDS. J Clin Gastroenterol. 1990;12:295–7.
26. Markowitz SM, Kerkering TM, Gervin AS. Biliary obstruction and cholestasis in AIDS: case report. Va Med. 1990;117:114–6.
27. Dong ZM, Murphy JW. Effects of the two varieties of *Cryptococcus neoformans* cells and culture filtrate antigens on neutrophil locomotion. Infect Immun. 1995;63:2632–44.
28. Springer DJ, Chatuverdi V. Projecting global occurrence of *Cryptococcus gattii*. Emerg Infect Dis. 2010;16:14–20.
29. Chen YC, Chang SC, Shih CC, Hung CC, Luhbd KT, Pan YS, Hsieh WC. Clinical features and in vitro susceptibilities on two varieties of *Cryptococcus neoformans* in Taiwan. Diagn Microbiol Infect Dis. 2000;36:175–83.