Published Online: 2025 December 31

Case Report

First Co-infection of Brucella and *Aspergillus niger-terreus* as Chronic Meningitis: A Case Report

Hamideh Moradi Shahrebabak [1], Mehdi Nourallahzadeh [1], Hossein Sajjad Savadkouhi [1], Seyyed Hamid Hosseini [1], Simin Dokht Shoaei [2,1,*]

[1] Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Clinical Research and Development Center, Imam Hossein Teaching and Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[*] ***Corresponding Author:*** Clinical Research and Development Center, Imam Hossein Teaching and Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: drsimin2@yahoo.com

Received: 19 July, 2025; **Revised:** 26 December, 2025; **Accepted:** 26 December, 2025

Abstract

Introduction: Chronic meningitis is a syndrome with neurologic signs and symptoms lasting more than 4 weeks with sustained abnormal cerebrospinal fluid (CSF). It has multiple differential diagnoses as infectious, autoimmune, neoplastic, and other group diseases. It may have two etiologies and complete evaluation should be done. Here we present a co-infection of meninges with Brucella and Aspergillus.

Case Presentation: The patient is a 36-year-old man with one-month neuropsychologic signs and symptoms. He had headache, vomiting, behavior disorder, and decreased level of consciousness. Cerebrospinal fluid analysis showed lymphocytic pleocytosis, low sugar, and increased protein. Brucella serology in serum and CSF was positive, concurrent with *Aspergillus niger-terreus* positive PCR in CSF.

Conclusions: This case has 4 important points: (1) Brucella meningitis is common, and this patient is the first case of Brucella and Aspergillus co-infection; (2) *Aspergillus niger* or *terreus* meningitis alone is rare, and this patient is the first coinfection of this fungus and Brucella; (3) all possible infectious and non-infectious diseases should be evaluated, and various pathogens should be considered based on the patient's immune status and endemicity; (4) identification of pathogenic fungal species is important to use effective drugs, contemplating antifungal sensitivity.

Keywords: Chronic Meningitis, Coinfection, Brucella, *Aspergillus niger-terreus*

1. Introduction

Chronic meningitis refers to a clinical syndrome caused by several etiologies, including infectious (Mycoses, Bacteria, Mycobacterium, Parasites.) autoimmune, neoplastic, and other group diseases. Neuropsychologic signs and symptoms, including decreased level and content of consciousness, focal neurologic deficits and meningeal irritation for more than 3 - 4 weeks with sustained abnormal cerebrospinal fluid cerebrospinal fluid (CSF) present this syndrome. Fungal infections have recently shown increased incidence in immunocompromised patients, and brucellosis should be noticed based on epidemiology (1). In spite of clinical impact and improvement in diagnostic tools, chronic meningitis remains a diagnostic challenge in clinical practice. Owing to non-specific clinical manifestations and paraclinical findings, it is difficult to distinguish different etiologies, resulting in delayed diagnosis especially when more than one disease is responsible.

Brucellosis is most commonly seen in the Mediterranean countries, the Balkans, the Persian Gulf, the Middle East, and Central and South America (2). Brucella melitensis is the most invasive species and can involve any part of nervous system as acute, subacute and chronic course (3). Laboratory confirmation is necessary by culture, serology, or molecular tests. Automated blood culture systems are more often positive than conventional cultures for sterile body

Copyright © 2026, Journal of Kermanshah University of Medical Sciences. This open-access article is available under the Creative Commons Attribution-NonCommercial 4.0 (CC BY-NC 4.0) International License (https://creativecommons.org/licenses/by-nc/4.0/), which allows for the copying and redistribution of the material only for noncommercial purposes, provided that the original work is properly cited.

How to Cite: Moradi Shahrebabak H, Nourallahzadeh M, Savadkouhi HS, Hosseini SH, Shoaei SD. First Co-infection of Brucella and Aspergillus niger-terreus as Chronic Meningitis: A Case Report. J Kermanshah Univ Med Sci. 2025;29(4):e166096. doi: https://doi.org/10.5812/jkums-166096

fluids including CSF. Serum agglutination test (SAT or Wright test) is usually recognized as the reference technique and ELISA is less specific. Molecular tests with high sensitivity and specificity provide early recognition (4).

