

Synergistic Integration of Traditional Chinese Medicine and Western Medical Intervention in the Treatment of Brain Abscess: A Case Report

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Brain abscess is life-threatening and carries a high risk of mortality. Despite advances in sensitive imaging techniques, effective antimicrobial therapies, and sophisticated surgical procedures, diagnosing and treating brain abscesses remains challenging. Although empirical antimicrobial therapy and neurosurgery are considered primary treatments for brain abscesses, their efficacy is limited by potential side effects including neutropenia development, the need for repeat surgeries, and the risk of new-onset epilepsy. Here, we present a case of a 52-year-old male patient who experienced paroxysmal convulsions accompanied by left-sided limb weakness and numbness for over 2 months. Despite a brain MRI revealing a multilocular cystic lesion in the right frontal lobe, with about 28 mm × 19 mm × 21 mm in size, the patient declined neurosurgical interventions. After completing a 6-week course of antimicrobial therapy, the patient sought traditional Chinese medicine (TCM) treatment. As a result, the patient remained free of paroxysmal convulsions for about 60 days after a 4-month TCM treatment. A follow-up MRI imaging at 8 months showed a reduction in the size of the lesion in the right frontal lobe to 8 mm × 4 mm. To the best of our knowledge, this is the first well-documented case of a brain abscess that was successfully managed with a combination of antimicrobial therapy and TCM. This case report suggests that TCM may provide significant supplementary benefits in managing infections like brain abscesses. However, further evidence from prospective studies is necessary to substantiate the efficacy of Chinese herbal medicine for the treatment of brain abscesses.

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Abbreviations: TCM, traditional Chinese medicine; MRI, magnetic resonance imaging; DWI, diffusion weighted imaging; ADC, apparent diffusion coefficient; CSF, cerebrospinal fluid; mNGS, metagenomic next-generation sequencing; XFHM, Xianfang Huoming Yin; ANP, Angong Niu Huang Pill.

Keywords: traditional Chinese medicine, brain abscess, paroxysmal convulsion, neutropenia, case report

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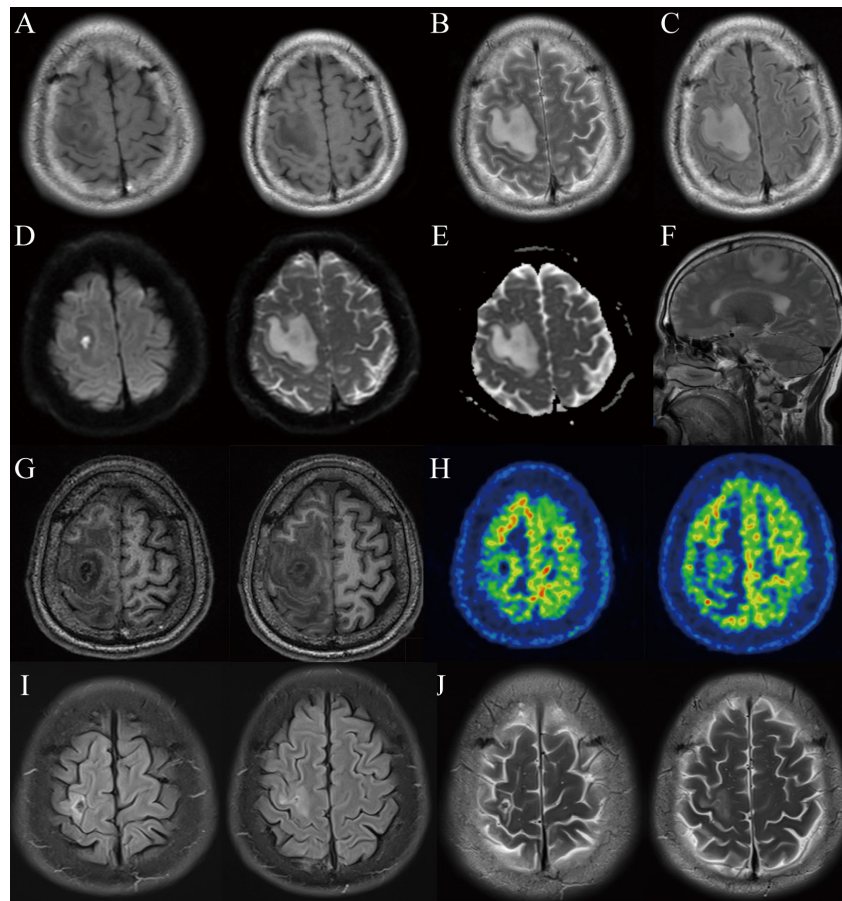


