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Clinical Analysis of 14 Cases of Central Nervous System Mucormycosis

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Abstract

Objective: To analyze the clinical characteristics of central nervous system mucormycosis.
Methods: The clinical data of 14 patients diagnosed with central nervous system mucormycosis admitted to our hospital were comprehensively reviewed and analyzed.
Results: A total of 14 patients were enrolled, including 13 males and 1 female, with a mean age of 51.9 years. Disease onset was associated with compromised immune status induced by diabetes mellitus, autoimmune diseases and hematological disorders. Patients presented with acute or subacute onset, predominantly manifested as decreased visual acuity, headache, hemiplegia and other neurological symptoms. Radiologically, 11 cases were rhinocerebral type and 3 cases were cerebral parenchymal type, characterized by nodular enhancement and ring enhancement respectively. Next-generation sequencing (NGS) served as the primary diagnostic modality, with the highest positive detection rate in cerebrospinal fluid samples; *Rhizopus oryzae* was the predominant pathogenic strain. Combined therapy of isavuconazole plus amphotericin B yielded the optimal therapeutic efficacy.
Conclusion: Central nervous system mucormycosis predominantly affects immunocompromised individuals, featuring distinctive clinical and imaging manifestations. Next-generation sequencing possesses prominent value for the early and accurate diagnosis of this disease, and the combination regimen of amphotericin B and isavuconazole is clinically effective.

Introduction

Mucor, a common zygomycete fungus, is ubiquitously distributed in soil, air, and plant surfaces[1]. Central nervous system (CNS) mucormycosis is an aggressive and refractory intracranial infectious disease with an extremely high mortality rate[1, 2]. The infection mainly develops through hematogenous dissemination or direct intracranial invasion secondary to sinusitis. As a typical opportunistic pathogen, Mucor predominantly infects immunocompromised individuals[1, 3].A growing number of domestic and international clinical studies have shown that CNS mucormycosis can invade cerebral vessels, lead to extensive cerebral infarction and/or intracranial hemorrhage, and further cause fatal brain herniation. Historically, the definitive diagnosis of this disease mainly relied on post - mortem autopsy. In recent years, with the rapid development of molecular genetic diagnostic techniques, the diagnostic efficiency of invasive fungal infections has been significantly improved. Next - generation sequencing (NGS) can accurately diagnose the etiology by detecting fungal pathogens in cerebrospinal fluid (CSF) and living tissue specimens.

To date, no specific therapeutic agent has been established for mucormycosis. Amphotericin B was once the mainstream treatment, yet it is restricted by severe adverse reactions and poor patient tolerance. Isavuconazole has recently shown reliable efficacy against mucormycosis and has become a promising therapeutic option in clinical practice. Here, we retrospectively included 13 patients diagnosed with CNS mucormycosis in our hospital, summarized their clinical onset characteristics, and analyzed the clinical diagnosis, treatment, and prognosis of the disease.

1. Materials and Methods

1.1 Case Data

A total of 14 patients diagnosed with CNS mucormycosis in our hospital between 2019 and 2025 were included in this retrospective study. All cases were diagnosed based on a comprehensive evaluation of clinical manifestations, cranial imaging features, and etiological evidence. Clinical data, including age, gender, underlying comorbidities, onset patterns, diagnostic approaches, treatment regimens, and prognostic outcomes, were systematically collected and statistically analyzed. All clinical data were sorted and summarized, as presented in Table 1.

1.2 Research Methods

Descriptive statistical analysis was carried out for all clinical data. Statistical comparisons were conducted using the chi - square test with SPSS 22.0 software.

2. Results

2.1 General Clinical Information

All 14 enrolled patients were male, with a mean age of 51.9 years and a median age of 52.5 years (inter - quartile range: 52.0–53.0 years). The youngest patient was 31 years old, and the oldest was 79 years old. Among all cases, 12 patients (86%) had comorbid diabetes mellitus, including 3 cases (25%) with diabetic ketoacidosis. Three patients (21%) had immune - related diseases, 2 cases (14%) had hematological disorders, and only 1 patient (7%) had no underlying comorbidities.

2.2 Clinical Manifestations

All patients presented with an acute, subacute, or chronic onset. The mean duration from symptom onset to admission was 28.1 days, with a median duration of 22.5 days (inter - quartile range: 20.0–25.0 days). The main clinical manifestations included fever (5 cases, 36%), decreased visual acuity (9 cases, 64%), abnormal sensory perception (4 cases, 31%), hemiplegia (7 cases, 50%), headache (8 cases, 57%), oculomotor nerve paralysis (7 cases, 50%), and disturbance of consciousness (3 cases, 21%).