Aspergillus meningitis is rare with nonspecific clinical presentation. The most common Aspergillus species causing invasive infection is *A. fumigatus*, followed A. flavus, *A. terreus*, and, less common *A. niger*. However, less common species that are often identified by molecular means have increasingly been reported to cause invasive infection. Most species initially appear as small, fluffy white colonies on culture plates within 48 hours from a normally sterile site, such as a needle biopsy or CSF, although blood cultures are rarely positive (5).

A. terreus has colony beige to cinnamon buff color with Columnar; biseriate; globose; small 2 - 2.5 µm conidia and globose accessory conidia along hyphae. It is increasingly detected as resistant to amphotericin B and more susceptible to newer azoles. *Aspergillus niger* has initially white colony, rapidly turning black with yellow reverse, microscopically radiate; biseriate; globose, black, with very rough conidia 4 - 5 µm. It is uncommon in invasive infections but causing superficial agent of otic disease and colonization (6).

Antibody detection is of limited utility because immunosuppressed hosts fail to mount an antibody response even with invasive infection. Detection of galactomannan (GM) by enzyme immunoassay (EIA) has contributed substantially to the diagnosis of invasive aspergillosis with controversy in optimal cut-offs (0.5 - 0.7). Other potential markers also include the nonspecific fungal marker β-d-glucan (BDG) (7). Polymerase chain reaction (PCR) is now accepted as an early diagnostic marker for IA, which may be more sensitive than other methods (6). The new metagenomic next-generation sequencing (mNGS) is a fast, unbiased, culture-free approach that can increase the pathogen species detection rate, such as fungi, helping clinicians improve the accuracy of clinical diagnosis and take therapeutic action as quickly as possible (8).

In this report, we present a case of co-infection of Aspergillus and Brucella chronic meningitis in a construction worker with no history of immune deficiency.

2. Case Presentation

The patient is a 36-year-old Afghan man, who lived in Iran in a village near Tehran for 20 years as a construction worker. He had headaches, dizziness, nausea, vomiting, and weight loss since a month ago and behavior disorder, lethargy, restlessness, confusion, delirium, ataxia, and arthralgia from one week before admission. He had no focal neurological deficits, nuchal rigidity, or Kernig's and Brudzinski's signs. Both pupils were midsize and reactive to light. Fundoscopy showed no uveitis and retinopathy. The cranial and peripheral nerve exams were normal. Chest, abdomen, musculoskeletal, and scrotum exams was all normal. The brain CT scan was normal. MRI presented small nonspecific white matter hyperintensity signals on T2-weighted and fluid attenuated inversion recovery (FLAIR). Unidentified bright objects were also observed in the frontal lobe. Chest CT scan, abdominopelvic ultrasonography was all normal. Cerebrospinal fluid analysis showed lymphocytic pleocytosis, low sugar, and increased protein (Table 1). Treatment with ceftriaxone, vancomycin, and acyclovir was started. Complete blood count, rheumatologic, renal, liver, thyroid, inflammatory, and toxicologic tests were normal. Biochemistry tests were normal other than resolving hyponatremia. The patient evaluation was continued with the impression of chronic meningitis. Serum VDRL, galactomannan (GM) antigen, and β-d-glucan (BDG) tests were negative. Brucella serology was reported positive in serum as Wright: 1/160, Coombs Wright: 1/160, 2ME:1/80 and in CSF as Wright:1/80, Coombs Wright:1/160 and 2ME1/40. No pathogen was obtained through microbial culture. Aspergillus PCR was negative for *A. fumigatus* and *A. flavus* but a positive PCR which could not differentiate *A. niger* from *A. terreus*, was detected in CSF by PCR, regarding *A. terreus* is inherently resistant to amphotericin B. The mNGS test was not available to further differentiation.

The treatment was changed to ceftriaxone, doxycycline, rifampin, and intravenous voriconazole. There was a rise in serum creatinine level, which normalized by discontinuation of vancomycin. After one week, the level of consciousness content slightly decreased, and a new Brain CT scan showed mild ventriculomegaly; dexamethasone was added, and he had clinical improvement with complete orientation after two days.

At the end of two weeks of treatment, the patient's symptoms improved. Due to financial problems treatment continued as oral doxycycline and rifampin, plus ceftriaxone and voriconazole in the form of outpatient parenteral antibiotic therapy (OPAT) from the third week. For one month there was no neurologic sequelae or drug side effects, but after that time (6 weeks of treatment) he moved to his country without informing anyone or coming to the hospital.

