

CASE REPORT

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Brain abscesses: the first report of disseminated *Nocardia beijingensis* infection in an immunocompetent individual in China

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Abstract

Nocardia is widely distributed in the natural environment and typically cause opportunistic infections. However, it is important to note that the pathogenicity of different *Nocardia* species may vary significantly. Here we reported the first case of brain abscess caused by *Nocardia beijingensis* (*N. beijingensis*) infection in China. A 70-year-old male immunocompetent individual came to our hospital for treatment due to headache. After examination, it was found that he had a brain abscess caused by *N. beijingensis*. By utilizing a combination of surgical intervention and antibiotic therapy, the patient ultimately achieved full recovery. In addition, we isolated this strain and displayed its ultrastructure through scanning electron microscopy. The phylogenetic tree was analyzed by 16 S rRNA sequence. A literature review of *N. beijingensis* infections in all immunocompetent and immunocompromised patients was presented. It highlighted that abscess formation appears to be a common manifestation of *N. beijingensis* infection, and *N. beijingensis* has become an emerging pathogen in immunocompetent individuals.

Keywords Brain abscess, Immunocompetent, Infection, *Nocardia beijingensis* (*N. beijingensis*), Phylogenetic tree

Introduction

Brain abscess is characterized as inflammatory lesions, and it is usually caused by pathogens encrust pus on the central nervous system [1, 2], with a mortality rate of approximately 50–55% [3, 4]. In all intracranial space-occupying lesions, the proportion of brain abscesses

is nearly 1–2% in developed countries and about 8% in developing countries [4]. According to a survey in northern Europe, the incidence of brain abscesses is 9 cases per million people every year, and it has been rising continuously in recent years [5]. Although *Nocardia* brain abscess is uncommon and estimated about 1–2% of all intracranial space-occupying lesions, it has the highest mortality rates of all bacterial brain abscesses, which has gradually raised widespread concern [6].

Brain abscess caused by *Nocardia* infection is characterized by cerebritis and central focal necrosis. *Nocardia* are aerobic actinomycetes ubiquitous in water and soil, which can cause local or disseminated infections primarily affecting immunocompromised patients such as AIDS, malignant neoplasms, hematopoietic stem cells or organ transplantation, diabetes, COPD, flora imbalance, chronic kidney disease, trauma [7]. To date, nearly 92

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Nocardia species have been identified, of which 54 have been identified as clinically significant pathogens [8–10].

Nocardia beijingensis (*N. beijingensis*) was initially isolated from sewage ditch soil in Beijing, the capital of China in 2001 by Wang et al. and was first reported as a human pathogenic pathogen primarily affecting immunocompromised patients in Thailand and Japan in 2004 [11, 12]. Here we reported the first case of brain abscess caused by *N. beijingensis* infection in China, which could raise the awareness of disseminated nocardiosis in immunocompetent individuals.

Case presentation

Clinical feature

A 70s male patient presented intermittent bilateral frontal headaches, swelling, fatigue, and unsteady gait, without any apparent causes 10 days ago. He had previously sought medical attention at a local hospital where a cranial Computed Tomography (CT) scan revealed extensive areas of low density in the left hemisphere of the cerebellum, as well as old lacunar infarcts in both basal ganglia and periventricular regions. Enhanced Magnetic Resonance Imaging (MRI) suggested a nodular lesion in the left cerebellar hemisphere, raising suspicion of a tumor with associated hemorrhage. The patient received treatment for a period of time but the efficacy was not good, so he came to our hospital for further treatment. Reviewing the medical records, a personal history of cerebral infarction was noted, without any other underlying conditions or medication use. After admission, the patient underwent a physical examination, with a body temperature of 36.8 °C, blood pressure of 118/78 mmHg, clear consciousness, soft mind, and fluent language. Bilateral pupils were equally large and round, with a left to right ratio of 2.5:2.5 mm. He was sensitive to light reflection and had normal eye movements. Bilateral facial patterns were symmetrical, and the facial sensation was symmetrical on both sides. The pharyngeal reflex existed. The muscle strength of the limbs was at level V, with normal muscle tone and normal tendon reflexes. The superficial sensation of the limbs was symmetrical on both sides, and the deep sensation was basically normal. Due

