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Case Report

Cryptococcoma in an immunocompetent patient: Unveiling the mystery of a rare rim-enhancing brain lesion ☆

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ABSTRACT

A 59-year-old immunocompetent male who initially presented with symptoms of stroke was found to have an incidental rim-enhancing lesion on magnetic resonance imaging (MRI) of the brain. This discovery led to a lumbar puncture to analyze the cerebrospinal fluid, resulting in the diagnosis of cryptococcoma. The patient was subsequently managed with liposomal amphotericin B, followed by consolidation and maintenance therapy with fluconazole. The patient achieved a positive outcome, demonstrating the effectiveness of early diagnosis and targeted treatment. The rarity of cryptococcoma in immunocompetent individuals makes this case particularly unusual and noteworthy. It underscores the need for more extensive research to enable prompt diagnosis and effective management.

Introduction

Cryptococcus is an encapsulated yeast, an opportunistic fungal pathogen that may lead to life- threatening infections such as meningoencephalitis and disseminated cryptococcosis. There are 2 main species most prevalent under this namely *Cryptococcus neoformans* and *Cryptococcus gatti*. *C. neoformans* is typically linked to immunocompromised individuals, while *C. gattii* infections are more commonly observed in immunocompetent patients. To the best of our knowledge, this case report presents a rare instance of cryptococcoma caused by *C. neoformans* in an immunocompetent individual with no risk factors.

Case description

Clinical presentation

A 59-year-old male from New York with chronic comorbidities of controlled diabetes mellitus, hypertension, hyperlipidemia,

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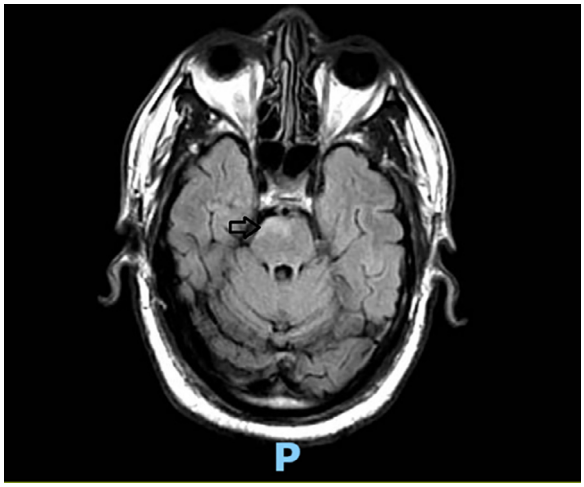

Fig. 1 – MRI of the brain without contrast. Right paramedian pons stroke with surrounding edema noted, (highlighted by black arrow).

benign prostatic hyperplasia and chronic kidney disease stage 2 along with a recent cerebrovascular accident which was associated with no residual deficits presented to the hospital for a brief episode of diplopia, dizziness and left upper extremity ataxia. On examination the following vitals were obtained: Temperature 98.3 F, heart rate 96 beats per minute, blood pressure 180/80 mmHg and respiratory rate 18 with pulse oximetry (SpO2) 96% on room air.

Diagnostic workup

The initial laboratory workup was unrevealing which included complete white cell count of 5,700 (reference range 3.5-10.5 10^3/uL), hemoglobin 10.3 (reference range 11.6-15.4 g/dL), platelets 190,000/uL (reference range 140-390 10^3/uL), creatinine 1.9 mg /dL (reference range 0.7-1.0 mg/dL) and remaining electrolytes and liver function tests in normal limits. C-reactive protein and erythrocyte sedimentation rate were normal. He was noted to have baseline quantiferon test negative. HIV screen tests were negative both in previous and current admission.