Table 1. Cerebrospinal Fluid Findings in Patient with Co-infection of Brucella and Aspergillus as Chronic Meningitis

Test	WBC	Lymph; %	Poly; %	RBC	Sugar; mg/dL	Protein; mg/dL
1st day	30	90	10	20	56	418
5th day	100	95	05	100	42	305

3. Discussion

Chronic meningitis is meningeal inflammation with signs and symptoms for at least 4 weeks without relief, including headache, lethargy, mental status changes, and fever with sustained abnormal CSF. It has many infectious and non-infectious etiologies to be considered as a challenging diagnostic entity and needs more complex diagnostic tests and treatments based on etiology (1).

New pathogens have been added to infectious etiologies, and molecular analysis provides important help to detect them. New mNGS provides identification of pathogens without the bias of a predetermined result (8).

Considering two etiologies may cause signs and symptoms, all clinical and paraclinical evaluations should be completed based on epidemiology and patient immune status.

Neurobrucellosis is common in endemic countries and is in the first diagnoses of chronic meningitis including in Iran. It involves every part of the central and peripheral nervous system, such as isolated meningitis, encephalitis, myelitis, peripheral neuritis and psychologic disorders, or any combinations of these syndromes. It is diagnosed by serology and culture. In brucella meningitis, CSF changes include mononuclear pleocytosis, high protein, and hypoglycorrhachia (9). Paraclinical confirmation is necessary by culture, serology, or molecular tests (6).

A case of Brucella and VZV co-infection in a 56-year-old woman with low consciousness, seizures, fever, and mood disorders has been reported. The brain CT revealed no pathological lesions, but MR showed non-specific plaques in the periventricular white matter. VZV was detected by molecular tests in CSF. The blood culture and the Wright test revealed the presence of Brucella spp (10).

Karsen has presented a meningitis case with Brucella and Mycobacterium co-infection. Patient was a 19-years-old stockbreeder who had severe headache, fever, vomiting, meningeal irritation symptoms, confusion and diplopia. STA test for brucellosis was positive at 1/80 titer in CSF and at 1/640 titer in serum with negative growth of Brucella spp. There was no clinical improvement. Repeated CSF smear yielded acid-fast bacteria. Tuberculosis meningitis was confirmed with the growth of *M. tuberculosis* on the 14th day of cultivation (BACTEC) of the CSF sample (11). A case of hydrocephalus due to brucella meningitis has been reported as our case (12). Coinfection of Brucellae and Aspergillus in meninges has not been reported.

Cerebral aspergillosis has the highest mortality of invasive aspergillosis syndromes; the incidence of cerebral aspergillosis is low and can't be easily determined because the diagnosis is often unsuspected, and it appears in patients with persistent immunosuppression and disseminated disease. Concomitant pulmonary infection is usually present in some patients. Isolated cerebral aspergillosis can occur in intravenous drug abusers or immunocompetent patients (13). Aspergillus has 250 species in 8 subgenera that are subdivided into a total of 27 sections and species complexes. Different probes are used for the detection and differentiation of Aspergillus spp. based on the detection of markers within the gene of Aspergillus and newly mNGS (8).

A. terreus is an emerging uncommon opportunistic pathogen, a common soil-related isolate, causing fatal disseminated infections in immunocompromised patients. Identification of *A. terreus* is increasingly important because of its resistance to antifungals, including amphotericin B, but improved susceptibility with newer azoles (14). Its presentations are low and described in case reports. A case of fungal meningitis caused by *A. terreus* in an immunocompetent patient with nasal and sinus polypectomy. He developed headache, fever, fits, loss of consciousness one week after surgery. Computed tomographic (CT) images showed pansinusitis, hydrocephaly, left lower lobe consolidation with right upper lobe linear atelectasis and mild ground glass density patches. Abnormal CSF culture was positive for Aspergillus (BACTEC) and mNGS showed high degree of similarity (above 99.7%) to *A. terreus* reference sequences. He had hydrocephaly as our case (15). Syndromes as endogenic endophthalmitis, post acupuncture spondylodiscitis with *A. terreus*, and other presentations has been reported (16, 17).

Aspergillus niger is found in soil, on plants, in food and condiments such as pepper, and is used in the chemical industry for a variety of applications, while being a possible pathogen to humans. The role of *A. niger* in invasive infection is less well proved, because of its low virulence, perhaps due to its large conidia, which cannot easily reach deep into lung parenchyma. It is a common colonizer and causes superficial infections, such as otitis externa (6).

