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### 1. Submitted to the journal "Aksona" (08-03-2024)

Yth. Editor Jurnal Aksona

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Kami dengan ini menyertakan sebuah laporan kasus dengan judul

"Meningoencephalitis Masquerading as Metabolic Encephalopathy: A Case Report in a 65-Year-Old Geriatric Patient". Laporan kasus ini menampilkan presentasi kasus meningoensefalitis pada pasien geriatri dengan gambaran klinis yang tidak biasa ditemukan pada kasus meningoensefalitis umumnya. Semoga dengan laporan kasus ini dapat memberi gambaran dan meningkatkan kewaspadaan pada teman sejawat terhadap kasus serupa di lapangan.

Demikian atas perhatiannya, kami sampaikan terima kasih.

Ferdinand Erwin, dr

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Fakultas Kedokteran, Universitas Katolik Widya Mandala Surabaya

### 2. First revision (20-08-2024)

Berikut kami lampirkan hasil review naskah "Meningoencephalitis Masquerading as Metabolic Encephalopathy ( A Case Report in a 65-Year-Old Geriatric Patient)", mohon diperbaiki sesuai dengan catatan yang telah diberikan, berikan tanda **Bold kuning** pada bagian-bagian mana yang telah diperbaiki

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Case Report

## Meningoencephalitis Masquerading as Metabolic Encephalopathy: A Case Report in a 65-Year-Old Geriatric Patient

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#### ABSTRACT

Introduction: Meningoencephalitis, an inflammatory condition affecting the brain and meninges. Varied etiologies, ranging from infectious pathogens or autoimmune disorders. The symptoms include headache, fever, altered mental status, seizure, or neurological deficits. Here we presented atypical case of elderly with meningoencephalitis.

Case: A 65-year-old female with a history of recurrent hyponatremia and hypokalemia presented to the emergency room with sudden loss of consciousness, vomiting, and behavioral changes persisting for a week. No abnormality found in neurological examination and brain CT-scan. Initial diagnosis of metabolic encephalopathy was made due to severe electrolyte imbalances. The patient's mental status improved after gradual correction of electrolytes. On the second day, she experienced generalized seizures and developed right-sided hemiparesis. Head MRI with contrast revealed diffuse dural thickening and leptomeningeal enhancement in both hemispheres, confirming meningoencephalitis. Intravenous ceftriaxone and dexamethasone were initiated, along with levetiracetam for seizures. On the next day, cerebrospinal fluid analysis showed Candida spores, but cultures were negative. Intravenous fluconazole was then added to the therapy. The patient demonstrated consistent neurological improvement over a two-week hospitalization.

**Conclusion:** Meningoencephalitis should be considered in elderly patients presenting with altered consciousness, even in the absence of fever or meningeal signs. Our case highlights the importance of neuroimaging and comprehensive CSF analysis for accurate diagnosis. While CSF culture remains the gold standard for diagnosis for fungal CNS infection, negative results of CSF culture should not delay the initiation of antifungal therapy. Early initiation of targeted antimicrobial therapy is crucial for favorable outcomes in such cases.

Keywords: Meningoencephalitis; Geriatric; Elderly; Candidiasis

Article Highlight: Describe the highlights of the manuscript

- Geriatric patient may present with subtle or nonspecific symptoms of meningoencephalitis such as confusion, altered mental status, or lethargy, rather than classic signs like fever and neck stiffness.
- 2. Negative CSF cultures of fungal infection should not delay the initiation of antifungal therapy.