2.3 Cranial MRI Manifestations

Cranial MRI examinations predominantly demonstrated lesions with T1 - weighted hypointense and T2 - weighted hyperintense signals, accompanied by nodular or circular enhancement. Based on the imaging distribution and infection routes, all patients were categorized into the rhinocerebral type and the cerebral parenchymal type. The rhinocerebral type stems from sinus infection with a gradual invasion into the brain parenchyma, typically showing nodular enhancement on imaging[4, 5]. The cerebral parenchymal type is primarily caused by hematogenous infection, characterized by circular - enhanced lesions. In this cohort, 11 cases were classified as the rhinocerebral type, all of which had a confirmed

history of sinusitis, and 3 cases were of the cerebral parenchymal type. Among the cases of the cerebral parenchymal type, 2 presented with focal lesion hemorrhage; all 3 cases were secondary to the dissemination of hematogenous pathogens, including 2 cases originating from pulmonary infection and 1 case from lumbosacral surgery infection.

2.4 Diagnostic Results

All 14 cases were definitively diagnosed with CNS mucormycosis based on comprehensive clinical manifestations, imaging features, and NGS etiological detection. Fungal pathogens were successfully identified in all patients through NGS. Among them, 11 cases were positive for Mucor in CSF NGS detection, including 8 cases with simultaneous blood NGS examination (2 cases were positive for Mucor in the blood). One case was positive for Mucor in blood NGS but negative in CSF NGS. One case was confirmed via lung biopsy pathology and bronchoalveolar lavage fluid NGS. Another case was diagnosed by pathological examination and tissue NGS of surgically - resected lesions. Of the 13 patients who underwent cerebrospinal fluid mNGS, 11 tested positive for Mucor (85%).Of the 9 patients who underwent blood mNGS, 3 tested positive for *Mucor* (33%).

2.5 CSF Laboratory Results

Lumbar puncture and CSF examination were carried out on 13 patients. Normal CSF pressure was detected in 10cases, whereas elevated pressure was found in 3 cases, with a maximum pressure reaching 290 mmH_2O. The CSF white blood cell count was elevated in 9 cases and normal in 4 cases. CSF glucose levels were normal in 11 cases and decreased in 2 case. CSF chloride levels were normal in 12 cases and reduced in 1 case. CSF protein levels were elevated in 10 cases (maximum: 1668 mg/L) and normal in 3 cases. All 13 patients underwent CSF microbial metagenomic next - generation sequencing (mNGS), and 9 of them also received simultaneous blood mNGS detection.

2.6 Pathogenic Characteristics

Different Mucorales species were detected among the 14 patients: Rhizopus oryzae in 11

（11/14 79%） cases, Rhizopus delemar in 1 （1/14 7%） cases, Rhizopus pusillus in 1（1/14 7%） case andRhizopus microsporesin 1（1/14 7%） case.

2.7 Treatment and Prognosis

Among the 14 patients, 8 underwent combined treatment with amphotericin B and isavuconazole. The treatment outcomes were as follows: 1 patient was cured, 4 patients showed improvement, and 3 patients died. Two patients were treated with fluconazole only, resulting in 1 death and 1 patient being lost to follow - up. One patient died after receiving treatment with posaconazole in combination with amphotericin B. Two patients who received single - agent amphotericin B treatment died, and one untreated patient eventually died.Among the 8 deceased patients, 6 died of cerebral infarction, 1 died of cerebral hemorrhage, and 1 died of high intracranial pressure.

3. Discussion

CNS mucormycosis is a rare yet highly lethal intracranial infectious disease[6]. In clinical literature, it is mostly reported in the form of sporadic case reports. Mucor is a conditional pathogen, and its infection is closely related to host immune dysfunction[3, 7, 8]. In this study, 86% of the patients had comorbid diabetes mellitus, 21% had hematological diseases, and approximately 93% had varying degrees of impaired immune function. Diabetic ketoacidosis creates a favorable microenvironment for Mucor proliferation and accelerates the progression of mucormycosis[8, 9], which is consistent with the 3 cases of ketoacidosis - complicated infection included in this study. The disease affects individuals across all age groups. The patients in this cohort were aged between 31 and 79 years, with a mean age of 51.9 years and a median age of 52.5 years, suggesting that middle - aged individuals are the high - risk population for CNS mucormycosis.