Figure 1. Imaging findings of the brain abscess. Initial brain MRI (A-F): Axial T1-weighted MR (A), T2-weighted MR (B), Flair MR (C), and sagittal T2-weighted MR (F) images show slightly long T1 and long T2 signal nodules in the right parietal lobe with inhomogeneous signals. Axial diffusion (D) with corresponding apparent diffusion coefficient (E) shows diffusion restriction of the right parietal lesion. Brain PET-CT on Day 5 (G-H): Axial PET-CT scans show a circular nodule in the right parietal lobe, with a clear boundary and a smooth inner margin. Brain MRI at 8 months (I-J): Axial T1-weighted MR (I) and T2-weighted MR (J) images show an elliptical-like abnormal signal shadow in the right frontal lobe.

INTRODUCTION

Brain abscess is a rare and challenging disorder that can be caused by bacteria, mycobacteria, fungi, or parasites [1]. The incidence of brain abscess is estimated to range from 0.4 to 0.9 cases per 1 000 000 population [1,2]. Brain abscesses typically present in middle age, with a median onset of 50 years, and affect men disproportionately, accounting for approximately 70% of cases [3]. The most common clinical manifestation of brain abscess is headache. Other symptoms include fever, cognitive impairment, nausea, vomiting, and seizures [4]. However, the classic triad of headache, fever, and focal neurologic deficits is observed in only 20% of patients [4]. Brain abscesses can originate from direct extension (chronic otitis media, mastoiditis, sinusitis, meningitis, or dental infections), hematogenous spread (endocarditis or pulmonary infections), severe head trauma, or neurosurgical procedures. Despite extensive investigation and

diagnostic testing, 20-30% of brain abscesses remain cryptogenic [5], with the source of infection being unidentified or obscure.

Currently, neurosurgery and empirical antimicrobial therapy constitute the major treatment for brain abscesses. However, neurological aspiration carries about a 20% risk of re-aspiration or secondary excision, while primary excision is more invasive and not always feasible [6]. On the other hand, antimicrobial therapy is also challenging due to the limited penetration of antibiotics into the abscess. A 6-8-week course of intravenous antimicrobials is recommended for aspirated or conservatively treated brain abscesses, while a shorter duration of 4 weeks is recommended for patients following excision [6]. A prolonged period of intravenous treatment can be taxing for patients, as it entails enduring discomfort from a long-term hospital stay, risks of hospital-acquired infections, and potential complications associated with venous

catheters, including infection, bleeding, and venous thrombosis. The mortality rates associated with brain abscesses over 1, 2-5, and 6-30 years are 21%, 16%, and 27%, respectively [7]. Despite advancements in imaging sensitivity, antimicrobial therapy efficacy, and surgical techniques, there is still a diagnostic and therapeutic challenge for brain abscesses.

In recent years, traditional Chinese medicine (TCM) has been widely used by more and more patients for its fewer side effects, minimal invasiveness, and activities in modulating the immune system and enhancing the body's inherent healing capabilities. The integration of TCM with Western medicine has garnered increasing attention, particularly in the treatment of complex and challenging conditions such as severe pneumonia [8], ulcerative colitis [9], and diabetes [10]. In this study, we present a case of cryptogenic brain abscess successfully treated with TCM following antimicrobial therapy, without neurosurgical interventions.

