International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Chronic Fungal Meningitis in A 34-Year-Old Male with Initially Normal Cerebrospinal Fluid, Later Diagnosed as Cryptococcus Neoformans Infection

Mr. Amit Kumar Pandey

Assistant Professor, Microbiology, People's college of paramedical science and research center

Abstract

A rare but potentially deadly illness, chronic fungal meningitis frequently manifests with vague symptoms and may initially go undiagnosed because of normal cerebrospinal fluid (CSF) results. Although infection in immunocompetent people is becoming more widely acknowledged, Cryptococcus neoformans is traditionally linked to immunocompromised hosts. We describe a rare case of chronic cryptococcal meningitis in a male immunocompetent patient, age 34, who first complained of constitutional symptoms and frequent headaches. The diagnosis was delayed because the initial CSF investigation was unremarkable. Cryptococcal infection was discovered through further examinations and subsequent clinical deterioration. This case emphasizes the difficulties in diagnosing persistent fungal meningitis and emphasizes the significance of strong clinical suspicion and recurrent CSF examination.

Keywords: Cryptococcal Meningitis, Cerebrospinal fluid (CSF), Immunocompetent hosts, Cryptococcus Neoformans, C-Reactive Protein.

Background

Chronic meningitis is characterized by inflammation of the meninges lasting over four weeks and can result from infectious, inflammatory, neoplastic, or autoimmune causes. Among infectious reasons, fungal meningitis is still uncommon and hard to identify because of its slow progression and frequently mild lab irregularities.

Cryptococcus neoformans is an encapsulated yeast frequently located in soil tainted by bird faces. Although cryptococcal meningitis mainly impacts those with HIV/AIDS or other types of immunosuppression, there are growing reports of cases in immunocompetent individuals. Timely diagnosis is essential, since postponed treatment is linked to considerable morbidity and mortality. Cryptococcal meningitis (CM) is a significant worldwide opportunistic infection, particularly in individuals with HIV/AIDS. Approximately 1 million instances of cryptococcal meningitis occur annually around the globe.

This case illustrates a patient who initially had normal CSF results but was subsequently diagnosed with cryptococcal meningitis, highlighting the diagnostic challenges linked to early-stage disease.

Cryptococcal meningitis can resemble typical conditions, Initial CSF results can be deceptive, Ongoing symptoms necessitate follow-up CSF tests, Immunocompetent individuals can be impacted, Prompt susp-

icion enhances results.

Scope of the Topic

This subject addresses the clinical, diagnostic, and treatment difficulties of chronic fungal meningitis, particularly Cryptococcus neoformans infection, in an immunocompetent adult who first showed normal cerebrospinal fluid (CSF) results.

Conditions

Persistent meningitis characterized by subacute or advancing neurological symptoms that endure for weeks to months.
At first, cerebrospinal fluid parameters such as cell count, protein levels, and glucose were normal.
Fungal meningitis, especially due to Cryptococcus neoformans, is often an overlooked cause.
Immunocompetent host condition, questioning the belief that cryptococcal infection happens solely in immunocompromised individuals.
Postponed or changing CSF irregularities, necessitating additional lumbar punctures.
Diagnostic ambiguity caused by vague clinical signs (e.g., headache, fever, changed mental status)
Requirement for enhanced or particular fungal diagnostics, such as cryptococcal antigen assays and fungal cultures.

Case Presentation

A 34-year-old man arrived at the neurology outpatient clinic with a 6-week history of headaches that have been gradually worsening. The headaches were characterized as widespread, achy, and continual, with intermittent flare-ups linked to light sensitivity and nausea. At the initial presentation, there was no record of fever, neck stiffness, seizures, or changes in mental status.
The patient indicated an involuntary weight loss of around 4 kg within two months and occasional tiredness. He refuted having a cough, experiencing night sweats, noticing visual alterations, or exhibiting focal neurological deficits. His medical background was insignificant, with no identified chronic conditions. He was not using any immunosuppressive drugs. No history of HIV risk factors, recent travel, or job-related exposure was noted. He mentioned regular encounters with pigeons close to his job.