### INTRODUCTION

Meningoencephalitis is inflammatory condition that affects the brain and the membranes surrounding it, known as the meninges .The etiology of meningoencephalitis can be attributed to a variety of infectious and noncauses.1,2 infectious Infectious causes meningoencephalitis include viral, bacterial, fungal, and parasitic infections. Viral causes are the most common and can include herpes simplex virus, varicella-zoster virus, and enteroviruses. Bacterial causes may include Streptococcus pneumoniae, Neisseria meningitidis, and Listeria monocytogenes. Fungal and parasitic causes are less common but can also lead to meningoencephalitis. Non-infectious causes of meningoencephalitis can include autoimmune conditions, such as autoimmune encephalitis. 1,3,4

According to reports from the 2019 Global Burden of Disease (GBD) Study, the global incidence of meningitis has decreased from 3.29 million (2.7–4.0) cases in 1990 to 2.51 million (2.11–2.99) cases in 2019. This research also showed that globally, approximately one-third of patients diagnosed with meningitis caused by viral meningitis. In Indonesia, the number of cases per 100,000 population is 21,400 (15,100 to 29,800) cases. Although there has been a 45% reduction in the overall mortality rate associated with meningitis from 1990 to 2019, the overall burden of the disease remains substantial. Previous studies have identified older individuals with bacterial meningitis as a

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distinct patient subgroup characterized by atypical clinical presentations, unusual bacterial pathogens, and a high frequency of adverse outcomes.<sup>6</sup>

#### CASE

A 65-year-old female patient, who had a previous history of recurrent hyponatremia and hypokalemia, was brought to the emergency room because of sudden loss of consciousness, repeated vomiting, and behavioral changes indicated by increased restlessness. The patient's family reported that they experienced behavioral changes for one week, such as increased irritation and restlessness. There was no reported fever, headache, or neck stiffness during this period.

The patient's vital signs were normal. However, a Glasgow Coma Scale (GCS) score of 10 (E3V2M5) indicated decreased responsiveness in neurological examination. Although the individual's mental health changed, there were no signs of specific neurological disorders, and there were no signs of meningeal inflammation, such as stiffness of the neck or any other meningeal sign. The first diagnosis of metabolic encephalopathy was made after laboratory tests showed a significant decrease in sodium (112 mEq/L) and potassium (2.56 mEq/L) levels.

Non-contrast computed tomography (CT) of the brain was performed promptly, and the examination show no signs of abnormalities or indications of cerebral edema. Once the patient is hospitalized, electrolyte imbalances are corrected gradually. During the first 48 hours, the patient's mental status and electrolyte levels improved.

An unexpected development occurred on the second day of hospital admission. Patients experience general seizures, followed by a period of altered mental status after the episode. On the examination, right-sided neurological deficits hemiparesis emerged. A subsequent non-contrast brain CT scan revealed no current intracranial abnormalities or indications of haemorrhage or infarction. The patient was subsequently administered levetiracetam at a dosage of 2 x 500mg.

Additional workup is required because of the development of neurologic symptoms and an unclear metabolic cause. Additional magnetic resonance imaging (MRI) of the brain with contrast shows diffuse dural thickening with abnormal leptomeningeal enhancement in both hemispheres (Figure 1). These results support the new diagnosis of meningoencephalitis.

To confirm the etiology of infection, a lumbar pucture procedure was performed. Remarkably, the cell count, glucose, or protein levels in the cerebrospinal fluid (CSF) did not show any abnormalities on examination. In contrast, Ziehl-Neelsen staining of CSF indicates the presence of *Candida* spores. Bacterial and fungal cultures in the CSF showed no signs of growth despite these microscopic studies. There were no positive results from polymerase chain reaction (PCR) studies of

CSF for well-known viral infections such as CMV, H5N1, and H1N1.

The patient was immediately started on comprehensive intravenous ceftriaxone 1 gram twice daily, intravenous fluconazole in a dose of 800 mg daily, intravenous dexamethasone, and levetiracetam was administered to treat seizures. The patient demonstrated consistent improvement in his neurological condition during his two-week hospitalization, which resulted in a improved mental status, reduction in seizures and resolution of the neurological deficits. Thereafter, MRI showed that the leptomeningeal enhancement had diminished. The patient returned with a comprehensive outpatient follow-up plan to monitor neurologic recovery and the address impact of these atypical meningoencephalitis symptoms.

