



## Case report

Multiple brain abscesses caused by *Nocardia asiatica*: Case report and literature reviewShanmu Jin<sup>a,b</sup>, Xiaopeng Guo<sup>a</sup>, Hao Xing<sup>a</sup>, Dingding Li<sup>c</sup>, Yu Wang<sup>a,\*</sup>, Wenbin Ma<sup>a</sup><sup>a</sup> Department of Neurosurgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China<sup>b</sup> 4+4 Medical Doctor Program, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China<sup>c</sup> Department of Laboratory Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China

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## ABSTRACT

*Nocardia* are opportunistic pathogens mainly affecting immunocompromised individuals. *Nocardia asiatica*, a novel species, can cause severe infections. We present a case of multiple brain abscesses due to *Nocardia asiatica*, discussing its diagnosis and treatment. In January 2022, a 27-year-old Chinese woman with a history of atypical membranous nephropathy presented with low-grade fever, cough, limb weakness, and headaches. Imaging revealed lung and brain lesions. Neurological symptoms worsened over time, culminating in recurrent seizures and severe headaches. A brain MRI confirmed multiple abscesses. Craniotomy and lesion removal were performed, leading to a diagnosis of brain abscesses caused by *Nocardia asiatica*. Empirical antibiotics were followed by targeted regimen. After successful treatment, the patient remained symptom-free during follow-ups. *Nocardia asiatica* multiple brain abscesses are exceedingly rare. This case underscores the importance of considering nocardiosis in immunosuppressed patients presenting with neurological symptoms. Timely neurosurgical intervention and effective antibiotic therapy are crucial. Metagenomic next-generation sequencing proved invaluable for rapid diagnosis. Treatment with trimethoprim-sulfamethoxazole (TMP-SMX) and a carbapenem followed by TMP-SMX alone achieved disease control. This case contributes to the understanding of *Nocardia asiatica* infections and highlights the role of neurosurgical procedures in managing disseminated nocardiosis.

## Introduction

*Nocardia* species are aerobic, Gram-positive, acid-fast, branching bacteria of the Actinomycetes order which are commonly found in soil and water, with more than 90 species identified and over 50 associated with human diseases [1]. They usually behave as opportunistic pathogens and affect immunocompromised patients, mainly causing lung, brain, or skin infections [2]. Here, we describe a case of multiple brain abscesses due to *Nocardia asiatica*, a novel *Nocardia* species which was first isolated from patients in Japan and Thailand in 2004 [3], and was classified as a member of the *Nocardia abscessus* complex [4]. Additionally, we provide a literature review on similar cases.

## Case report

In January 2022, a 27-year-old Chinese woman under immunosuppressant treatment was admitted to the neurosurgery department, with a

primary complaint of three months of low-grade fever and cough, alongside one month of limb weakness and headaches. Her medical history included a diagnosis of atypical membranous nephropathy seven years ago. Over the past two years, her renal condition had been successfully managed with hydroxychloroquine (0.1 g twice daily) and prednisolone (12.5 mg once daily), maintaining normal serum albumin and creatinine levels.

In late October 2021, the patient presented with low-grade fever, cough, and occasional blood-tinged sputum, accompanied by no chest pain or breathing difficulties. A chest computed tomography (CT) scan identified a smooth-edged soft tissue mass with lobulation in the lower lobe of her left lung, measuring approximately 3.1 cm × 2.7 cm. In November, she received outpatient treatment from our respiratory department. A positron emission tomography (PET)/CT scan discovered a 5.0 cm × 3.0 cm × 6.8 cm mass closely associated with the posterior pleura near the descending aorta in the basal segment of the left lower lung, with a maximum standardized uptake value (SUVmax) of 17.4