CASE PRESENTATION

A 52-year-old male patient presented with paroxysmal convulsions accompanied by left-sided limb weakness and numbness over 2 months. On January 8, 2023, he experienced left limb convulsions, and then a whole-body tonic-clonic seizure with trismus and loss of consciousness for 10 minutes. Subsequently, he complained of weakness and numbness in his left limb and was admitted to a local hospital in Chenzhou, China. The patient experienced fever, cough, and general fatigue in mid-December 2022 and recovered spontaneously within 2 weeks without definitive diagnosis and treatment. He had no history of seizure disorder, chronic sinusitis, dental infection, surgery, head trauma, heart disease, or receiving immunosuppression treatment. His family history was unremarkable. Brain magnetic resonance imaging (MRI), showed a slightly long T1 and long T2 signal nodule measuring about 8 mm × 7 mm in the right parietal lobe, with heterogeneous signal intensity (Figure 1). The nodule demonstrated high signal intensity on T2/FLAIR and diffusion weighted imaging (DWI) sequences. Correspondingly, its apparent diffusion coefficient (ADC) map showed low signal intensity, suggesting restricted diffusion. Large patches of edema with long T1 and long T2 signals were observed around the lesion. The definitive diagnosis remained elusive, with brain abscess, metastatic tumor, and subacute cerebral infarction being considered. Sodium valproate, vancomycin, ceftriaxone, and mannitol were administered to the patient.

On January 11, the patient experienced another paroxysmal convulsion and was transferred to a tertiary hospital in Guangzhou, China. On admission, he was conscious and afebrile. His complete blood count was

normal. Blood and urine cultures were unremarkable. The erythrocyte sedimentation rate was slightly elevated at 17 mm/h (normal range: 0-15 mm/h), while the C-reactive protein was at 8.8 mg/L (normal range: 0-10 mg/L). A lumbar puncture and cerebrospinal fluid (CSF) analysis was performed, and the results were found to be within normal ranges. CSF testing for autoimmune encephalitis-specific IgG antibodies was negative. And a metagenomic next-generation sequencing (mNGS) test on the patient's cerebrospinal fluid did not detect any pathogenic microorganisms. In addition, serum tumor markers, including AFP, CEA, CA19-9, TPSA, FPSA, SCC, β -hCG, and FER, were negative. PET/CT results (Figure 1) revealed a circular-shaped nodule in the right parietal lobe, measuring about 20 mm × 18 mm, with a smooth inner margin. There was a ring-shaped enhancement observed in FDG uptake and a slight enhancement in DOPA uptake. A large area of low density was present peripheral to the lesion, with no radioactive uptake detected. Collectively, these findings favored a diagnosis of an infectious disease, specifically a brain abscess, rather than a primary brain tumor.

INTERVENTIONS

The patient refused neurosurgical interventions but wanted to seek conservative anti-infective therapy. He received meropenem (2 g, iv, q8h) and vancomycin (1 g, iv, q12h) intermittently over 6 weeks. A repeat brain MRI on Day 25 showed enlargement of a multilocular cystic lesion in the right frontal lobe, about 28 mm × 19 mm × 21 mm in size, accompanied by significant surrounding brain parenchymal edema. Unfortunately, following 4 weeks of antimicrobial treatment, the patient had leukopenia and neutropenia on Day 33 and even agranulocytosis on Day 40. Thus, the patient was administered granulocyte-stimulating factors, and his leukocyte and neutrophil counts normalized within 4 days. Changes in white blood cell count and neutrophil count are shown in Figure 2.