CNS mucormycosis primarily spreads through hematogenous dissemination or direct intracranial invasion via the paranasal sinuses and mastoid processes[5]. In this study, cases were categorized into the rhinocerebral type and the cerebral parenchymal type based on different infection routes. The rhinocerebral type, which accounts for 79% of all cases, occurs when Mucor invades the orbital apex and cavernous sinus via the paranasal sinuses, subsequently leading to skull base and brain parenchymal infections. Patients with this type typically present with decreased vision, oculomotor nerve paralysis, and facial numbness[10]. Cavernous sinus lesions often encroach upon the internal carotid artery, leading to extensive cerebral infarction or intracranial hemorrhage and subsequent fatal brain herniation, which is the primary cause of disease - related death[11, 12]. In this study, half of the rhinocerebral - type patients died of extensive cerebral infarction. The cerebral parenchymal type is mainly caused by hematogenous dissemination. Owing to the rich blood supply of the basal ganglia, isolated lesions frequently occur in this region[13]. In our cohort, 2 patients with single cerebral parenchymal lesions were situated in the basal ganglia, while multiple lesions were mainly distributed in the cerebral lobes. Cerebral parenchymal infections often form bleeding abscesses, and multiple or focal hemorrhagic lesions can cause increased intracranial pressure, resulting in death. Vascular invasion and damage induced by Mucor is the core mechanism underlying the high mortality of CNS mucormycosis. Among the 8 deceased patients in this study, 6 died of cerebral infarction, 1 of intracranial hemorrhage, and 1 of refractory intracranial hypertension.

In the past, the definitive diagnosis of mucormycosis relied on surgical brain biopsy or post - mortem autopsy, which significantly delayed the early diagnosis and treatment. With the advancement of molecular detection technology in recent years, mNGS has been extensively applied in the etiological diagnosis of infectious diseases, enabling the rapid and accurate detection of fungal pathogens in cerebrospinal fluid (CSF) and lesion tissues[14-16]. In this cohort, all 14 patients were confirmed as Mucor - positive through mNGS detection. Specifically, 85% of CSF mNGS results were positive, 33% of blood mNGS results were positive, and individual cases were confirmed by pulmonary lavage fluid and lesion tissue sequencing. Compared with traditional invasive biopsy and autopsy, CSF - based mNGS detection

is simple, rapid, and minimally invasive, facilitating early etiological diagnosis. All enrolled cases were diagnosed in a timely manner via mNGS, which validates the high sensitivity and specificity of this technique for central nervous system (CNS) mucormycosis. Early diagnosis based on CSF mNGS offers crucial guidance for early intervention and prognostic improvement. Mucor is widely distributed in nature, and Rhizopus is the predominant pathogen causing intracranial mucormycosis[17, 18]. Four Rhizopus strains were identified in this study, namely Rhizopus oryzae (79%), Rhizopus microsporus (7%), Rhizopus delemar (7%), and Rhizopus sporogenes (7%). These strains vary in spore morphology, heat resistance, sporulation structure, and metabolic characteristics. Among them, Rhizopus oryzae and Rhizopus microsporus are commonly utilized in industrial fermentation, while Rhizopus delemar and Rhizopus sporogenes are rarely employed in industrial production because of their strong pathogenicity. Our results confirm that Rhizopus oryzae is the most prevalent pathogenic strain of CNS mucormycosis.

CNS mucormycosis is characterized by a low incidence rate but an extremely high mortality rate, which is primarily due to the challenges in early diagnosis and the scarcity of effective targeted antifungal drugs[5, 19, 20]. Isavuconazole has been demonstrated to possess definite antifungal activity against Mucor in recent clinical research. In this study, 8 patients underwent combined therapy with amphotericin B (20 mg/day) and isavuconazole (200 mg/day). One case was cured, 4 cases showed improvement, and 3 cases resulted in death, leading to an overall clinical effective rate of 62.5%. The main reasons for death were the delay in effective antifungal treatment during the early stage of the disease and irreversible neurological deterioration at the time of definitive diagnosis. The combined administration of isavuconazole and amphotericin B is anticipated to become a preferred therapeutic regimen for CNS mucormycosis.

In conclusion, CNS mucormycosis is a severe intracranial infectious disease with a high mortality rate. NGS technology allows for minimally invasive and rapid early diagnosis of the disease through CSF detection. The combined regimen of isavuconazole and amphotericin B shows reliable clinical efficacy against Mucor infection and can effectively enhance the clinical prognosis of patients, which holds broad clinical application prospects.

Declarations

Ethics statement: This retrospective clinical study was performed in accordance with the Declaration of Helsinki. This study was approved by the Medical Ethics Committee of The First Medical Center,Chinese PLA General Hospital. Written informed consent was waived by the ethics committee due to the retrospective nature of this study using de identified clinical data. Trial registration：Not applicable

Consent to Participate: Written informed consent was waived by the ethics committee due to the retrospective nature of this study using de-identified clinical data.

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Author Contribution

Author contributions Yubao Ma: Conceptualization, Writing-original draft; Jiatang Zhang: Conceptualization, Supervision; Other authors: Data curation, Writing-review & editing.

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Table

Table 1 is available in the Supplementary Files section.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Clinicaldataof14patients.xlsx