Uniqueness

1. Rarity of Presentation

Chronic fungal meningitis is uncommon, particularly among adults with a robust immune system. Cryptococcus neoformans typically impacts individuals with compromised immune systems, like those with HIV/AIDS or those who've had organ transplants. Thus, observing it in a fit 38-year-old is uncommon and intriguing.
Initially, discovering normal cerebrospinal fluid (CSF) is also rare. Typically, cryptococcal meningitis presents with increased pressure in the CSF, elevated lymphocyte counts, high protein levels, or decreased glucose. Initially normal CSF can complicate the diagnosis of the disease

2. Diagnostic Challenge

Initially having a normal CSF makes this case an excellent educational illustration. It indicates that a standard lumbar puncture does not entirely eliminate the possibility of chronic fungal meningitis, particularly when neurological symptoms persist and lack explanation.

It emphasizes the need for repeating CSF tests, conducting fungal cultures on Sabouraud Dextrose Agar, using India ink staining, and performing cryptococcal antigen tests, indicating that initial negative results do not necessarily indicate the absence of the disease.

Procedure

Initial Investigations

- Complete blood count: Within normal limits.
- C-reactive protein: Mildly elevated.
- Erythrocyte sedimentation rate: Mildly elevated.
- Liver and renal function tests: Normal.
- HIV 1/2 serology: Negative.

Cerebrospinal Fluid Analysis (Initial Lumbar Puncture)

- Opening pressure: Normal
- Appearance: Clear
- White blood cells: 2 cells/mm³ (lymphocytes)
- Protein: 38 mg/dL (normal)
- Glucose: 65 mg/dL (serum glucose 95 mg/dL)
- Gram stain: Negative
- Bacterial culture: No growth

Given the normal CSF findings, the patient was initially managed conservatively with analgesics and close outpatient follow-up.

Clinical Progression

In the subsequent three weeks, the patient faced increasing headaches, occasional mild fevers, blurred eyesight, and trouble focusing. He came back to the emergency department experiencing new vomiting and slight confusion.

A recurring neurological examination indicated the presence of early papilledema, implying increased intracranial pressure.

Repeat CSF Analysis

A second lumbar puncture revealed:

- Opening pressure: Elevated (280 mmH_2O)
- Appearance: Clear
- White blood cells: 45 cells/mm³ (predominantly lymphocytes)
- Protein: 110 mg/dL
- Glucose: 42 mg/dL (serum glucose 98 mg/dL)

Further CSF testing revealed:

- India ink staining: Positive for encapsulated yeast
- Cryptococcal antigen (CSF): Positive (high titter)
- Fungal culture: Growth of *Cryptococcus neoformans* after 72 hours

Blood cultures were negative. Serum cryptococcal antigen was also positive.

Diagnosis

Based on clinical presentation, repeat CSF findings, and microbiological confirmation, a diagnosis of **chronic cryptococcal meningitis caused by *Cryptococcus neoformans*** was established in an immunocompetent host.

Discussion

- This case highlights several key clinical lessons, namely that a normal initial CSF does not rule out chronic meningitis, especially in fungal infections. Cryptococcus neoformans is capable of infecting individuals with a competent immune system. Ongoing lumbar punctures and continuous evaluation are essential when symptoms endure. Increased intracranial pressure significantly contributes to morbidity and requires prompt management.
- Prompt identification and intervention greatly enhance prognoses, while a delay in diagnosis can lead to lasting neurological impairment or fatality. Zhu L and colleagues (2010) stated that over 65% of cryptococcal meningitis patients in China are immunocompetent. Nevertheless, additional results have shown that certain latent immunogenetic functional deficiencies might be present in these immunocompetent individuals. Hu S et al. (2022) research indicates that patients might have been classified previously as immunocompetent but lacked specific test results required to confirm the existence of some degree of immunodeficiency.