Due to the side effects of antibiotics and concerns about the potential complications of surgical intervention, the patient sought TCM treatment. After a 6-week course of antimicrobial therapy, the patient visited the outpatient clinic at Longhua Hospital of Shanghai University of Traditional Chinese Medicine on February 23, 2023. On examination, the patient was oriented and cooperative. Muscle strength was 5/5 in the left proximal upper extremity and left lower extremity and 4/5 in the left distal upper extremity. The superficial sensation was decreased in the left distal upper limb. Cranial nerve function was intact, with no evidence of facial asymmetry, dysarthria, or dysphagia. There were no signs of meningeal irritation. Reflexes were normal and symmetric in the upper and lower extremities, without any abnormal reflexes.

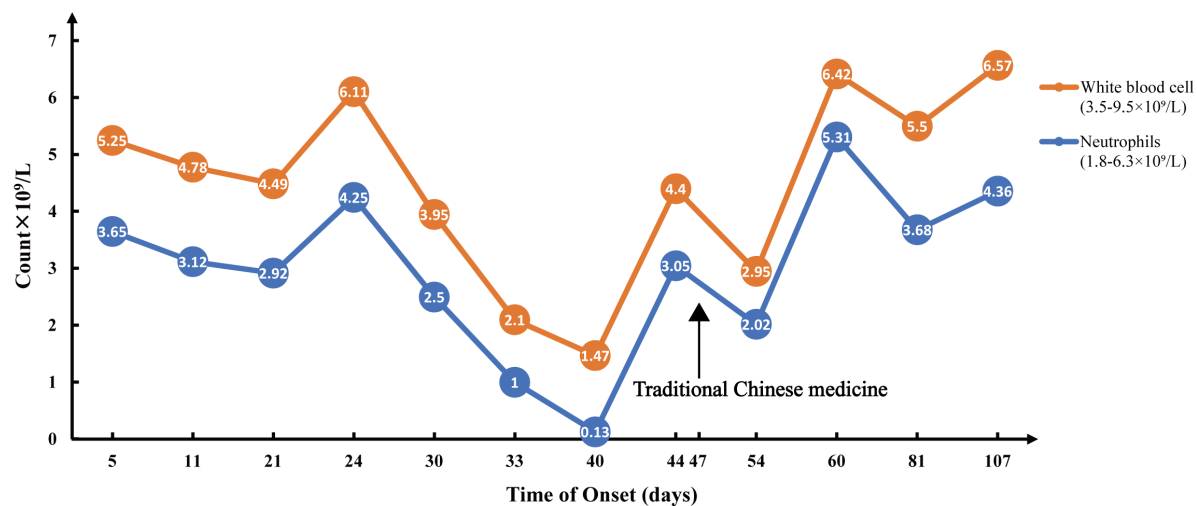


Figure 2. Changes in white blood cell count and neutrophil count from Day 5 to Day 107.