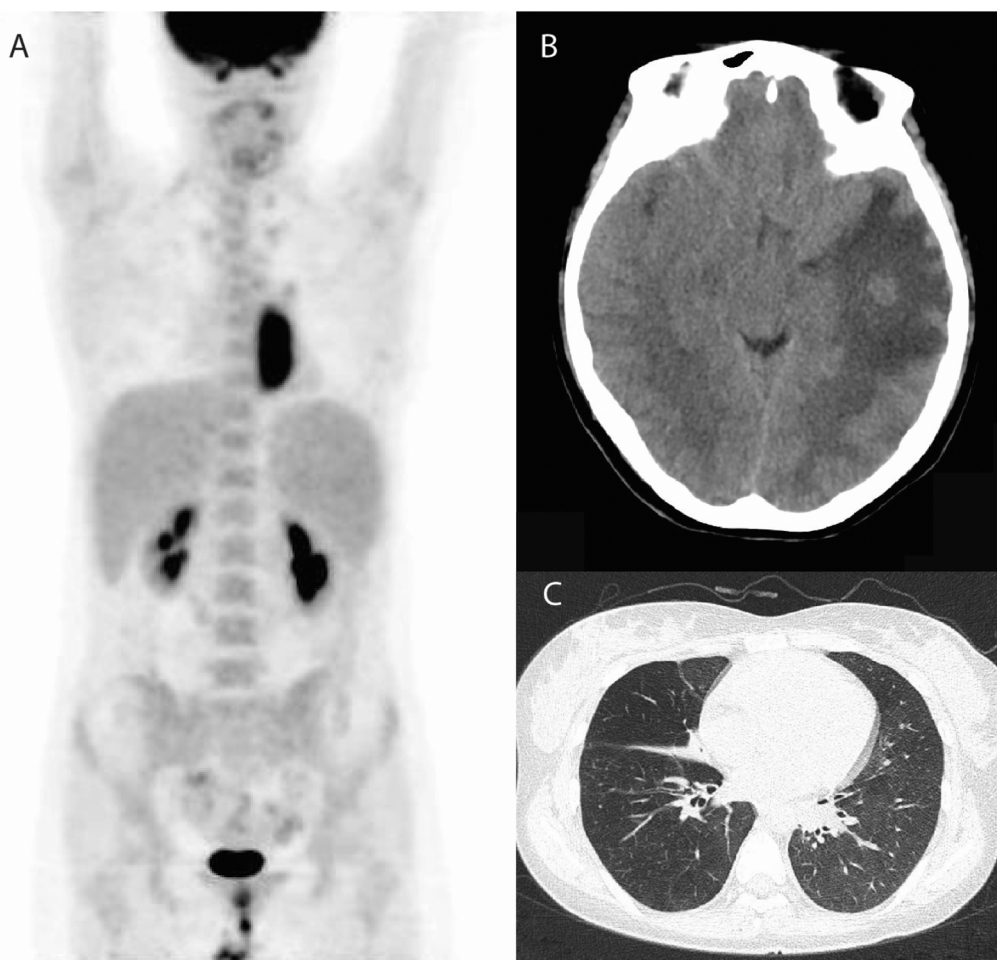
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**Fig. 1.** (A) PET/CT scan in October 2021. High radiotracer uptake is seen in the left lower lung. (B) Head CT scan in December 2021. Abnormal intensities are seen in the left hemisphere. (C) Chest CT scan in January 2022. Atelectasis and bronchial dilation are seen in the right middle lung.

(Fig. 1(A)). No tumor cells were found in the bronchoalveolar lavage fluid (BALF) and brush cytology examination. Following two weeks of oral moxifloxacin and intravenous ceftriaxone, her temperature gradually returned to normal from a peak of 39.4 °C. A follow-up CT scan demonstrated a patchy high-density area in the lower lobe of the left lung which exhibited uniform and significant enhancement.

In mid-December, the patient experienced recurrent episodes of left upper limb weakness, each lasting for approximately 10 min, without accompanying symptoms such as headaches, vomiting, loss of consciousness, or limb numbness. She did not seek medical attention at that time. Later, the patient had an episode of loss of consciousness, limb convulsions, and leftward mouth deviation, followed by headaches and dizziness upon regaining consciousness. A head magnetic resonance imaging (MRI) detected small nodular lesions with edema in the right uncinate gyrus, left basal ganglia-temporal lobe-insula, and left temporal-parietal junction. She received treatment with mannitol and sodium valproate.