### DISCUSSION

Fungal central nervous system (CNS) infections can be categorized into two main groups: those that affect a healthy host, including Cryptococcus, Coccidioides, Histoplasma, Blastomyces, and Sporothrix species, and those that cause opportunistic infections in immunocompromised individuals, such as Candida, Aspergillus, Zygomycetes, and Trichosporon species. 7 Candida species are typically part of the normal human flora and seldom lead to central nervous system (CNS) diseases unless there is a compromise in host defenses. Several factors contribute to the dissemination of Candida into the bloodstream and potentially the CNS. These factors include prematurity, broad-spectrum antibiotic usage, hyperalimentation, malignancy, presence of indwelling catheters, corticosteroid treatment, neutropenia, surgery, diabetes mellitus, thermal injuries, and intravenous drug abuse.<sup>2,7</sup> Although Candida albicans is the predominant species isolated in cases of Candida meningitis, other species such as Candida tropicalis, Candida glabrata, Candida lusitaniae, and Candida parapsilosis have also been reported.8,9

The clinical presentation of fungal meningitis is typically less predictable compared to bacterial meningitis. Patients often exhibit symptoms consistent with the chronic meningitis syndrome, defined as meningitis that shows no improvement or worsens over a period of at least 4 weeks. Clinical observations tend to lack specificity, with patients commonly displaying general weakness or a failure to thrive. <sup>2,8,10</sup> Common symptoms may include fever, headache, lethargy, confusion, nausea, vomiting, stiff neck, or neurological deficits, although typically only a subset of these symptoms will be initially evident. In some cases, patients may present with symptoms resembling subacute dementia. Raised intracranial pressure and its associated symptoms can manifest acutely or develop gradually as the disease progresses.<sup>2</sup> Fungal meningitis is consistently a primary consideration in the differential diagnosis of patients presenting with the chronic meningitis syndrome. However, it is crucial to also consider numerous other infectious and noninfectious conditions, particularly tuberculous or carcinomatous meningitis. 9,11

In elderly patients, meningoencephalitis can present with unique challenges and complexities. As people age, their immune systems may weaken, making them more susceptible to infections. Furthermore, the symptoms of meningoencephalitis in older adults may be atypical or mistaken for other age-related conditions, leading to potentially delayed diagnosis and treatment. These factors, coupled with the potential for more severe outcomes in the elderly population, make meningoencephalitis a significant concern in this age group.<sup>12</sup> According to previous clinical presentation reports. the meningoencephalitis in elderly patients often includes typical symptoms such as headaches, neck stiffness, vomiting, and fever. Additional symptoms may include confusion, altered mental status, and seizures. 12,13

Cerebrospinal fluid findings in fungal meningitis have been extensively investigated. Typically, there is a mononuclear pleocytosis observed, with cell counts ranging from 20 to 500 cells/mm3. The proportion of polymorphonuclear (PMN) leukocytes varies, generally remaining well below 50%. In some instances, PMN leukocytes predominate, a phenomenon more frequently observed in meningitis caused by fungi such as Aspergillus, Scedosporium, Blastomyces, or the agents of mucormycosis. Cerebrospinal fluid protein concentrations typically show elevation in cases of fungal meningitis. When protein concentrations are notably high. Glucose concentrations in CSF during fungal meningitis tend to be decreased, although they may occasionally appear normal.<sup>2,8,11</sup> While culture examination remains the gold standard for diagnosing fungal meningitis, some cases exhibit negative results in CSF culture tests. Voice R.A. et al. also reported that only 44% of candidiasis meningitis patients demonstrated Candida growth upon initial CSF culture examination. Subsequent reevaluation of initially negative samples, employing modified examination techniques, yielded a total of 88% of samples with positive Candida cultures. 14

Because *Candida* meningitis is associated with low morbidity rates, there have been no randomized controlled trials conducted to assess the optimal treatment approach. As outlined in the clinical practice guidelines for the management of candidiasis by the Infectious Diseases Society of America, last updated in 2016, the initial therapy for *Candida* meningitis typically involves liposomal Amphotericin B (AmB) at a dosage of 5 mg/kg daily, with or without oral flucytosine administered at 25 mg/kg four times daily. However, the optimal duration of this initial therapy has not been thoroughly studied.<sup>2,15</sup> Fluconazole has demonstrated efficacy as a step-down therapy or as an alternative therapy, typically administered at a dosage of 400–

