Cerebral Cryptococcomas: A Systematic Scoping Review of Available Evidence to Facilitate Diagnosis and Treatment

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Background

- Recommendations for managing patients with cerebral cryptococcomas are scarce across multiple clinical guidelines.
- Due to the deficiency of high-quality data coupled with an increasing number of at-risk patients, the purpose of this review is to describe the demographic characteristics, causative pathogen, intracranial imaging, surgical and/or pharmacological interventions, as well as outcomes of patients with cerebral cryptococcomas to improve recognition and management.

Methods

- We conducted a scoping review in accordance with the PRISMA guidelines using PubMed and Web of Science.
- Reports were included if the following details were presented: (1) site of infection; (2) treatment details which at least include the specific antifungal therapy administered, if applicable; and (3) patient outcome.

Limitations

- We chose to complete a scoping systematic review due to the lack of an available comprehensive review about cerebral cryptococcomas.
- Our analysis only included 47 individual patients derived from 40 reports. In order to abstract consistent data each report, we had to exclude publications that did not provide information on the site of infection; treatment regimen at least including the specific antifungal therapy administered, if applicable; and patient outcome.
- Specific details about the pharmacological treatments administered, such as the route, dose, and/or duration, were often not reported, which limited our abilities to provide clear treatment recommendations, but may be due to the paucity of recommendations provided in the guidelines.
- Few reports clearly delineated “induction” therapy versus “maintenance” therapy.
- The duration of “induction”, “maintenance”, and corticosteroid therapy was longer in patients who survived than those who died, which could represent survival-related selection bias.
- Due to the inherent difficulties of diagnosing cerebral cryptococcomas, many additional cases may be unrecognized and, therefore, not reported.

Results

Table 2. Comparisons between cerebral cryptococcomas caused by *C. neoformans* and *C. gattii*.

	C. neoformans	*C. gattii*
Prevalence *	74%	26%
Clinical manifestations		
• Headache	56%	50%
• Altered mental status or confusion	52%	25%
• Visual disturbances	16%	13%
• Seizures	16%	0%
• Fever	20%	25%
• Chills	0%	13%
• Fatigue	16%	25%
• Weight loss	4%	13%
• Papilledema	20%	25%
• Upper extremity weakness	20%	13%
• Time from symptom onset to presentation (days), median (range)	30 (3–365)	29 (3–270)
Radiographic findings		
• One or more lesions throughout the brain parenchyma	40%	56%
• Perilesional edema	77%	47%
• Hydrocephalus	71%	33%
Treatment regimens		
• Amphotericin B-based formulation	88%	100%
• Amphotericin B-based formulation in combination with flucytosine or fluconazole	57%	89%
• “Induction” therapy duration among survivors (days), median (range)	42 (10–60)	38 (7–84)
• “Maintenance” therapy duration among survivors (days), median (range)	126 (60–730)	317.5 (12–365)
Follow-up, median (range)	302.5 (30–4380)	279 (7–1460)

*, based on the 34 cases in which an organism was isolated and speciated [19,22,23,24,26,27,28,29,30,32,34,36,37,39,41,44,45,46,47,50,52,53,54].

- A total of 40 records representing 47 individual patients were included, of which the median age was 48.5 years, 75% were male, and 60% reported a significant past medical, surgical, or social history.
- C. neoformans was isolated more often than C. gattii (74% vs. 26%, respectively).
- Patients most often presented with headache, altered mental status and/or confusion, and vomiting occurring over a median of 30 days; though few were noted to have significant findings on physical examination. More than 50% of patients had a single cerebral cryptococcoma lesion, whereas perilesional edema was present in 73% of cases.
- Surgical intervention occurred in 49% of patients.
- An amphotericin B-based formulation was administered as “induction” therapy to 91% of patients, but combined with flucytosine or fluconazole in only 58%, for an overall median of 42 days. Fifty two percent of patients received “maintenance” therapy for a median of 126 days, in which fluconazole was most often used.
- Corticosteroids were administered to approximately 30% of patients for a median of 31.5 days.
- Overall, mortality was 34%.

Conclusions

- Based on our findings, management should include antifungal therapy for a minimum of 6 months with considerations for concomitant corticosteroids in the setting of perilesional edema, as well as surgical intervention.
- Emphasis should be placed on providing well-documented treatment details in future case reports and series to allow for the development of more concise evidence-based recommendations.

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