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Indian Journal of Microbiology Research

Journal homepage: www.ijmronline.org

Case Series

Unveiling the menace: a case series of fungal meningitis with galactomannan and beta-D-glucan detection and the efficacy of amphotericin B and flucytosine treatment

Rachana Patel[1*], Bhavinkumar Bhagubhai Patel[2], Trupti Jansari[1], Amit Pravin Chauhan[1], Tanuja Javadekar[1]

[1]Shreemati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth deemed to be University, Piparia, Vadodara, Gujarat, India

[2]Bhailal Amin General Hospital, Gorwa, Vadodara, Gujarat, India

Abstract

Fungal meningitis is a rare but serious infection of the central nervous system with high morbidity and mortality, especially when diagnosis is delayed. Standard CSF analysis often fails to identify the aetiology, making early detection challenging. This case series explores the utility of CSF fungal biomarkers—galactomannan and beta-D-glucan—in diagnosing fungal meningitis and the clinical outcomes following prompt antifungal therapy.

We describe three critically ill adult patients diagnosed with fungal meningitis of varying aetiologies. All cases had initial negative routine CSF studies, cultures, and Bio Fire panels. Diagnosis was confirmed using elevated CSF galactomannan and beta-D-glucan levels. Each patient was treated with liposomal amphotericin B and flucytosine, followed by step-down therapy with voriconazole. All patients showed neurological recovery without residual deficits and were successfully discharged after prolonged ICU care.

This series underscores the diagnostic challenges posed by fungal meningitis and the pivotal role of adjunctive CSF biomarkers in early detection. The use of galactomannan and beta-D-glucan assays significantly enhanced diagnostic sensitivity in our patients. Early initiation of appropriate antifungal therapy based on these biomarkers contributed to favourable outcomes.

CSF galactomannan and beta-D-glucan are valuable diagnostic tools for fungal meningitis, especially in cases with negative conventional workups. Timely diagnosis and antifungal therapy with amphotericin B and flucytosine can lead to full neurological recovery, even in critically ill patients.

Keywords: Amphotericin B, Beta-D-glucan, Flucytosine, Fungal meningitis, Galactomannan.

Received: 10-06-2025; **Accepted:** 07-09-2025; **Available Online**: 20-09-2025

1. Introduction

Although fungal meningitis is not so common but once detected with suspicion, it should be treated aggressively as can lead to life threatening condition. Bacterial meningitis is more common, but fungal meningitis is rare and serious condition that affects the membranes surrounding the brain and spinal cord. Our case series highlights the significance of diagnostic challenges especially the role of fungal biomarkers for diagnosing the fungal meningitis, early response to inj. amphotericin B and flucytosine. Objective of our case series was to emphasize the diagnostic test for fungal marker in Cerebro-spinal fluid (CSF) and good response to the treatment modalities.

2. Case Description

2.1. Case 1

A female of 84 years admitted with c/o right upper limb weakness since early morning, followed by slurred speech

*Corresponding author: Rachana Patel
Email: rachana.roze@gmail.com

https://doi.org/10.18231/j.ijmr.11710.1768021632

and right side facial weakness. On arrival to ER (Emergency Room), patient was conscious and oriented to time, place and personand had right upper limb power grade 3/5. Urgent MRI Brain stroke protocol and blood investigations (**Table 1**) were done and showed no bleed or infarct like acute changes. Patient was shifted to ICU for close monitoring and observation. Tab. Ecosprin 75 mg, Tab. Clopidogrel 75 mg and Atorvas 40mg, was started. Patient had persistent slurred speech and increase in right upper limb weakness so repeat MRI was done and showed - Mild chronic micro-vascular ischemic changes, Age related cerebral involutional changes, fluid in the right mastoid air cells. EEG was done suggestive of moderate to severe encephalopathy with left hemispheric continuous slowing.

On 3rd day Lumbar puncture was done and sent CSF fluid for examination. CSF fluid R/M was normal (**Table 2**) GeneXpert, KOH stain, Gram stain, AFB stain, BioFire -all were negative. Repeat 3rd MRI brain s/o abundant leptomeningeal enhancement noted along the left cerebral sulci. Empirically IV Acyclovir 900mg TDS was started. Blood culture, urine culture and CSF culture were sent. IV Noradrenaline infusion started in view of hypotension targeting mean arterial pressure (MAP) more than or equal to 65 mm of Hg, gradually GCS declined to E1V1M4 so endotracheal intubation was done and kept on mechanical ventilatory support.