800 mg daily (equivalent to 6–12 mg/kg), owing to its ability to achieve excellent levels in both CSF and brain tissue. The treatment continued until all clinical signs, symptoms, and abnormalities in CSF and radiological findings have resolved.<sup>15</sup>

### CONCLUSION

In conclusion, meningoencephalitis poses particular challenges in elderly patients due to potential atypical symptoms and the risk of delayed diagnosis. Therefore, clinicians should maintain a high index of suspicion for meningoencephalitis in elderly patients, particularly when encountering decreased consciousness. Prompt recognition and initiation of treatment are crucial to prevent severe outcomes. While CSF culture remains the gold standard for diagnosis for fungal CNS infection, negative results of CSF culture should not delay the initiation of antifungal therapy. Overall, early recognition, appropriate diagnosis, and timely treatment are imperative in managing fungal meningitis, particularly Candida meningitis, to improve patient outcomes and reduce the risk of complications.

#### Acknowledgment

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### **Conflict of Interest**

The authors have no conflicts of interest to disclose for this report

### **Funding**

No funding was received for this case report.

### **Author Contribution**

Author: examined the patient, contributed to data collection and manuscript description, and wrote the manuscript.

Co-author: examined the patient together with the author, contributed to data collection, and reviewed the manuscript.

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### TABLES AND FIGURES

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Figure 1. A non-contrast head CT scan reveals diffuse dural thickening with abnormal leptomeningeal enhancement in both the left and right cerebral hemispheres.

# 3. First revision submitted (25-08-2024)

Berikut kami lampirkan revisi terhadap masukan yang telah diberikan. Atas masukannya kami ucapkan terima kasih.

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4. Paper accepted for publication (09-09-2024)

# [AKSONA] Editor Decision

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Nita Kurniawati, Ferdinand Erwin:

We have reached a decision regarding your submission to AKSONA , "Meningoencephalitis Masquerading as Metabolic Encephalopathy: A Case Report in a 65-Year-Old Geriatric Patient".

Our decision is to: Accept Submission

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# **Letter of Acceptance (LoA)**

Dear Author(s)

We have pleasure to inform you that your manuscript (code: 55844), titled "Fungal Meningoencephalitis Masquerading as Metabolic Encephalopathy: A Case Report in a 65-Year-Old Geriatric Patient" by Nita Kurniawati and Ferdinand Erwin, has been accepted for publication in AKSONA. You will be contacted again by us for a proofreading of your manuscript. Please respond within the given time to ensure timely publication.

We are looking forward for your future submission

Editor in Chief,

Dr. Paulus Sugianto, dr., Sp.N(K), FAAN.

5. Paper Published (29-01-2025)

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# Fungal Meningoencephalitis Masquerading as Metabolic Encephalopathy: A Case Report in a 65-Year-Old Geriatric Patient

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### **ABSTRACT**

**Introduction:** Infectious pathogens or autoimmune disorders can cause meningoencephalitis. Symptoms include headache, fever, altered mental status, seizure, or neurological deficits. Symptoms frequently manifest atypically in the elderly, which can result in delayed treatment. This case emphasizes how important it is to consider meningoencephalitis in elderly patients with altered consciousness, even without typical signs of it.

Case: A 65-year-old female with a history of recurrent hyponatremia and hypokalemia arrived at the emergency room with sudden loss of consciousness, vomiting, and behavioral changes that persisted for a week. The neurological examination and brain CT scan revealed no abnormalities. Severe electrolyte imbalances prompted the initial diagnosis of metabolic encephalopathy. Following progressive electrolyte correction, the patient's mental condition improved. On the second day, she had generalized seizures and developed right-sided hemiparesis. An MRI of the head with contrast showed thicker dura mater and leptomeningeal enhancement in both hemispheres, indicating meningoencephalitis. Ceftriaxone and dexamethasone were administered intravenously, along with levetiracetam, to treat seizures. The next day, cerebrospinal fluid analysis showed *Candida* spores, but cultures were negative. Intravenous fluconazole was then added to the therapy. Throughout her two-week stay, the patient's neurological condition improved consistently.