In late December, the patient presented to our hospital's emergency department with worsening headaches and projectile vomiting. A head CT scan revealed abnormal densities accompanied by extensive surrounding edema (Fig. 1(B)). A head MRI displayed circular and nodular lesions in the left temporal-occipital lobe and the right of cerebral falx, which manifested as isointense on T1-weighted imaging (T1WI), mixed intensities on T2-weighted imaging (T2WI), ring enhancements on contrast, centrally hyperintense on diffusion-weighted imaging (DWI), and centrally hypointense on apparent diffusion coefficient (ADC) map, causing shallowing of local sulci, narrowing of the left lateral ventricle,

and a slight rightward shift of midline structures (Fig. 2). Measures to alleviate intracranial pressure were promptly initiated.

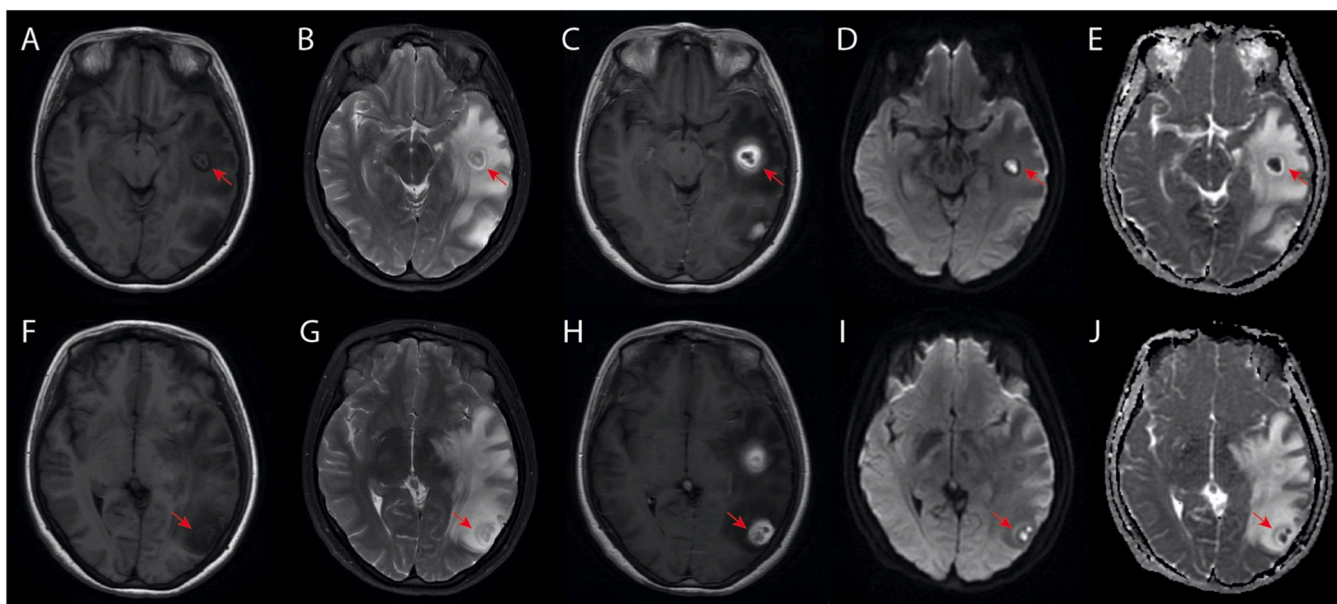
In January 2022, a PET/CT scan indicated a hyperdense nodule with peripheral high radiotracer uptake (SUVmax 7.5) in the left temporal lobe, with no abnormal radioactive findings observed in the lungs. A lumbar puncture showed a cerebrospinal fluid (CSF) pressure of 250mmH<sub>2</sub>O, a total white blood cell count of  $2 \times 10^6$ /L (composed of 100% mononuclear cells), a total protein level of 0.31 g/L, chloride at 129 mmol/L, and glucose at 3.2 mmol/L. Cytological and microbiological examinations of the CSF yielded negative results.

During current hospitalization, no abnormalities were found in the initial physical examination on admission. A chest CT scan suggested atelectasis in the right middle lung, as well as bronchial dilation with mucus plug indicating infection (Fig. 1(C)).