The patient developed acute kidney injury, for which renal replacement therapy was initiated. Autoimmune encephalopathy panel was negative. Fungal markers (Galactomannan and Beta-D Glucan) from serum and CSF were sent and all came positive. Soi.v liposomal amphotericin-B (3 mg/kg) + Tablet flucytosine (20 mg/kg) 500 mg QDS was started, patient neurologically improved with GCS 10/10 over period of 3-5 days, without focal neurological deficit. EEG was done s/o- moderate encephalopathy. Along with hemodynamic improvement there was neurological improvement so patient was extubated and over the period of time AKI was also resolved. Patient was stable so was discharged on tablet voriconazole 200 mg BID for 7 days.

Table 1: Blood investigations

	Day 1	Day 7	Day 12	Day 16		Day of discharge
Hb	11.5	9.7	10.1	10.3		10
WBC	6860	14,020	9380	11,230		9740
Platelet	2,37,000	1,97,000	1,52,000	2,45,000		3,24,000
Na	140	130	135	139	145	144
K	4.2	5.5	3.7	4.2	3.8	3.4
Cl	109	101	101	100		104
HCO_3	27.6	22.7	28.5	36.4		35.1
Urea	20	90	143	56		
S. Creat	0.92	3.78	4.24	1.15	1.0	1.09
CRP	13.3	90.5	25	65		9.5
PCT	0.06		0.27			
S. galactomannan		1.15		23.42		
S. beta-D-glucan		144.55		0.43		
CSF galactomannan		3.4				
CSF beta-D-glucan		248.38				
Blood culture		No growth				
Urine culture		No growth				
CSF BioFire		Not detected				

Hb: Hemoglobin; WBC: White blood cell count; CRP: C-reactive protein; PCT: Procalcitonin; CSF: Cerebrospinal fluid

Table 2: CSF investigations

CSF	Cell count	Differential count	protein	CSF glucose	Chloride	LDH	Matching glucose	Galactomannan	Beta-D-glucan
Sample 1	<5		82	60	120	41	114	3.4	248.38

2.2. Case 2

A 73 year old male patient known case of Hypertension and Ischemic Heart Disease (recent post CABG) presented with complaint of generalized weakness since 4-5 days and decreased appetite. No history of vomiting, loose stools or burning micturation.

On the day of admission patient had temperature of 101.2' F, hence blood culture and urine culture were sent and Antibiotic cefoperazone+sulbactum iv 3gm BD and Teicoplanin 400mg started and given for 7 days. Routine blood investigations (**Table 3**) were done and in view of altered LFT, USG Abdomen was done s/o Minimal ascites, mildly inflamed wall of cecum and ascending colon, rest of findings were normal. Neurologist and Nephrologist reference was done advised to send Free Light Chain Assay and Serum Protein Electrophoresis which were negative. Urine culture s/o E-coli so Antibiotics escalated to Inj.Meropenem 1 gm TDS. MRI Brain done on 2nd day forgeneralized weakness and Drowsiness s/o Small patchy subacute-to-chronic infarct in the left occipital lobe in paramedian location. Few scattered foci of FLAIR hyperintensity in bilateral frontal deep white matter. Age related cerebral involution changes.

HRCT Chest done on 2nd day i/v/o Breathlessness s/o Trace to mild bilateral pleural effusion. Minimal interstitial edema in the bilateral lung parenchyma also observed as described. Patient had having intermittent fever spikes.

In view of altered sensorium, CSF analysis was done on 4th day, CSF routine was normal (**Table 4**). CSF Bacterial and fungal culture and BioFire came negative. While CSF fungal markers were revealed (Galactomannan and beta D-glucan positive) So IV amphotericin- B (Liposomal) and Tablet *flucytosine* 1000 mg twice a day was started. Serum fungal markers came negative. Blood c/s didn't show any growth.

