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Case report

A case of cryptococcoma in an immunocompetent man with polysubstance use

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ABSTRACT

Cryptococcus most commonly affects the pulmonary and central nervous systems in patients who are immunocompromised. It is most likely to present as meningitis. However, it can affect immunocompetent patients in the cerebral parenchyma. Here we describe a rare case of cryptococcoma in an immunocompetent male patient who originally presented with headache and possible seizure-like activity and had IV drug use as a risk factor. Cryptococcomas are a rare manifestation of the disease, and can present due to Cryptococcus gatti. Definite diagnosis is dependent on culture of the organism and treatment includes a long course of anti-fungals

Background

Cryptococcosis most commonly affects the pulmonary and central nervous systems and seen in patients who have human immunodeficiency virus (HIV) or other immunodeficiencies [1]. Common species include *Cryptococcus neoformans and Cryptococcus gatti* [2]. Transmission occurs through inhalation of mammal and bird feces [3]. Primarily, the disease affects the lung and then spreads in a hematogenous route. For the disease to pass the blood-brain barrier, it indicates that host defenses are compromised [1]. Cryptococcocis is most likely to present as meningitis. However, in immunocompetent patients, cerebral parenchyma is more likely to be involved as cryptococcomas [4]. Here we describe a rare case of cryptococcoma in an immunocompetent male patient who originally presented with headache and possible seizure-like activity.

Objective

To describe clinical presentation of cryptococcoma in an immunocompetent male with IV drug use as risk factor.

Case

A 52-year-old male with untreated hypertension, atrial fibrillation, and hepatitis C, presented to the emergency department with acute frontal throbbing, severe headache for a couple days. There was associated nausea, vomiting, and vision changes. He reported suspicious seizure-like activity, with loss of consciousness and tongue biting, and right lower extremity weakness, which progressed throughout his body. Social history was significant for homelessness and polysubstance use including opioid, cocaine, and fentanyl use. Vitals and physical exam were unremarkable. On presentation, WBC was 9.5 × 10 * 3/uL with 20.7 % lymphocytes. As seen in Table 1, ESR was also elevated. Liver function tests and renal tests were within normal limits. HIV, VDRL, and RPR were negative and hepatitis C PCR was negative for active disease. QuantiFERON gold was positive, however patient was without evidence of active pulmonary disease. Immunoglobulins were all within normal limits.

CT head was remarkable for a small area of hypodensity in the left frontal lobe white matter favoring vasogenic edema. The scan was followed by an MRI of the brain with and without contrast which showed abnormal signal intensity with enhancement in the left frontoparietal region, most prominently centered in the region of the left pars marginalis with a small area of possible restricted diffusion in the immediate subcortical white matter. There was also faint signal intensity on the FLAIR imaging in the sulci of the adjacent posterior left frontal lobe (Fig. 1). Infectious disease (ID), neurology, and neurosurgery were all consulted. EEG was negative for seizure activity. Patient was started on Keppra 500 mg twice daily for seizure prophylaxis due to reported history.

Original cerebrospinal fluid (CSF) results were consistent with bacterial infection as seen in Table 2; however, opening pressure was not recorded on original procedure. Patient was started on vancomycin and

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Table 1
Labs on presentation.

Lab type	Value	Normal Range
WBC	9.5 × 10 * 3/uL	4.0–11.0 × 10 * 3/uL
Hgb	16.9 g/dL	14.0–18.0 g/dL
Platelets	272 × 10 * 3/uL	150–450 × 10 * 3/uL
Glucose	107 mg/dL	70–109 mg/dL
BUN	18 mg/dL	6–20 mg/dL
Creatinine	0.7 mg/dL	0.7–1.2 mg/dL
Sodium	131 meq/L	133–145 meq/L
Potassium	4.9 meq/L	3.5–4.8 meq/L
Chloride	95 meq/L	97–110 meq/L
Alk phos	118 u/L	40–130 u/L
Total bilirubin	0.8 mg/dL	< 1.0 mg/dL
AST	17 U/L	0–40 U/L
ALT	12 U/L	0–41 U/L
Lactic acid	1.8 mmol/L	0.5–2.2 mmol/L
ESR	27 mm/hour	0–15 mm/hour
CRP	< 1 mg/L	0–5 mg/L