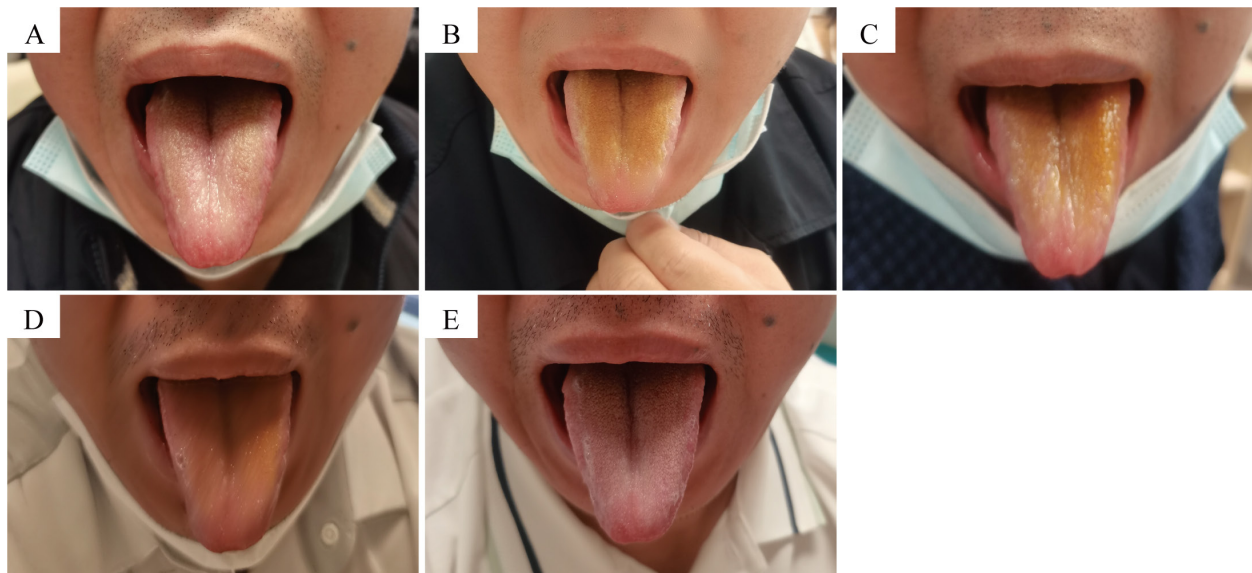


Figure 3. Tongue manifestations across different visits. (A) Visit 1: The tongue presented with a red body and a yellow, greasy coating. (B–D) Visits 2 to 4: The tongue showed a red body with a thick, yellowish-brown, and greasy coating, indicating the exacerbation of the pattern of phlegm dampness-heat toxicity. (E) Visit 6: The tongue exhibited a pale red body with a thick white coating, suggesting a resolution of the pattern of phlegm dampness-heat toxicity and an improvement in the patient's condition.

Given the patient's red tongue with a yellow greasy coating (Figure 3), and a wiry, slippery, rapid pulse, he was diagnosed with the pattern of phlegm dampness—heat toxicity, and upper invasion of the brain orifice based on the TCM theory. Thus, we prescribed Chinese herb granules based on modified Xianfang Huoming Yin (XFHM), along with Angong Niu Huang Pill (ANP), and antelope horn powder for 14 days (Appendix A: Table S1).

RESULTS

On the second visit (March 9, 2023) to the outpatient clinic, the patient complained three times of paroxysmal convulsions without loss of consciousness during the treatment period. A brain MRI on Day 54 indicated a reduction in the size of a multilocular cystic lesion in the right frontal lobe, measuring approximately 21 mm × 16 mm × 15 mm, with decreased surrounding brain parenchymal edema. The patient reported an improvement in weakness and numbness of the left upper limb following