**Conclusion:** Fungal causes should be considered in cases with unclear meningoencephalitis in the elderly, even if fever or meningeal signs are not present. Although CSF culture continues to be the gold standard for diagnosing fungal CNS infection, negative results should not delay the start of antifungal therapy. Early initiation of targeted antimicrobial therapy is crucial for successful results in these cases.

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### INTRODUCTION

Meningoencephalitis is a serious inflammatory condition that affects the brain and the membranes surrounding known meninges. Meningoencephalitis has several infectious and noninfectious causes.<sup>1,2</sup> Viral, bacterial, fungal, and parasitic infections are among the infectious causes of meningoencephalitis. The most prevalent causes are viral infections, such as herpes simplex virus, varicella-zoster virus, and enterovirus. Streptococcus pneumoniae, Neisseria meningitidis, and Listeria monocytogenes are three possible bacterial causes. Fungal and parasitic infections can cause meningoencephalitis, despite their rarity. Noninfectious causes of meningoencephalitis include autoimmune disorders. like autoimmune encephalitis. 1,3,4

The 2019 Global Burden of Disease (GBD) Study showed that the global incidence of meningitis has decreased from 3.29 million (2.7–4.0) cases in 1990 to 2.51 million (2.11–2.99) cases in 2019. The report revealed that viral meningitis caused almost one-third of meningitis diagnoses globally.<sup>5</sup> In Indonesia, there are 21,400 cases per 100,000 people (range: 15,100 to 29,800). Although meningitis-related fatality rates have decreased by 45% between 1990 and 2019, the disease's overall impact remains significant.<sup>5</sup>

The prevalence of central nervous system (CNS) fungal infections has shown an increasing tendency. These infections may manifest clinically as meningitis, meningoencephalitis, abscesses, or vascular disease. Meningoencephalitis appears to be the most common clinical manifestation of candidiasis in the CNS. Other symptoms include endophthalmitis, brain abscesses, vasculitis, intraventricular infection, hydrocephalus, calcifications, and cranial neuropathies. Stroke lesions may also appear in extremely rare cases.<sup>6,7,8</sup>

Several Candida species, such as C. albicans, C. tropicalis, C. lusitaniae, and C. parapsilosis, are associated with human illness.9 Diverse patient demographics exhibit specific vulnerabilities to different Candida infections impacting the central nervous system. The species C. albicans is frequently from both immunocompromised immunocompetent patients. However, its frequency has been decreasing over the last decade. 6,10 Candida meningitis usually occurs in cases of disseminated candidiasis, especially among immunocompromised people, those with underlying immune deficiencies, or patients who have undergone neurosurgical procedures.6,9

Previous studies have indicated that elderly people with bacterial meningitis are a unique patient subgroup with unusual symptoms, unusual bacterial pathogens, and a high rate of adverse outcomes.<sup>11</sup> This unusual presentation in elderly patients can lead to

misdiagnosis and treatment. Approximately 6% of those with disseminated candidiasis are estimated to have undetected neuroinfections.<sup>6</sup> Also, past studies have shown that Candida infections of the CNS can present in altered mental status without meningeal symptoms, potentially leading to delayed diagnosis and treatment.<sup>12</sup> Another diagnostic challenge is that CSF cultures have poor diagnostic accuracy in patients with Candida meningitis. 13,14 In elderly patients with altered consciousness, the causes and differential diagnoses are wide-ranging and often atypical. In this case, we provide an atypical presentation of meningoencephalitis to raise awareness among healthcare professionals and encourage prompt and appropriate treatment, which is crucial for improving patient outcomes.

### **CASE**

A 65-year-old female patient with a history of recurrent hyponatremia and hypokalemia was admitted to the emergency room due to sudden loss of consciousness, repeated vomiting, and behavioral changes characterized by increasing restlessness. For a week, the patient's family noticed behavioral changes, such as increased agitation and restlessness. There was no report of fever, headaches, or neck stiffness during this period.