Patient was kept on NIV in view of respiratory distress. Later on for worsening respiratory distress, severe tachypnoea, tachycardia, drowsiness, endotracheal intubation was done and patient was kept on Mechanical ventilatory support. Repeat blood c/s along with ET secretion c/s were sent for analysis, from which blood culture grew Gram positive bacterial growth, while ET secretion culture grew *Klebsiella Pneumoniae* bacterial growth, iv antibiotic was given according to culture and sensitivity. X-Pert Carba R Assay from ET culture revealed NDM and OXA-48 positive, anti-fungal (Injection + Tablet) were continued. Serum galactomannan came negative, while Beta-D-Glucan was still positive (334.87) so antifungal were continued. Cytomegalo virus DNA PCR was negative. Patient was gradually weaned off from ventilator. Patient had c/o oozing from CABG dressing site, pus swab c/s was sent for analysis, which grew *Acinetobacter Baumannii* bacterial, IV antibiotic was escalated according to sensitivity report. Patient was later on decannulated from tracheostomy as GCS was 15/15, ambulated and shifted out of ICU. Wound culture sent again on 30th day of admission, culture reports on *Staphyloccoccus hemolyticus* so antibiotics were continued according to culture sensitivity. Sternal wire removal was done procedure remained uneventful, patient remained hemodynamically stable, afebrile, took orally well hence patient was discharged. Patient was hospitalized for nearly 35 days in hospital.

Table 3: Blood investigations

	Day of admission	Day 10	Day 20	Day 25	Day 30	Day of discharge
Hb	11.3	10.9	11.1	9.9	10.3	10.6
WBC	10830	13130	15,490	15330	15850	12560
Platelet	142000	458000	391000	540000	452000	357000
Na	139	137	139	132	132	133
K	5	4.2	4.1	4.4	4	4.7
Cl	103	101	103		102	102
HCO_3	19.8	28.3	27.7		22.2	22
Urea	103	113	118			
S. Creat	2.64	2.38	2.6	2.1	2.51	2.61
CRP	123.2	69.48	56.6	39	91.8	56.90
PCT	2.92	8.7	1.1		1.46	
S. galactomannan	0.95	0.32			0.46	
S. beta-D-glucan	334.87	461.69			256	
Blood Culture	No growth					
Urine Culture		*E.coli*				
CSF BioFire		Not detected				

Hb: Hemoglobin; WBC: White blood cells; CRP: C-reactive protein; PCT: Procalcitonin; CSF: Cerebrospinal fluid

Table 4: CSF investigations

CSF	Cell count	Differential count	Protein	CSF glucose	Chloride	LDH	Matching glucose	Galactomannon	Beta-D-glucan
Sample 1	<10		61	56	120	41	108	3.82	165.52
Sample 2	<5		63	60	113	59	107	0.42	13.43

2.3. Case 3

A male of 79 years presented with complaints of altered mental status and drowsiness without any co-morbidities. He had history of recent hospitalization within 90 days for circumcision and chikungunya fever. Patient was admitted in ward and shifted to ICU in view of hypotension and hypoxia. After sending blood investigations (**Table 5**), blood culture and urine culture BL-BLI was started. On arrival to ICU GCS- E2 V2 M5, pupils were bilaterally equal and reacting to light, no focal neurological deficit, no signs of meningeal irritation. In view of persistent fever and patient not improving, CT scan from head to pelvis was done, which showed no abnormalities. Neuro-physician opinion was taken and CSF was planned and done for diagnostic purpose. ANA and ANCA negative. MRI brain with contrast enhanced venography was done revealed no acute findings and brain parenchymal abnormalities seen. Fungal marker in the form of galactomannan and Beta-D-Glucan were sent and turned to be positive. Meanwhile patient was intubated and ventilated in view of GCS<7 and hypotension. Injectable amphotericin 3 out mg/kg and flucytosine 100 mg/kg/day were started and given for 28 days. After 3-5 days of starting amphotericin and flucytosine patient neurologically improved GCS – 8/10 E-3 V-T and M-5 without any focal neurological deficit. Voriconazole was given for 14 days, after 1 month Decannulation was done. Patient was discharged after approximate 50 days of admission.

3. Discussion

Humans inhale numerous fungal spores daily, most of which are cleared by alveolar macrophages and neutrophils within the respiratory tract. Among pathogenic fungi, Aspergillus fumigatus and Aspergillus flavus are the most common species associated with invasive infections, though other species have been reported to cause CNS disease.

Fungal meningitis presents significant challenges in critical care because of its nonspecific symptoms, diagnostic limitations, and restricted therapeutic options. This series emphasizes the importance of early recognition, rapid diagnostic evaluation, appropriate antifungal therapy, and careful monitoring to optimize patient outcomes.