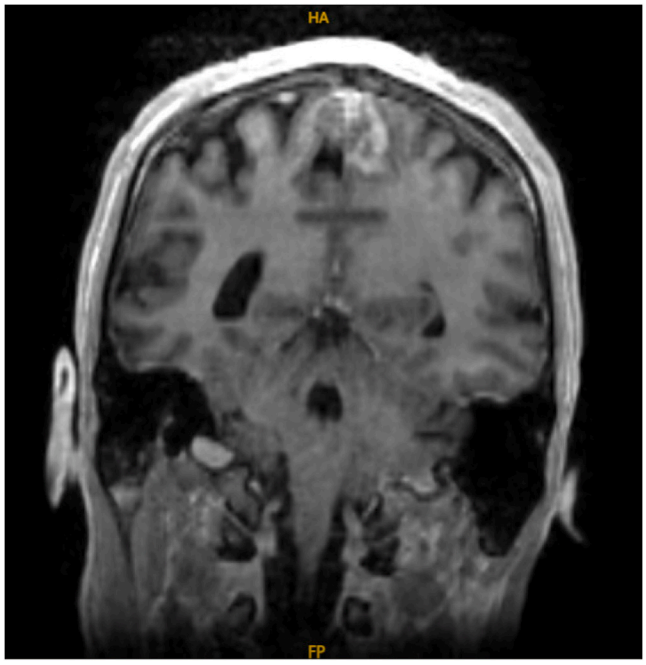

Fig. 1. MRI brain showing Cryptococcoma lesion. Coronal postcontrast T1 shows abnormal signal intensity with enhancement in the left pars marginalis.

Table 2
CSF Results.

	Value	Normal Range
CSF appearance	Slightly cloudy, xanthrochromia absent	
CSF glucose	26 mg/dL	40–80 mg/dL
CSF protein	127	15–45 mg/dL
CSF lactic acid	0.0 mmol/L	0–2 mmol/L
CSF LDH	26 u/L	7–30 u/L
CSF RBC count	517c/uL	No reference range
CSF WBC count	495c/uL	No reference range
CSF seg	41 %	No reference range
CSF lymph	50 %	No reference range
CSF mono	9 %	No reference range

cefepime, and PICC line was placed for anticipation of long-term antibiotic use for suspected bacterial meningitis. Blood cultures and urine cultures had no growth. A few days after being on antimicrobials, CSF cryptococcus antigen was positive in titers 1:4. Antimicrobials were discontinued, and patient was started on intravenous liposomal amphoteric 3 mg/kg every 24 h and parenteral flucytosine 2 g every 6 h. Notably, CSF PCR was negative for *Cryptococcus neoformans*. At this time, diagnosis of cryptococcoma due to likely *Cryptococcus gatti* was made. Second lumbar puncture showed opening pressure to be 25 cm H2O, and resulted in improvement of neurologic symptoms. Hospital course was complicated by acute kidney injury (AKI) secondary to amphotericin administration.

After a four-week induction therapy regimen, patient was to continue parenteral fluconazole 800 mg daily for consolidation and then parenteral fluconazole 200 mg daily for maintenance for 12 months.

Discussion

Cryptococcosis is the most common fungal disease of the central nervous system and primarily affects immunocompromised individuals [1]. This includes patients who have HIV, hepatitis B or C, chronic renal disease, diabetes mellitus, oncological diseases, rheumatologic conditions and solid organ transplantation. While our patient had reported hepatitis C, PCR showed no viral load. While he was extensively tested for evidence of immunocompromise, no such underlying cause was identified. Furthermore, cryptococcoma is a rare manifestation of this fungal disease. The most common manifestation is meningoencephalitis with over 1 million cases per year [5]. It is pertinent that the patient's CSF PCR was negative for *Cryptococcus neoformans*, leading to the belief that the infection was most likely caused by *Cryptococcus gatti. C. gatti* has been more likely associated with cryptococcoma in immunocompetent patients compared to the *neoformans* variant [6].

The most common symptoms of cryptococcoma as reported in the literature were headaches of vomiting, changes in consciousness or mental status, and cranial dysfunction. Seizure was less likely reported. Only one case report stated that patient presented with fever [7]. These symptoms arise from increased intracranial pressure, which can lead to inflammation and mass effect because of blockage of drainage of the CSF [8]. MRI findings include hypointensity in T1 and hyperintensity in T2 sequences with peripheral edema and enhancement after contrast gadolinium injection, as seen in our patient (Fig. 1). The lesions were most likely seen in the cerebrum [9,10]. Definitive diagnosis for cryptococcoma relies on culture of the organism, which remains the gold standard. Since the infection is often confined to localized lesion, obtaining a lumbar puncture as done with this patient [11]. Furthermore, cryptococcosis manifestation in the CNS has been associated with increased opening pressure on lumbar puncture, making it a valuable diagnostic tool. We did not conduct a biopsy of the lesion for confirmatory pathology due to suspicion of increased intracranial pressure on admission.

The Infectious Disease Society of America (IDSA) recommends liposomal amphotericin B at 0.7–1.0 mg/kg per day intravenously and flucytosine 100 mg/kg per day orally divided into four doses for four weeks of induction therapy. Consolidation therapy should be done for eight weeks with 800 mg of fluconazole daily, and then maintenance therapy with 200 mg of fluconazole for six to twelve months [12].