Simmonds reported a 68-year-old woman with a background of hypertension, stroke and rheumatoid arthritis treating with methotrexate presented with a 4-week history of gradual deterioration and increasing confusion with new onset right-sided weakness. Her initial CT scan revealed a rim enhancing mass lesion with surrounding edema in the left parietal lobe for which she underwent CT scan-guided biopsy. Microbiology culture of the 2 biopsy samples yielded *A. niger*. She was started on the antifungal agent voriconazole then posaconazole, with recovery (18).

Another case of a 67-year-old previously immunocompetent female who was treated with corticosteroids for COVID-19 one-month prior was admitted for altered mental status (AMS). Subsequent imaging and biopsy demonstrated invasive CNS *A. niger*. This report draws attention to the detrimental immunosuppressive effects of corticosteroid therapy in COVID-19 (19).

Our patient was an immunocompetent construction worker without any immunosuppressive drug use.

Signs and symptoms of chronic meningitis and CSF changes in infectious and noninfectious etiologies are similar, non-specific, and overlap with each other. So, evaluation should be complete to find combined diseases. In endemic areas, infection with two pathogens at the same time should not be ignored, and physicians should use a variety of methods to augment the detection rate of the pathogen.

This case has four points of importance: (1) Brucella meningitis is common, and this patient is the first case of Brucella and Aspergillus co-infection in meninges; (2) *A. niger* or *A. terreus* meningitis alone is rare, and this patient is the first co-infection of *A. niger* or *A. terreus* and Brucella in meninges; (3) all possible infectious and non-infectious diseases should be evaluated for rapid diagnosis and prevention of neurological complications, and various pathogens should be considered based on the patient's immune status and endemicity; (4) identification of pathogenic fungal species is important for using effective drugs, contemplating antifungal sensitivity.

3.1. Conclusions

In chronic meningitis, it is important to investigate all possible infectious etiologies agents (Bacterium, Fungi, …) and other non-infectious diseases to confirm rapid diagnosis and prevent neurological complications. Consideration of various pathogen should also involve the patient's immune status and endemicity.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Study concept and design and drafting of the manuscript H. M. S., M. N., H. S. S., and S. H. H.: data gathering.

Conflict of Interests Statement: The authors have no conflict of financial and non-financial interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to patient privacy.

Ethical Approval: This study is approved under the ethical approval code of IR.SBMU.RETECH.REC.1404.058

Funding/Support: This study has no funding/support.

Informed Consent: There was no new treatment regimen, procedure or intervention. He knew report is used only for training purposes. He was agreed to participate in this case report with Implied consent, as presenting smile with no disagreement when talking about case reporting. He was anonymized surely; names and other identifiers are not included in the text or images.

References

1. Aksamit AJ. Chronic Meningitis. *N Engl J Med*. 2021;**385**(10):930-6. [PubMed ID: 34469648]. https://doi.org/10.1056/NEJMra2032996.
2. Tuon FF, Gondolfo RB, Cerchiari N. Human-to-human transmission of Brucella - a systematic review. *Trop Med Int Health*. 2017;**22**(5):539-46. [PubMed ID: 28196298]. https://doi.org/10.1111/tmi.12856.
3. Hatami H, Hatami M, Soori H, Janbakhsh AR, Mansouri F. Epidemiological, clinical, and laboratory features of brucellar meningitis. *Arch Iran Med*. 2010;**13**(6):486-91. [PubMed ID: 21039003].
4. Araj GF. Update on laboratory diagnosis of human brucellosis. *Int J Antimicrob Agents*. 2010;**36 Suppl 1**:S12-7. [PubMed ID: 20692128]. https://doi.org/10.1016/j.ijantimicag.2010.06.014.
5. Gautier M, Normand AC, Ranque S. Previously unknown species of Aspergillus. *Clin Microbiol Infect*. 2016;**22**(8):662-9. [PubMed ID: 27263029]. https://doi.org/10.1016/j.cmi.2016.05.013.
6. Martin J, Blaser MD, Jeffrey I, Cohen MD, Steven M, Holland MD. *Mandell Douglas & Bennett, Principles and Practice of Infectious Diseases*. 10th ed. Philadelphia: Churchill Livingston; 2025.
7. Thompson G3, Boulware DR, Bahr NC, Clancy CJ, Harrison TS, Kauffman CA, et al. Noninvasive Testing and Surrogate Markers in Invasive Fungal Diseases. *Open Forum Infect Dis*. 2022;**9**(6):ofac112. [PubMed ID: 35611348]. [PubMed Central ID: PMC9124589]. https://doi.org/10.1093/ofid/ofac112.
8. Zhao Y, Zhang W, Zhang X. Application of metagenomic next-generation sequencing in the diagnosis of infectious diseases. *Front*