Based on the patient's medical history, symptoms, and radiological findings, the primary diagnosis under consideration was brain abscess, with a high likelihood of pulmonary infection as the source. The suspected brain abscesses had developed cystic walls, necessitating surgical removal primarily for lesion elimination and diagnostic confirmation. Other possibilities such as brain metastasis from lung cancer, primary central nervous system lymphoma, and glioma were not completely ruled out.

The patient underwent neuronavigation-guided craniotomy for the resection of lesions in the left temporal and occipital lobes. The lesion in the right central region had decreased in size without increase in radiotracer uptake, so it was left untreated during the surgery. The lesion excised from the left temporal lobe measured approximately



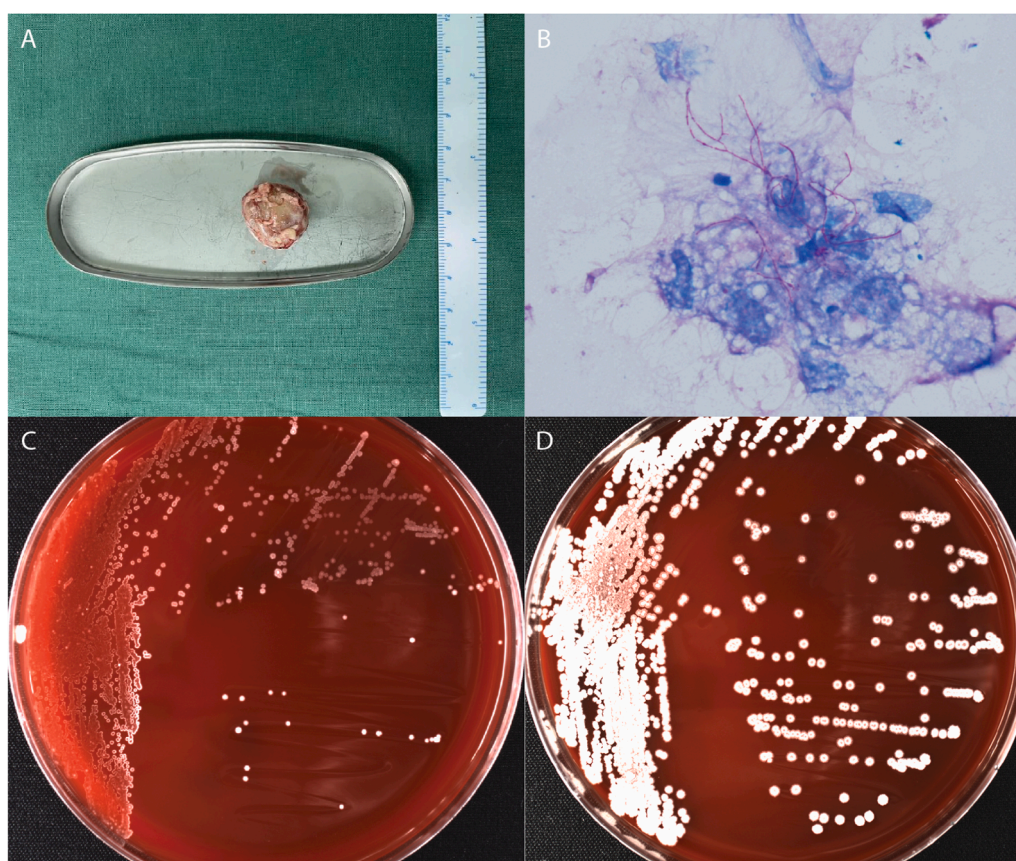


**Fig. 2.** (A-E) The left temporal lesion (red arrow). Imaging on T1WI (A), T2WI (B), contrast (C), DWI (D), and ADC (E) is shown, respectively. (F-J) The left occipital lesion (red arrow). Imaging on T1WI (F), T2WI (G), contrast (H), DWI (I), and ADC (J) is shown, respectively.

3 cm × 3 cm × 3 cm (Fig. 3(A)). Intraoperative frozen pathology revealed significant neutrophil infiltration and abscess formation in the brain tissue, supporting the diagnosis of brain abscess.