Our findings highlight the need for heightened awareness among healthcare professionals and better access to advanced diagnostic tools. The conventional diagnostic modalities for CNS fungal infections often have limited sensitivity, making diagnosis difficult. In this context, CSF biomarkers such as galactomannan and beta-D-glucan serve as valuable adjuncts, enabling earlier identification of fungal pathogens. In one study, the combined sensitivity and specificity of these biomarkers exceeded 85% for detecting CNS fungal infections. Although fungal meningitis is more common in immunocompromised patients, it may also occur in immunocompetent individuals, as observed in our series and in earlier reports by Elsawy *et al*.[1] and Pettit *et al*.[2]

Table 5: Blood and CSF investigations

	Day of admission	Day 10	Day 20	Day 25	Day 30	Day of discharge
Hb	9.4	11.9	8.9	9.5	10.2	9.6
WBC	10,500	10,370	10,640	13,600	8110	9570
Platelet	367000	2,05,000	3,14,000	118000	2,85,000	261000
Na	120	132	131	129	141	131
K	3.7	3.2	3.9	4.7	4.5	4.8
Cl	83	105	104	94	107	89
HCO_3	26.6	25.2	21.7	25.2	26	29
Urea	13	17	80	91	33	
S. Creat	0.7	1.3	1.26	1.35	1	1.02
CRP	178	133	81	12.2	37	15.6
PCT	78.33	2.49	0.52	1.38	-	-
S. galactomannan	-	1.05	1.17	-	0.48	-
S. beta-D-glucan	-	>523.43	129.24	-	59.60	-
Blood culture	-	-	-	-	-	-
Urine culture	-	-	-	-	-	-
CSF BioFire	-	-	-	-	-	-

Hb: Hemoglobin; WBC: White blood cell count; Na: Sodium; K: Potassium; Cl: Chloride; HCO_3^- = Bicarbonate; CRP: C-reactive protein; PCT: Procalcitonin; CSF: Cerebrospinal fluid.

Table 6: CSF investigations

CSF	Cell count	Differential count	Protein	CSF glucose	Chloride	LDH	Matching glucose	Galactomannon	Beta-D-glucan
Sample 1	10	L-100%	60	46	116	24	212	6.03	155

Similar to our findings, Chong *et al*. have shown that CSF galactomannan and beta-D-glucan are useful in diagnosing fungal meningitis.[3,4] A high index of suspicion is crucial for detecting such infections, as emphasized by Rathish *et al*.[5] and Desai *et al*.[6] unlike our cases, Hiraga *et al*. reported successful treatment with voriconazole and corticosteroids, with diagnosis established by CSF galactomannan.[7] Forster *et al*. further demonstrated that combining galactomannan with beta-1, 3-D-glucan improved the diagnostic yield compared to either marker alone.[8]

As described by Tang *et al*., fungal meningitis remains a life-threatening condition in which early diagnosis and prompt initiation of antifungal therapy are essential for survival.[9] Memória *et al*. reported successful treatment with liposomal amphotericin B and itraconazole, a therapeutic approach similar to ours.[10] Shariati *et al*. and Walsh et al. have also advocated for early diagnosis and antifungal treatment in CNS aspergillosis.[11,12] In one comparative study, liposomal amphotericin B plus flucytosine demonstrated superior efficacy and fewer adverse effects compared to voriconazole, supporting our choice of induction therapy in these cases. This aligns with findings from Schwartz *et al*. who reported improved survival rates when combination therapy was initiated early in invasive CNS aspergillosis.[13] Kourkoumpetis *et al*. highlighted that delayed antifungal treatment was associated with a twofold increase in mortality among CNS fungal infection cases.[14] Moreover, Perfect *et al*. in the updated IDSA guidelines reinforce the integration of biomarker-based diagnosis and early combination antifungal therapy for optimal outcomes.[15]

However, as this series is retrospective and involves a small number of patients, the results cannot be generalized, and larger prospective studies are needed.

4. Conclusion

Biomarker in the form of CSF galactomannon and Beta-D-glucan facilitated early diagnosis of fungal infection. We also revealed that in such cases usage of liposomal amphotericin with flucytosine can be very useful for treatment without major adverse drug reactions.

5. Clinical Significance

This case series underscores the diagnostic utility of CSF galactomannan and beta-D-glucan assays in the early identification of fungal meningitis, particularly when conventional CSF studies and cultures are negative. By facilitating rapid diagnosis, these biomarkers allow for prompt initiation of targeted antifungal therapy, which is critical for improving survival and neurological outcomes.

In our experience, the combination of liposomal amphotericin B and flucytosine, followed by voriconazole as consolidation therapy, proved effective and was well tolerated, aligning with current Infectious Diseases Society of America (IDSA) recommendations. Early diagnosis and treatment not only improve prognosis but can also reduce the duration of ICU and hospital stay, thereby minimizing healthcare costs and complications.