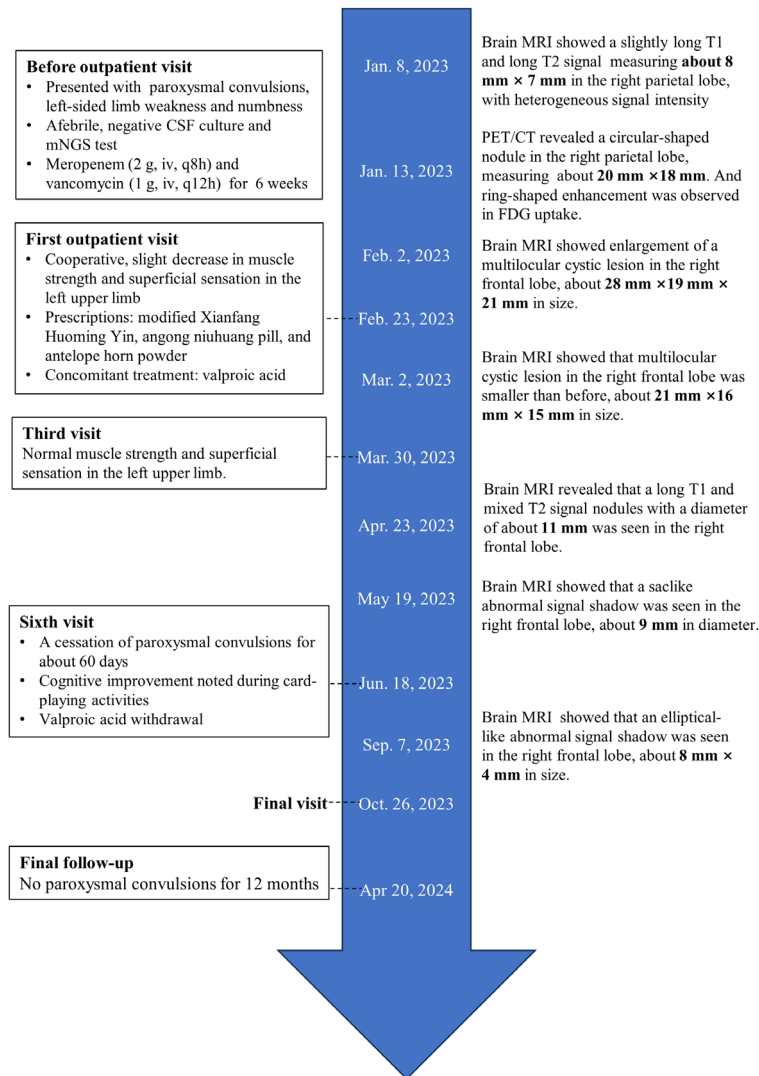


Figure 4. The timeline of this case. MRI, magnetic resonance imaging.

TCM treatment. His muscle strength improved to 5/5 in the left proximal upper extremity and 5-/5 in the distal upper extremities. And the superficial sensation was normal. By a similar TCM pattern, the patient continued TCM treatment.

Following subsequent visits, the patient exhibited a decreasing frequency of paroxysmal convulsions, with accompanying changes in brain imaging revealing a reduction in nodular size and peripheral cerebral parenchymal edema. In addition, the leukocyte and neutrophil counts were normal from Day 60 to Day 107 following TCM treatment (Figure 2). Detailed tongue manifestation is provided in Figure 3. All the granules were prepared by Sichuan Neo-Green Pharmaceutical Technology Development Co. Ltd., Sichuan, China.

A follow-up brain MRI at 8 months revealed the presence of an elliptical-like abnormal signal shadow

measuring approximately 8 mm × 4 mm within the right frontal lobe (Figure 1). We conducted a final telephone follow-up with the patient on April 20, 2024. The patient reported being in good health and free from paroxysmal convulsions for approximately 12 months. A timeline detailing the interventions and imaging findings is provided in Figure 4.

DISCUSSION

Brain abscesses are life-threatening conditions with a significant risk of mortality. A population-based cohort study reported that in-hospital mortality from brain abscess increased with age, rising from 4.22% in patients aged 0-14 years to 17.83% in those over 60 years, with no significant sex/gender difference. Advanced age, stroke, septicemia, pneumonia, meningitis, hepatitis, immuno-

compromise, and congenital heart disease are associated with an increased risk of mortality in brain abscess [2,11].

In this report, we present a case of a patient who experienced paroxysmal convulsions and left-sided limb weakness, ultimately diagnosed with a brain abscess. The patient's prior symptoms of fever, cough, and fatigue may have indicated a pulmonary infection, which is a known predisposing factor for brain abscess. Cryptogenic brain abscesses often lack distinctive features in progression, clinical presentations, and physical examination, which can easily result in missed diagnoses, inappropriate treatment, and unfavorable outcomes. A study of two cryptogenic brain abscess cases also found that the patients exhibited only limb dysfunction, with no other signs of infections based on medical history, complete blood count, CRP levels, or CSF examination. Further aspiration and culture of pus ultimately identified the pathogen [12]. The patient in this study declined neurological interventions. Despite an extensive workup, the etiology and source of infection remained undetermined. A systematic review and meta-analysis demonstrated that approximately 32% of cultures obtained from brain abscesses yield negative results [13]. Common causes of negative culture results include an intact abscess capsule, prior antibiotic administration, and limitations in diagnostic methods.