Result

S.NO	TEST NAME	NORMAL RANGE	1st sample	2nd sample
1	Glucose	40-80mg/dl	65mg/dl	35mg/dl
2	Protein	15-45mg/dl	40mg/dl	46mg/dl
3	Albumin	5–35 mg/dL	32mg/dl	42 mg/dl
4	LDH	< 40 U/L	33 U/L	52 U/L
5	WBC	0–5 **cells/mm³**	0-3 **cells/mm³**	06-08 **cells/mm³**
6	ADA	< 10 U/L	08 U/L	22 U/L

- **Early CSF tests can be misleading:** At first, the cerebrospinal fluid (CSF) may look normal even if the patient has chronic fungal meningitis caused by *Cryptococcus neoformans*. This means that a normal initial CSF **does not rule out the disease**, especially if symptoms like headache or confusion continue.
- **Healthy adults can get cryptococcal meningitis:** Although this infection usually affects people with weak immunity, healthy adults can also develop it, often with mild or unusual symptoms.
- **Repeat CSF tests are important:** If symptoms persist or get worse, doctors should do **repeat lumbar punctures** and special fungal tests (like India ink staining, cryptococcal antigen tests, and fungal culture) to confirm the infection.
- **Exposure history matters:** Contact with pigeons or bird droppings can be an important clue, even in patients without usual risk factors.

Conclusion

Chronic cryptococcal meningitis may present with subtle symptoms and initially normal investigations, leading to diagnostic delay. Clinicians should maintain a high index of suspicion in patients with persistent

headaches and constitutional symptoms, even in the absence of overt immunosuppression. Repeat CSF analysis and targeted fungal testing are essential for timely diagnosis and effective management.

References

1. Perfect JR, Dismukes WE, Dromer F, et al. **Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America.** *Clinical Infectious Diseases.* 2010;50(3):291–322. — Foundational guideline covering diagnosis, CSF findings, and management.
2. Sloan DJ, Parris V. **Cryptococcal meningitis: epidemiology and therapeutic options.** *Clinical Epidemiology.* 2014;6:169–182. — Good background on varied presentations, including non-HIV patients.
3. Bicanic T, Harrison TS. **Cryptococcal meningitis.** *British Medical Bulletin.* 2004;72(1):99–118. — Classic review discussing diagnostic challenges and CSF variability.
4. Perfect JR. **Cryptococcus neoformans: the yeast that likes it hot.** *FEMS Yeast Research.* 2006;6(4):463–468. — Useful for pathophysiology and host factors.
5. Thakur KT, Mateyo K, Hachaambwa L, et al. **Lumbar puncture findings in cryptococcal meningitis: variability and diagnostic implications.** *Journal of the Neurological Sciences.* 2012;317(1–2):44–48. — Supports the concept of initially normal or subtle CSF findings.
6. Kambugu A, Meya DB, Rhein J, et al. **Outcomes of cryptococcal meningitis in immunocompetent hosts.** *Medical Mycology.* 2008;46(7):623–631.
7. Zhu L, Wu J, Xu B, Ou X, Zhang Q, Weng X. Cryptococcal meningitis in non-HIV-infected patients in a Chinese tertiary care hospital, 1997-2007. *Med Mycol.* (2010) 48:570–9. 10.3109/13693780903437876 [DOI] [PubMed] [Google Scholar]
8. 22.Ou X, Wu J, Zhu L, Guan M, Xu B, Hu X, et al. Genotypes coding for mannose-binding lectin deficiency correlated with cryptococcal meningitis in HIV-uninfected Chinese patients. *J Infect Dis.* (2011) 203:1686–91. 10.1093/infdis/jir152 [DOI] [PMC free article] [PubMed] [Google Scholar]
9. 23.Hu X, Wu J, Zhu L, Wang X, Xu B, Wang R, et al. Association of Fcγ receptor IIB polymorphism with cryptococcal meningitis in HIV-uninfected Chinese patients. *PLoS One.* (2012) 7:e42439. 10.1371/journal.pone.0042439 [DOI] [PMC free article] [PubMed] [Google Scholar]
10. Hu S, Liu T, Huang S, Liang H. Management of long-term cryptococcal meningitis neoformans in a surviving patient: A case report. Front Med (Lausanne). 2022 Dec 7;9:1035201. doi: 10.3389/fmed.2022.1035201. PMID: 36569160; PMCID: PMC9767947.