Previous studies have demonstrated that early initiation of combination antifungal therapy significantly improves survival in CNS aspergillosis and that delayed treatment is associated with markedly higher mortality. Therefore, incorporating CSF fungal biomarker testing into routine workup for patients with unexplained meningoencephalitis could transform clinical practice by enabling faster, evidence-based therapeutic decisions.

6. Ethical Approval

This study was approved by Institutional ethical approval with ref. no. SVIEC/on/Medi/RP/June/25/72.

7. Source of Funding

None.

8. Conflict of Interest

None.

References

1. Elsawy A, Almaghrabi R, Elsaid T, Alshehri M, Almaghrabi A. *Aspergillus terreus* meningitis in immunocompetent patient: a case report. *Front Microbiol*. 2015;6:1353.
2. Pettit AC, Kropski JA, Castilho JL, Schmitz JE, Rauch CA, Mobley BC, et al. The index case for the fungal meningitis outbreak in the United States. *N Engl J Med*. 2012;367(22):2119–25.
3. Chong GM, Maertens JA, Lagrou K, Driessen GJ, Cornelissen JJ, Rijnders BJ. Diagnostic performance of galactomannan antigen testing in cerebrospinal fluid. *J Clin Microbiol*. 2016;54(2):428–31.
4. Malani AN, Singal B, Al Sous O, Summons TA, Durkin MM, Pettit AC. (1,3)-β-d-glucan in cerebrospinal fluid for diagnosis of fungal meningitis associated with contaminated methylprednisolone injections. *J Clin Microbiol*. 2015;53(3):799–803.
5. Rathish B, Wilson A, Warrier A, Pillay R, Thomas J. *Aspergillus fumigatus* meningitis in an immunocompetent young woman. *Indian J Pathol Microbiol*. 2020;63(3):488–90.
6. Desai SD, Seth S, Shah A, Vaishnav B. *Aspergillus* meningoencephalitis in a patient with human immunodeficiency virus infection: normal cerebrospinal fluid does not mean absence of meningitis. *Indian J Sex Transm Dis AIDS*. 2016;37(2):185–9.
7. Hiraga A, Aoki R, Nakamura KI, Kuwabara S. Rapidly progressive *Aspergillus* meningitis successfully treated with voriconazole and corticosteroids. *Neurol Sci*. 2018;39:577–9.
8. Forster J, Hoenigl M, Suerbaum S, Wagener J, Dichtl K. Serologic biomarkers in Candida and Aspergillus infections of the central nervous system: A comparison of galactomannan, mannan and β-1,3-D-gucan testing from serum and cerebrospinal fluid. *Mycoses*. 2022;65(7):709–14.
9. Tang HJ, Liu WL, Chang TC, Li MC, Ko WC, Wu CJ, et al. Multiple brain abscesses due to *Aspergillus fumigatus* in a patient with liver cirrhosis: a case report. *Medicine (Baltimore)*. 2016;95(9):e2813.
10. Memória Jr JR, Lopes Rufino EP, do Rêgo Aquino PL, Vaz Guimarães Filho F, Maranhão Neto T, de Vasconcelos HKNB. Brain aspergilloma in an immunocompetent individual: a case report. *Surg Neurol Int*. 2020;11:211.
11. Shariati A, Didehdar M, Rajaeih S, Moradabadi A, Ghorbani M, Falahati V, et al. Aspergillosis of central nervous system in patients with leukemia and stem cell transplantation: a systematic review of case reports. *Ann Clin Microbiol Antimicrob*. 2021;20(1):44.

12. Walsh TJ, Anaissie EJ, Denning DW, Herbrecht R, Kontoyiannis DP, Marr KA, et al.; Infectious Diseases Society of America. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis*. 2008;46(3):327–60.
13. Schwartz S, Ruhnke M, Ribaud P, Corey L, Driscoll T, Cornely OA, et al. Improved outcome in central nervous system aspergillosis, using voriconazole treatment. *Blood*. 2005;106(8):2641–5.
14. Kourkoumpetis TK, Desalermos A, Muhammed M, Mylonakis E. Central nervous system aspergillosis: a series of 14 cases from a general hospital and review of 123 cases from the literature. *Medicine (Baltimore)*. 2012;91(6):328–36.
15. Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, 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.

Cite this article: Patel R, Patel BB, Jansari T, Chauhan AP, Javadekar T. Unveiling the menace: a case series of fungal meningitis with galactomannan and beta-D-glucan detection and the efficacy of amphotericin B and flucytosine treatment. *Indian J Microbiol Res*. 2025;12(3):423–428.