The ESCMID study on infections of the brain recommends using 3rd-generation cephalosporin combined with metronidazole for the empirical treatment of community-acquired brain abscess. Meropenem can be considered an alternative in this condition [6]. In this case, the patient was administered meropenem and vancomycin for about 6 weeks. However, he suffered from leukopenia, neutropenia, and even agranulocytosis from week 4 to week 5 following antimicrobial treatment. Antibiotically-induced neutropenia remains a rarely reported side effect. A systematic review of case reports spanning from 1968 to 2020 determined that glycopeptides and beta-lactam antibiotics are the most frequently reported causative factors of acute antibiotic-induced neutropenia [14]. Further, a study on antibiotic-induced agranulocytosis using the Japanese adverse drug event report database showed that reporting odds ratios for vancomycin and meropenem were 3.54 and 0.98 [15]. These findings indicate that prolonged vancomycin use in this case may have contributed to agranulocytosis. Therefore, vigilance is warranted when employing long-term, high-dose antibiotic therapies to monitor for neutropenia.

Based on TCM theory, brain abscess is often categorized as the "brain carbuncle." Accordingly, the patient was diagnosed with the syndrome of phlegm dampness-heat toxicity, and upper invasion of brain orifice. The patient's red tongue, yellow coating, and wiry, slippery, and rapid pulse align with the presence of the pathogenic heat and toxin. As extreme heat generates wind, the

symptom of paroxysmal convulsions is also attributed to pathogenic heat and toxins. The greasy coating, symptoms of weakness, and numbness are considered external manifestations of pathogenic dampness. Under this syndrome, we prescribed a Chinese herbal formula derived from XFHM, along with ANP, and antelope horn powder.

XFHM is a well-known traditional Chinese herbal formula documented in the Ming Dynasty in China. XFHM is recognized for its efficacy in clearing heat, detoxifying toxins, alleviating swelling, invigorating blood circulation, softening hardness, and relieving pain. A retrospective study in Taiwan from 2004 to 2013 found that XFHM (18.2%), Jia-Wei-Xiao-Yao-San (9.1%), and Chai-Hu-Shu-Gan-San (8.4%) were three of the most frequently prescribed Chinese herbal formulas for mastitis patients [16]. Studies have reported that XFHM can attenuate synovium inflammation by regulating the differentiation of T, B, and NK cells, inhibiting T cell migration, and suppressing the NF- κ B and JAK/STAT signaling pathways [17,18]. Modified XFHM formulas are derived from the original formula by incorporating additional Chinese herbs to enhance their effects. *Astragali Radix* (Huang-Qi), for instance, exhibits positive effects on immune modulation, antiviral activity, antitumor properties, antihyperglycemic activities, and anti-inflammatory activity [19]. *Astragali Radix* has been found to enhance exercise performance and meliorate exercise-induced and post-stroke fatigue [20,21].

ANPs, a well-known patent Chinese medicine, have been used for centuries in Asia. Reviews showed that ANPs have been associated with shorter duration of symptoms such as headache, fever, convulsions, coma, and pyramidal signs in the treatment of viral encephalitis [22]. Serum levels of NSE, TNF- α , IL-6, and MMP-9 were also significantly elevated in the ANP group compared with the non-ANP group in children with severe viral encephalitis [23]. Moreover, antelope horn powder has been extensively employed in China for the treatment of febrile seizures in children. Its anti-febrile convulsive mechanism may involve the upregulation of 5-HT expression through the ER- β /TPH2/5-HT pathway and the inhibition of neuroinflammation [24]. Consequently, TCM treatment has prominent anti-inflammatory, anti-convulsant, and immune regulation effects.