to concerns about intracranial infection, in addition to blood tests, we also extracted cerebrospinal fluid from the patient for testing. The laboratory results were shown in Table 1, where the patient's blood infectivity indicators were elevated and abnormal cerebrospinal fluid indicators indicated the presence of intracranial infection.

Imaging examination

Upon admission, the patient underwent cranial MRI examination, which revealed bilaterally scattered patchy and focal abnormal signals in the frontal and parietal white matter, periventricular region, and basal ganglia. These signals appeared confluent in some localized areas. On T1-weighted imaging (T1WI), the signals were slightly decreased or isointense, while on T2-weighted imaging (T2WI) and FLAIR imaging, the signals were increased. No apparent diffusion restriction was observed on diffusion-weighted imaging (DWI). A lesion was observed in the left cerebellar hemisphere, characterized by indistinct borders. T1WI showed slightly decreased signals, while T2WI, FLAIR, and DWI showed high signals. Additionally, the surrounding area exhibited edema. In Fig. 1A, a distinct abscess lesion was seen, suggesting the possibility of an infection. Figure 1B and C depict postoperative MRI images acquired immediately after surgery and two weeks post-surgery, respectively. These images demonstrate the changes following the left cerebellar lesion resection, gradual resorption of pneumocephalus in the surgical area, and a reduced range of multiple enhancing lesions in the left cerebellum compared to the previous scan.

Etiological examination

During the excision of cerebellar lesion, a large abscess was identified in the left cerebellar hemisphere and promptly sent for examination. Histopathological analysis (Fig. 2A) revealed the presence of suppurative inflammation with abscess formation. Microscopic examination of the smears (Fig. 2B) revealed clusters of Gram-positive bacteria, while acid-fast staining (Fig. 2C) demonstrated red-colored bacterial filaments. Scanning electron microscopy (Fig. 2D) revealed rough, long, filamentous bacteria. After three days of incubation, blood agar plate culture exhibited white, dry, wrinkled colonies, which were identified as *N. beijingensis* by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS, Hangzhou YiDan biology technology co., ltd) (Fig. 2E). The antibiotic susceptibility results were summarized in Table 2.

Treatment and outcome

During the patient's hospitalization, continuous mannitol was administered to reduce intracranial pressure. On the second day of hospitalization, brain MRI revealed

Table 1 Laboratory examination results of the patient

Laboratory indicators	Result	Reference range
White blood cell count	12.83 × 10 ⁹ /L	3.50–9.50 × 10 ⁹ /L
C-reactive protein	42.4 mg/L	≤ 10.0 mg/L
Serum total protein	60.1 g/L	65.0–85.0 g/L
Serum albumin	34.9 g/L	40.0–55.0 g/L
Osmotic pressure	273 mosm/L	275–300 mosm/L
Pan's test (CSF)	Positive	Negative
Protein quantification (CSF)	108.3 mg/dl	≤ 45.0 mg/dl
Glucose quantification (CSF)	5.45 mmol/L	2.50–4.50 mmol/L

Abbreviations Cerebrospinal fluid (CSF)