Empirical antibiotics of ceftriaxone and metronidazole were

administered postoperatively. When acid-fast branching bacilli were observed on smears of the abscess pus, and nocardial infection was suspected (Fig. 3(B)), the antibiotic regimen was adjusted to intravenous meropenem 2 g three times a day and oral trimethoprim-



**Fig. 3.** (A) The resected left temporal lesion. The lesion is shown in cross section. (B) Modified Kinyoun staining of abscess pus. Acid-fast filamentous bacilli with hyphae-like branching are observed. (C & D) Culture of abscess pus. Dry chalky-white colonies with earthy smell are observed on a blood agar plate after culturing at 36 °C for three (C) and five (D) days, respectively.

**Table 1**  
Reported cases of multiple brain abscesses due to *Nocardia asiatica*.

Case number	Year	Country	Age (in years)	Sex	Predisposing factor		Extracranial focus	Neurological symptom	Brain surgery	Positive sample	Speciation method	Antimicrobial therapy	Outcome
					Underlying disease	Medication							
1 [13]	2012	Lebanon	49	M	Myasthenia gravis, malignant thymoma	Prednisone, mestinon	Anterior mediastinum	No	No	Pericardial effusion	Unspecified	Imipenem, amikacin, TMP-SMX	Alive
2 [14]	2016	Japan	65	M	Autoimmune hemolytic anemia	Prednisolone	Lung	Headache	Resection	Brain abscess	16S rRNA	Ceftriaxone, TMP-SMX	Alive
3 [15]	2017	Korea	51	M	Systemic lupus erythematosus, diabetes	Danazol, hydroxychloroquine, methotrexate, prednisolone	No	Limb weakness, dysarthria, dizziness, nausea, vomiting	Aspiration	Brain abscess	16S rRNA	TMP-SMX, ceftriaxone	Expired
4 [16]	2019	India	37	M	HIV infection	Tenofovir, lamivudine, efavirenz	Lung, subcutaneous tissue, pancreas	No	No	Subcutaneous and pancreatic abscesses	16S rRNA	Amikacin, meropenem, TMP-SMX	Alive
5 [17]	2020	India	53	M	HIV infection	No	No	Headache, gait ataxia	Drainage	Brain abscess	16S rRNA, MALDI-TOF MS	TMP-SMX	Alive
6 [18]	2022	China	49	M	No	No	Lung	Headache	No	BALF	mNGS	TMP-SMX, linezolid, ceftriaxone, minocycline	Alive
7 [19]	2023	Ecuador	63	M	Adult-onset Still's disease, type 2 diabetes mellitus	Prednisone, methotrexate, etanercept	Lung, subcutaneous tissue	Hemiparesis, alteration in consciousness	Biopsy	Brain abscess	16S rRNA	Levofloxacin, amikacin, linezolid, TMP-SMX	Expired
8 (present case)	2023	China	27	F	Atypical membranous nephropathy	Hydroxychloroquine, prednisolone	Lung	Limb weakness, seizure, headache, dizziness, vomiting	Resection	Brain abscess	mNGS	Meropenem, TMP-SMX	Alive

sulfamethoxazole (TMP-SMZ) three tablets (240 mg/1200 mg) four times a day. Specimen culture subsequently confirmed the presence of *Nocardia* (Fig. 3(C & D)), with metagenomic next-generation sequencing (mNGS) identifying it as *Nocardia asiatica*. The strain was sensitive to the majority of antibiotics tested, including cefotaxime, ceftriaxone, erythromycin, minocycline, cefepime, ceftazidime, imipenem, linezolid, tigecycline, and TMP-SMZ.

After complete relief from symptoms, the patient was discharged and continued the antibiotic treatment for six weeks. The intravenous meropenem was then discontinued, and the treatment transitioned to oral TMP-SMZ only, which was maintained for five months. The patient no longer required antiepileptic medication and did not experience seizures after the surgery. The last follow-up at our outpatient clinic was in August 2023, and the patient's condition remained favorable.