The patient's vitals were normal. In contrast, a Glasgow Coma Scale (GCS) score of 10 (E3V2M5) indicated decreased responsiveness in neurological examination. Although the individual's mental health changed, there were no signs of specific neurological disorders, nor were there any signs of meningeal inflammation, such as neck stiffness or any other meningeal sign. Laboratory tests revealed a significant decrease in sodium (112 mEq/L) and potassium (2.56 mEq/L) levels, leading to the first diagnosis of metabolic encephalopathy.

A non-contrast computed tomography (CT) scan of the brain was immediately performed and showed no abnormalities or cerebral edema. Hospitalization gradually corrects electrolyte imbalances. The patient's mental status and electrolyte levels improved over the first 48 hours. On the second day of hospitalization, something unexpected happened. Patients experience general seizures followed by a period of altered mental status. The test revealed right-sided neurological deficits, including hemiparesis. A subsequent non-contrast brain CT scan revealed no current intracranial abnormalities or indications of hemorrhage or infarction. The patient was then given two doses of levetiracetam, 500 mg each.

Further examination is necessary due to the development of neurological symptoms and an unclear metabolic cause. A contrast-enhanced magnetic



resonance imaging (MRI) scan of the brain revealed thickening dura mater and leptomeningeal enhancement rin both hemispheres (Figure 1). These results support the new diagnosis meningoencephalitis. The patient was promptly put on comprehensive intravenous ceftriaxone (1 gram twice daily), intravenous dexamethasone, and levetiracetam to treat the seizures.

The next day, a lumbar puncture was conducted to confirm the infection's cause. The cerebrospinal fluid (CSF) surprisingly showed no abnormalities in terms of cell count, glucose, or protein levels. In contrast, potassium hydroxide (KOH) staining in CSF revealed the presence of *Candida* spores. Despite the microscopic examinations, bacterial and fungal cultures in the CSF showed no indication of growth. Tests using polymerase chain reaction (PCR) on CSF did not show any signs of common viruses like CMV, H5N1, and H1N1.



Figure 1. Brain MRI reveals diffuse dural thickening with abnormal leptomeningeal enhancement in both the left and right cerebral hemispheres.

Based on the CSF examination intravenous fluconazole 800 mg per day was added as an antimicrobial treatment. Throughout her two-week hospitalization, the patient's neurological condition improved consistently, resulting in an improved mental status, fewer seizures, and the resolution of neurological deficits. MRI showed the leptomeningeal enhancement had decreased. The patient returned with a comprehensive outpatient follow-up plan to monitor neurologic recovery and treat the effects of these atypical meningoencephalitis symptoms.

### DISCUSSION

In this case report, we emphasized the importance of accurately diagnosing the fungal cause of meningitis in older patients, as atypical symptoms can potentially delay diagnosis and treatment. Of the different types of fungal infections that can happen in the central nervous system (CNS), there are two main groups: those that affect a healthy host, such as Cryptococcus, Coccidioides, Histoplasma. Blastomyces, and Sporothrix species, and those that affect immunocompromised individuals, such as Candida, Aspergillus, Zygomycetes, and Trichosporon species. 15 Candida species are commonly found in the normal human flora and rarely cause central nervous system (CNS) diseases unless host defenses are compromised. Several factors lead to the spread of Candida into the bloodstream and, potentially, the central nervous system. These factors include broad-spectrum antibiotic prematurity, use, hyperalimentation, malignancy, the presence of corticosteroid indwelling catheters, treatment, neutropenia, surgery, diabetes mellitus, thermal injuries, and intravenous drug misuse. $\frac{2.15}{C}$  C. albicans is the predominant species isolated in cases of Candida meningitis, but others, such as C. tropicalis, C. glabrata, C. lusitaniae, and C. parapsilosis, have also been reported. 16,17