This is the first well-documented report utilizing antimicrobial therapy and TCM based on modified XFHM combined with ANP and antelope horn powder in the treatment of brain abscesses. Throughout this case study and a 5-month follow-up period, TCM has proven to be both safe and effective for this patient. These findings suggest that TCM could serve as a valuable adjunct therapy in the treatment of complex infections such as brain abscesses. The efficacy of integrating TCM at an early stage with antibacterial treatments to shorten the duration

of antibiotic therapy and minimize adverse events in the management of brain abscesses merits further investigation.

Nevertheless, this case report has some limitations. Firstly, due to its nature as a case report, definitive causality cannot be established, and the generalizability of the findings may be limited. Secondly, MRI measurements may lack uniformity as the patient underwent brain scans at different hospitals. Finally, the proposed mechanisms of action for this traditional Chinese medicine are based on previous studies, and further validation of these hypotheses requires additional experiment evidence.

CONCLUSION

In conclusion, this case report suggested that a combination of antimicrobial therapy and TCM treatment was associated with the resolution of paroxysmal convulsions and weakness in a patient with a brain abscess. The modified XFHM may play a significant role in modulating inflammatory responses. While these preliminary findings are encouraging, further research is necessary to validate the efficacy and explore the potential of TCM in the treatment of brain abscesses.

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Ethics statement: Informed consent was obtained from the patient's guardian for the publication of all images, clinical data, and other data included in the manuscript.

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Appendix A

Table S1. Traditional Chinese Medicine Prescriptions

Formula/ patent Chinese medicine	Compositions in Chinese Name	Compositions in the Latin name	Daily dosage	Effects and mechanism
Modified Xianfang	Jin Yin Hua	<i>Lonicerae japonicae</i> Flos	30 g	anti-inflammation, antipyretic,
Huoming Yin*	Bai Zhi	<i>Angelicae dahuricae</i> Radix	12 g	antimicrobial (bacteria, viruses,
	Fang Feng	<i>Saposhnikovia</i> Radix	9 g	fungi), anticonvulsion, and
	Chen Pi	<i>Citri reticulatae</i> Pericarpium	9 g	immune regulation effects
	Dang Gui	<i>Angelicae sinensis</i> Radix	9 g	
	Chi Shao	<i>Paeoniae Rubra</i> Radix	10 g	
	Ru Xiang	<i>Olibanum</i>	6 g	
	Mo Yao	<i>Myrrha</i>	6 g	
	Zao Jiao Ci	<i>Gleditsiae spina</i>	12 g	
	Zhe Bei Mu	<i>Fritillariae thunbergii</i> Bulbus	9 g	
	Tian Hua Fen	<i>Trichosanthis</i> Radix	24 g	
	Wu Gong	<i>Scolopendra</i>	6 g	
	Quan Xie	<i>Scorpio</i>	6 g	
	Hu Zhang	<i>Polygoni cuspidati</i> Rhizoma et Radix	30 g	
	Ma Bian Cao	<i>Verbena officinalis</i>	30 g	
	Hong Teng	<i>Sargentodoxa cuneata</i>	30 g	
	Di Yu	<i>Sanguisorbae</i> Radix	30 g	
	Yi Yi Ren	<i>Coicis semen</i>	30 g	
	Da Huang	<i>Rhei</i> Radix et Rhizoma	9 g	
	Huang Qi	<i>Astragali</i> Radix	45 g	
	Pu Gong Ying	<i>Taraxaci</i> Herba	30 g	
	Gan Cao	<i>Glycyrrhizae</i> Radix et Rhizoma	9 g	
Angong Niu Huang Pill			0.5 pill, twice daily	anti-inflammation, antioxidation, antipyretic, antimicrobial (bacteria, viruses, fungi), anticonvulsion, anti-cell death, antiedema, antithrombotic, and neuroprotective effects
antelope horn powder			0.6 g, twice daily	anti-inflammatory, antipyretic, analgesic, anticonvulsant, antithrombotic, anticoagulation, and antihypertensive effects

*The formulation was prepared as oral granules and is to be administered twice daily.