## Discussion

The central nervous system (CNS) is the most common extrapulmonary location for nocardiosis, with an incidence of up to 44% in patients with disseminated infections [5]. On the other hand, cerebral nocardiosis frequently coexists with pulmonary disease, as only 20% of extrapulmonary lesions occur without a primary lung lesion [6]. Nevertheless, isolated CNS disease remains possible [7]. Patients may be neurologically asymptomatic, or present with headache, nausea, vomiting, seizures, aphasia, hemiparesis, and alterations in consciousness [6]. The one-year mortality rate in cases of nocardial brain infection varies from 20% to 40% [8–11]. Multiple abscesses are reported in 38% of patients with CNS nocardiosis, where the mortality rate rises to 66% [12].

A PubMed search of English literature yielded a total of seven cases documenting multiple brain abscesses attributed to *Nocardia asiatica* [13–19]. The current case represents the first occurrence in a female patient and also stands as the youngest case reported to date (Table 1).

All but one case was under immunosuppressive conditions, with five undergoing long-term treatment with oral glucocorticoids, and two were positive for human immunodeficiency virus (HIV). Six patients presented with identifiable extracranial infection foci, with the lung was being the most prevalent site. Only two patients were neurologically asymptomatic, with the others mainly complaining of headache and limb weakness.

Neurosurgical interventions were undertaken in five cases. Indications for neurosurgical procedures on nocardial brain lesions include the presence of large abscesses (diameter  $\geq 25$  mm) with a thick capsule, absence of positive extracranial samples, continuous clinical deterioration despite empirical antimicrobial treatment, the existence of mass effect causing brain displacement, and close proximity to the ventricles [20]. Regarding diagnosis, neurosurgical aspiration or excision facilitates pathogen identification and drug susceptibility testing, which is evidenced by the fact that brain abscess samples from the reviewed cases tested 100% positive for *Nocardia asiatica*. In terms of therapy, neurosurgical aspiration or excision served as a means for source control. On this aspect, craniotomy and complete excision of the abscess and its capsule are considered more effective than aspiration and drainage [12]. A recent retrospective study reported better outcomes for patients who underwent neurosurgery than those who did not [21]. However, selection bias and confounding by indication should be acknowledged, since neurosurgery may not be pursued in patients with either very mild or severe disease. For instance, the two cases without neurological symptoms in this review did not undergo brain surgery.

Obtaining an unequivocal diagnosis often necessitates pathogen identification at the species level. Commonly employed methods for this purpose include 16S RNA sequencing, matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS), and mNGS. With increasingly lower cost, shorter turnaround time, and more simplified interpretation, mNGS is gaining popularity in clinical practice [22]. It has proven particularly beneficial in cases like ours, where a

precise diagnosis was crucial.

TMP-SMX stands out as the primary antimicrobial choice to treat brain nocardiosis [2], which was received by all eight cases. It is recommended for its high penetration into the CNS, low rate of resistance among *Nocardia* species, and good oral bioavailability. Initial combination therapy with the addition of a high-dose  $\beta$ -lactam antibiotic is advocated, where a carbapenem (imipenem or meropenem) is generally favored over a third-generation cephalosporin (cefotaxime or ceftriaxone) according to the susceptibility profiles [20]. Among carbapenems, meropenem is the preferred choice when the patient has a history of seizures [23,24], which is relevant in our specific case.

In summary, we have presented a case of multiple brain abscesses caused by *Nocardia asiatica* that was effectively managed. Craniotomy was performed to remove the mature abscesses, achieving both lesion debulking and specimen sampling. mNGS played a key role in providing a rapid and definitive diagnosis alongside traditional culture methods. A two-stage antibiotic regimen was implemented, consisting of intensive therapy with TMP-SMX and a carbapenem for the initial six weeks and consolidation therapy of TMP-SMX alone for the subsequent five months. This approach resulted in stable disease control and successful treatment.

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No funding was received for conducting this case report study.

## Ethical approval

This case report study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Peking Union Medical College Hospital.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Authorship statement

All authors meet the International Committee of Medical Journal Editors (ICMJE) authorship criteria.

## CRedit authorship contribution statement

SJ conceived this case report study and drafted the manuscript. XG, HX, YW, and WM managed the patient. DL provided the original images of microbiological examination. XG, HX, DL, YW, and WM critically revised the manuscript. All authors read and approved the final manuscript.

## Declaration of Competing Interest

The authors declare there are no competing interests.

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