Fungal meningitis has less predictable clinical manifestations than bacterial meningitis. Patients frequently exhibit symptoms of chronic meningitis syndrome, which is defined as meningitis that persists or worsens for at least four weeks. Patients typically exhibit nonspecific clinical observations, such as general weakness or a failure to thrive.<sup>2,17,18</sup> Fever, headache, lethargy, confusion, nausea, vomiting, stiff neck, or neurological deficits are some of the most common symptoms, although only a subset of these will be present at first. In some cases, patients may have symptoms resembling subacute dementia. Raised intracranial pressure and related symptoms can manifest acutely or gradually as the disease advances.<sup>2</sup> Fungal meningitis is always a main concern in the differential diagnosis of chronic meningitis syndrome patients. However, it is important to examine various other infectious and noninfectious conditions, including tuberculous or carcinomatous meningitis. 16,19

Meningoencephalitis in the elderly can provide particular challenges and complexities. As people age, their immune systems may weaken, making them infections. susceptible to Furthermore. symptoms of meningoencephalitis in the elderly may be atypical or misdiagnosed as other age-related illnesses, thus delaying diagnosis and treatment. These factors, together with the possibility of more severe population, outcomes in the elderly meningoencephalitis a major concern in this age range.<sup>20</sup> According to previous reports, the clinical presentation of meningoencephalitis in elderly people frequently involves common symptoms such as headaches, neck stiffness, vomiting, and fever. Confusion, impaired mental status, and seizures are among the possible further symptoms.<sup>20,21</sup>



Researchers have extensively investigated cerebrospinal fluid findings in fungal meningitis. A mononuclear pleocytosis is usually observed, with cell counts between 20 and 500 cells/mm<sup>3</sup>. Although it varies, the percentage of polymorphonuclear (PMN) leukocytes is often far below 50%. Sometimes, PMN leukocytes are the most common type. Fungi such as spergillus, Scedosporium, Blastomyces, or the agents of mucormycosis cause meningitis more frequently. Cerebrospinal fluid protein concentrations typically show elevation in cases of fungal meningitis. Glucose concentrations in CSF during fungal meningitis tend to be decreased, although they may occasionally appear normal.<sup>2,17,19</sup> Although culture examination continues to be the most reliable method for diagnosing fungal meningitis, some cases show negative results in CSF culture tests. According to Voice et al., only 44% of candidiasis meningitis patients showed Candida growth during their initial CSF culture examination. Reevaluation of previously negative samples using modified examination techniques resulted in a total of 88% of samples having positive *Candida* cultures. 14

No randomized controlled trials have evaluated the appropriate treatment approach for Candida meningitis due to its low morbidity rates. The Infectious Diseases Society of America last updated its guidelines for practice candidiasis management in 2016. For people with Candida meningitis, they said that liposomal amphotericin B (AmB) at a dose of 5 mg/kg daily, with or without oral flucytosine at 25 mg/kg four times a day, should usually be the first treatment. However, the optimal duration of this initial treatment has not been thoroughly studied.<sup>2,12</sup> Fluconazole has shown efficacy as a step-down or alternative therapy, with a common dose of 400-800 mg daily (equal to 6-12 mg/kg), due to its ability to achieve excellent levels in both CSF and brain tissue. The treatment continued until all clinical signs, symptoms, CSF abnormalities, and radiological findings had resolved. 12

### **CONCLUSION**

Meningoencephalitis presents particular challenges in elderly patients due to the potential of atypical symptoms and the risk of delayed diagnosis. As a result, clinicians must uphold a high level of suspicion for meningoencephalitis in elderly patients, especially if they have diminished consciousness. Prompt recognition and treatment are crucial to avoiding serious results. Even though CSF culture remains the gold standard for diagnosing fungal CNS infections, the initiation of antifungal therapy should not be delayed due to negative CSF culture results. Overall, early recognition, appropriate diagnosis, and prompt treatment are critical in managing fungal

meningitis, particularly *Candida* meningitis, in order to enhance patient outcomes and reduce the risk of complications.

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### **Author Contributions**

Author: examined the patient, contributed to data collection and manuscript description, and wrote the manuscript.

Co-author: examined the patient together with the author, contributed to data collection, and reviewed the manuscript.

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