One of the more significant findings in this patient is his extensive history of intravenous drug use. The patient endorsed a twenty-five year history of intravenous drug use involving heroin and fentanyl-laced products. While case reports are limited, there has been evidence of cryptococcus meningitis in patients with IVDA although mechanism is uncertain [13,14]. Furthermore, one case series identified four cases of disseminated cryptococcosis in a similar geographic region within one year time, potentially pointing to a contaminant in the substances used leading to the disease [15].

Conclusion

We present a case of cryptococcoma in a 52-year-old male with past medical history of hypertension, atrial fibrillation, hepatitis C, and polysubstance use. Cryptococcomas should be included in differential

diagnosis for solitary brain lesions in both immunocompromised and immunocompetent patients. Treatment method consists of long-term anti-fungal therapy. It is possible that intravenous drug use was the risk factor for nidus of infection in this patient.

Consent

The patient has provided consent for publication. No images were used.

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CRediT authorship contribution statement

Radhika Malhotra: Writing – Original Draft (main contributor), Review & Editing. Zachary Lodato: Writing – Original Draft, Review & Editing. Patrick Brunk: Review & Editing. Anjella Manoharan: Review & Editing. Kaveh Hajifathalian: Review & Editing, Supervision. Diana Finkel: Review & Editing, Supervision. Smita Mahendrakar: Review & Editing, Supervision.

Conflict of interest

Radhika Malhotra, Zachary Lodato, Patrick Brunk, Anjella Manoharan, Kaveh Hajifathalian, Diana Finkel, Smita Mahendrakar all report no conflicts.

References

[1] Berkefeld J, Enzensberger W, Lanfermann H. Cryptococcus meningoencephalitis in AIDS: parenchymal and meningeal forms. Neuroradiology 1999;41(2):129–33.
[2] Goldman DL, Khine H, Abadi D, Lindenberg DJ, La P, Niang R, Casadevallet A. Serologic evidence for Cryptococcus neoformans infection in early childhood. Pediatrics 2001;107(5):E66.
[3] Klock C, Cerski M, Goldani LZ. Histopathological aspects of neurocryptococcosis in HIV-infected patients: autopsy report of 45 patients. Int J Surg Pathol 2009;17(6):444–8.
[4] Yu YQ, Jiang XX, Gao YJ. MRI of a pituitary cryptococcoma simulating an adenoma. Neuroradiology 1995;37(6):449–50.
[5] Yang CL, Wang J, Zou LL. Innate immune evasion strategies against Cryptococcal meningitis caused by Cryptococcus neoformans. Exp Ther Med 2017;14(6):5243–50.
[6] Kidd SE, Hagen F, Tscharke RL, Hunyh M, Bartlett KH, Fyfe M, et al. A rare genotype of Cryptococcus gattii caused the cryptococcosis outbreak on Vancouver Island (British Columbia, Canada). Proc Natl Acad Sci U S A 2004;101(49):17258–63.
[7] Li Q, You C, Liu Q, Liu Y, et al. Central nervous system cryptococcoma in immunocompetent patients: a short review illustrated by a new case. Acta Neurochir (Wien) 2010;152(1):129–36.
[8] Ngan NTT, Flower B, Day JN. Treatment of cryptococcal meningitis: how have we got here and where are we going? Drugs 2022;82(12):1237–49.
[9] Gultasli NZ, Ercan K, Orhun S, Albayrak S. MRI findings of intramedullary spinal cryptococcoma. Diagn Inter Radio 2007;13(2):64–7.
[10] Kesler R, Maertens P. Pontine cryptococcoma in a nonimmunocompromised individual: MRI characteristics. J Neuroimaging 1999;9(2):118–21.
[11] Odhiambo FA, Ngare W, Ndinya-Achola JO. Detection rate of Cryptococcus neoformans in cerebrospinal fluid specimens at Kenyatta National Hospital, Nairobi. East Afr Med J 1997;74(9):576–8.
[12] Perfect JR, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of america. Clin Infect Dis 2010;50(3):291–322.
[13] Monno L, Angarano A, Montagna MT, Coppola S, Carbonara S, Bellasario A. Chronic cryptococcal meningitis in an intravenous drug addict without evidence of infection by HIV-1,2 in southern Italy. Eur J Epidemiol 1994;10(6):773–4.
[14] Nerin Sanchez C, Hermida Lazcano I, Martinez Alvarez R, Arazo Garces P, Figueras Villalba P, Aguirre Errasti JM. Cryptococcal meningitis in an intravenous drug abuse HIV negative person. Med Interna 1997;14(5):264–5.
[15] Shorman M, Evans D, Gibson C, Perfect J. Cases of disseminated cryptococcosis in intravenous drug abusers without HIV infection: a new risk factor? Med Mycol Case Rep 2016;14:17–9.