Cell Infect Microbiol. 2024;**14**:1458316. [PubMed ID: 39619659]. [PubMed Central ID: PMC11604630]. https://doi.org/10.3389/fcimb.2024.1458316.

9. Shoaei S, Farahbakhsh M, Haghighi M, Hadavand F. Epileptic Seizure: An Atypical Presentation in Brucellosis. *Case Reports in Clinical Practice*. 2016;**1**(3):85-8.
10. Allahyari F, Halabian R, Nejad JH. VZV Encephalitis with Brucella coinfection-case report. *Oxf Med Case Reports*. 2023;**2023**(11):omad121. [PubMed ID: 38033406]. [PubMed Central ID: PMC10686003]. https://doi.org/10.1093/omcr/omad121.
11. Karsen H, Karahocagil MK, Irmak H, Demiroz AP. [A meningitis case of Brucella and tuberculosis co-infection]. *Mikrobiyol Bul*. 2008;**42**(4):689-94. [PubMed ID: 19149093].
12. Razzaghi R, Banaee S, Erami M, Kosha H. [Hydrocephalus due to brucella meningitis: A case report]. *J Arak Univ Med Sci*. 2012;**14**(7):109-15. FA.
13. Antinori S, Corbellino M, Meroni L, Resta F, Sollima S, Tonolini M, et al. Aspergillus meningitis: a rare clinical manifestation of central nervous system aspergillosis. Case report and review of 92 cases. *J Infect*. 2013;**66**(3):218-38. [PubMed ID: 23178421]. [PubMed Central ID: PMC7112586]. https://doi.org/10.1016/j.jinf.2012.11.003.
14. Thakur R, Shishodia SK, Sharma A, Chauhan A, Kaur S, Shankar J. Accelerating the understanding of Aspergillus terreus: Epidemiology, physiology, immunology and advances. *Curr Res Microb Sci*. 2024;**6**:100220. [PubMed ID: 38303967]. [PubMed Central ID: PMC10831165]. https://doi.org/10.1016/j.crmicr.2024.100220.
15. Elsawy A, Faidah H, Ahmed A, Mostafa A, Mohamed F. Aspergillus terreus Meningitis in Immunocompetent Patient: A Case Report. *Front Microbiol*. 2015;**6**:1353. [PubMed ID: 26648927]. [PubMed Central ID: PMC4664626]. https://doi.org/10.3389/fmicb.2015.01353.
16. Panigrahi PK, Roy R, Pal SS, Mukherjee A, Lobo A. Aspergillus terreus endogenous endophthalmitis: report of a case and review of literature. *Indian J Ophthalmol*. 2014;**62**(8):887-9. [PubMed ID: 25230968]. [PubMed Central ID: PMC4185171]. https://doi.org/10.4103/0301-4738.141065.
17. Jin Y, Yin X. Aspergillus terreus spondylodiscitis following acupuncture and acupotomy in an immunocompetent host: case report and literature review. *Front Cell Infect Microbiol*. 2023;**13**:1269352. [PubMed ID: 38239504]. [PubMed Central ID: PMC10794653]. https://doi.org/10.3389/fcimb.2023.1269352.
18. Simmonds L, Mitchell S, White B, Crusz SA, Denning D. Aspergillus niger infection in an immunosuppressed patient confined solely to the brain. *BMJ Case Rep*. 2017;**2017**. [PubMed ID: 28331021]. [PubMed Central ID: PMC5372240]. https://doi.org/10.1136/bcr-2016-218658.
19. Saleh H, Abraham P, Chahine H, Subbiah S, Grace-Abraham N. A Rare Case of Invasive Central Nervous System Aspergillus niger in a Previously Immunocompetent Patient After Corticosteroid Treatment for COVID-19. *Cureus*. 2024;**16**(4). e57923. [PubMed ID: 38725734]. [PubMed Central ID: PMC11081636]. https://doi.org/10.7759/cureus.57923.