An extensive evaluation identified an ischemic stroke in the right paramedian pons on computed tomography (CT) imaging. Subsequent magnetic resonance imaging (MRI) of the brain showed an infarct with surrounding edema that was disproportionate for a typical stroke. This prompted an extensive discussion between neurologist and radiologist for consideration of an MRI with intravenous contrast to further investigate the findings. The MRI with intravenous contrast of the brain was performed and it revealed the right para-midline area restricted diffusion in the pons. The anterior and central T2 FLAIR signal abnormality was found associated with a 9-millimeter size rim-enhancing lesion contacting the ventral surface of the pons. These findings were consistent with small para-midline pontine acute infarct secondary to anterior process affecting the small pontine perforating vessel (Figs. 1-3).

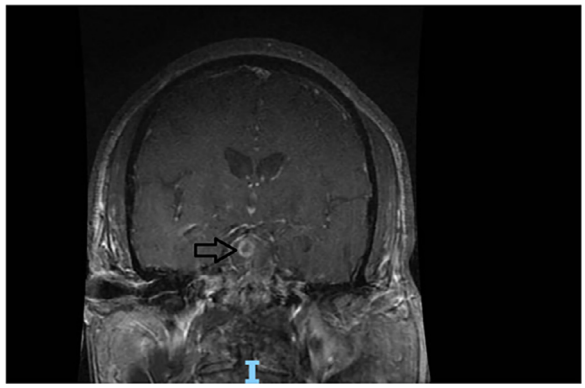

Fig. 2 – MRI of the brain with and without contrast coronal section.

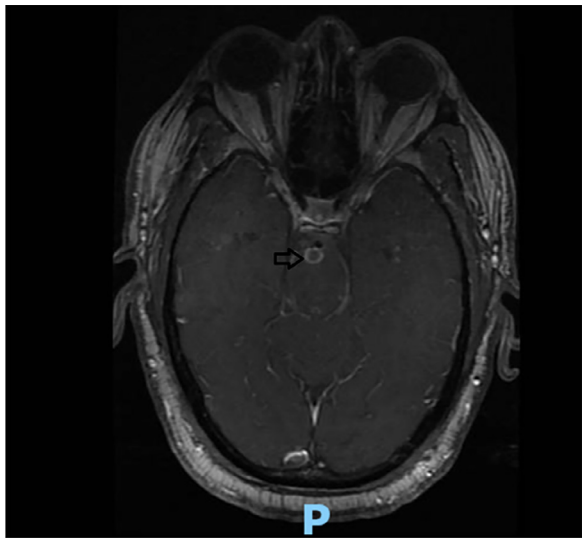

Fig. 3 – MRI of the brain with and without contrast transverse section showing 9-millimiter ring enhancing lesion in the pons along with right pontine infarct (highligted by black arrows).

This incidental finding prompted further investigation into underlying pathological processes. Bacterial, viral, fungal, and autoimmune etiologies were considered in the differential diagnosis. The patient underwent lumbar puncture which showed elevated white blood cells. Routine bacterial cultures and viral studies returned negative. Extensive autoimmune panels both in serum and cerebrospinal fluid (CSF) were unrevealing, however, cryptococcal antigen returned positive (Table 1).

The CSF cryptococcal antigen returned positive with a titer of 1:60. Simultaneous serum cryptococcal antigen titer was 1:80. Eventual CSF culture showed *C. neoformans* grubii which had intermediate resistance to micafungin. The minimum inhibitory concentrations for posaconazole were 0.25, voriconazole was 0.12, fluconazole was 8 and amphotericin B was 4.

Table 1 – Cerebrospinal fluid analysis.

Opening Pressure	36 mm H_2O (normal 10-20)
Appearance	Clear
Color	Colorless
CSF Lactate dehydrogenase	23 U/L (normal <40)
Total Nucleated Cells	629 (normal 0-5)
RBC	0 (normal 0-5)
CSF Neutrophils	16% (normal 0%-6%)
CSF Lymphocytes	80% (normal 0%-40%)
CSF Monocytes	3% (normal 0%-30%)
CSF Cryptococcal Titer	1:60
CSF Culture	*Cryptococcus neoformans* Grubii Posaconazole 0.25 Voriconazole 0.12 Fluconazole 8 Amphotericin 4

Management

The patient received induction therapy with amphotericin B liposome for 6 weeks. He had poor tolerance for flucytosine (severe nausea and vomiting). Due to amphotericin B liposome his renal function declined and ultimately precipitated in renal failure rendering him dependent on hemodialysis. He has successfully completed consolidation and maintenance therapy with fluconazole. The patient is currently doing well without any relapse of infection.

Discussion

The incidence of cryptococcal infections in immunocompetent individuals, while historically considered uncommon, is increasingly being acknowledged in recent medical literature (20%-40%) [1]. These infections attributed to strains of *C. gatti/neoformans* species complexes, often represent pervasive fungal infections bearing considerable mortality rates [2]. Common risk factors to consider besides uncontrolled HIV/AIDS include transplant, hematological malignancies, autoimmune disorders, uncontrolled diabetes mellitus, cirrhosis and chronic alcohol intake [3]. It is interesting to note that *C. gattii* infections are more commonly observed in immunocompetent individuals with uncertain risk factors as compared to *C. neoformans* which is associated with HIV/AIDS and other immunodeficiency states [4]. Presentation of either of these infections in the form of intracranial cryptococcoma however is sparse [5,6]. It is interesting to note that *C. neoformans* grubii is thought to be the more common strain prevalent in New York City however a larger scale analysis is needed [7].

Cryptococcus typically affects immunocompromised individuals and often presents as meningitis. Cryptococcal meningitis is known to cause ischemic stroke due to vasculitis, but in this case, the complication included a perforator infarct leading to cryptococcoma, a mass that can easily be misdiagnosed. Cryptococcomas though rare are usually found in the frontal or parietal lobes or basal ganglia, with pons involvement being exceptionally uncommon. Notably, our patient, who had well-managed diabetes and multiple negative HIV screenings, was uniquely diagnosed with pontine cryptococcoma caused by *C. neoformans* [5,6]. The patient was managed successfully with cumbersome antifungal therapy according to the guideline which included phases of induction, consolidation and maintenance therapy for at least 1 year to decrease the risk of relapse [8].

Cryptococcus inhabits diverse environmental niches, including avian excrement, soil and decaying vegetation. Inhalation of cryptococcus spores initiated pulmonary acquisition of the infection, with the respiratory tract serving as the principal portal of entry. Inhalation of the cryptococcal spore was thought to be the prime event in the case discussed above, though the patient did not have any respiratory complaints and the chest imaging (X-ray and CT chest) on evaluation was completely normal.

As demonstrated in our case, magnetic resonance imaging (MRI) is a better modality in diagnosing cryptococcoma as compared to computed tomography [9]. Individuals diagnosed with cryptococcal infections necessitate an extended duration (12-18 months) of antifungal treatment, comprising induction, consolidation and maintenance phases [10,11]. In certain instances where prolonged or repeated induction antifungal therapy failed to yield a resolution, surgical intervention has been attempted to achieve a cure. However, relying solely on imaging findings is not recommended for the management of these complex infections as cryptococcoma brain lesions may endure over extended durations with or without surrounding edema [12].

Despite the advancement in medical literature, the mortality associated with cryptococcosis remains as high as 25% likely due to the heterogeneous nature of their underlying conditions and diagnostic delays stemming from low suspicion [8]. Hence, timely diagnosis and implementation of effective antifungal therapy remains crucial in mitigating these adverse outcomes.

Conclusion

Cryptococcoma, traditionally associated with immunocompromised individuals, is increasingly being diagnosed in immunocompetent patients. Our case underscores this concerning trend, highlighting the need for heightened awareness within the medical community regarding the diagnosis, prompt management and potential severity of cryptococcosis specially in those individuals previously considered low risk.

Patient consent

An informed consent was obtained from the patient for consideration of use of medical information for publication purposes without revealing any identifying information.

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