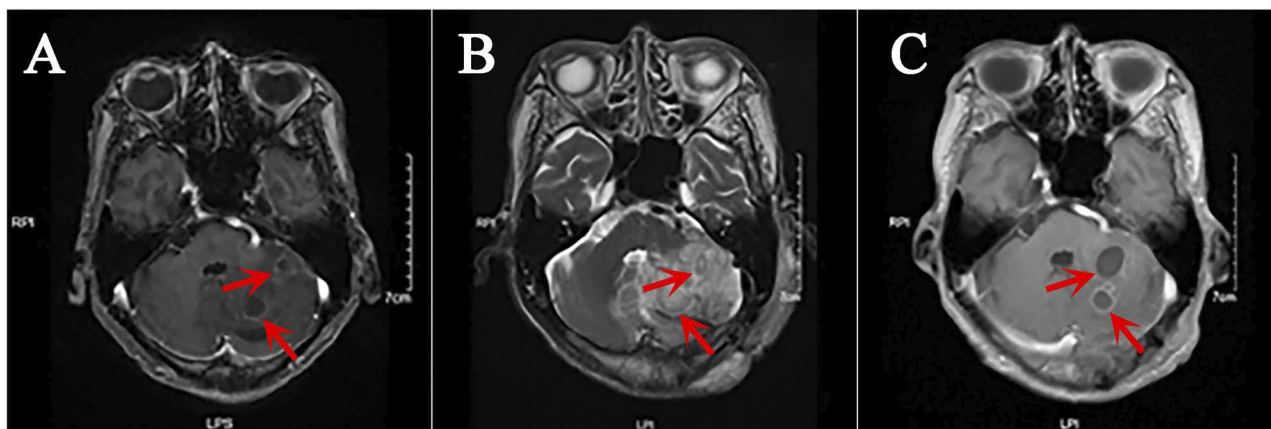


Fig. 1 MRI images of the patient's head. (A) MRI images of the patient upon admission. (B) MRI images of the patient after surgery. (C) MRI images of the patient two weeks after surgery. The locations of Abscess lesions were indicated by the red arrow

the presence of abscess. A single dose of vancomycin was administered for antimicrobial therapy. On the fifth day, the patient underwent cerebellar lesion resection. Following the incision of the left cerebellar hemisphere, purulent fluid was observed to discharge from a location approximately 2 cm deep to the left midline. After closure of the breach, the edematous area around the abscess was dissected, and a large abscess was completely excised for pathological and pathogen examinations. Based on the preoperative magnetic resonance images, the lateral part of the cerebellum was partially resected, and the remaining infected tissue was removed. The surgical field was thoroughly irrigated with a saline solution containing vancomycin, adequate hemostasis was achieved, and a gelatin sponge adhered to the surgical site was used to prevent further bleeding. After ensuring no active bleeding, dural defects were repaired with artificial dura mater, fascia was reconstructed, the bone flap was repositioned, and fixation was performed with titanium screws and plates. Layered closure was achieved with subcutaneous and skin sutures. Postoperatively, the patient received a combination of vancomycin, meropenem, linezolid, and trimethoprim-sulfamethoxazole (TMP-SMX) for antimicrobial therapy. After 24 days, the patient's infection markers decreased to normal levels, the brain lesion on the MRI diminished, and the patient remained stable, allowing for discharge. Following discharge, the patient continued oral administration of linezolid and sulfamethoxazole/trimethoprim for 30 days. The treatment plan for the patient was presented in Fig. 3

Phylogenetic tree of *N. beijingensis* ZJPPH1

The nucleotide sequences of the 1540-bp 16 S rRNA were verified and utilized to perform phylogenetic analysis by the Molecular Evolutionary Genetics Analysis (MEGA) software version 11 through the minimum-evolution method. A phylogenetic tree was constructed utilizing

the sequence of *N. beijingensis* ZJPPH1 (GenBank number: PP267164) from the isolate of this study along with 29 available sequences with the highest homology retrieved from GenBank. The nucleic acid sequence of the present isolate revealed 99.37% similarity with *N. beijingensis* strain IFM 0841 (Fig. 4).

Discussion

Brain abscess is a life-threatening infection, and the mortality rate increases with prolonged illness [5]. Approximately 70% of surviving patients will experience sequelae such as epilepsy or neurological deficits [13]. Generally speaking, head trauma, chronic ear infections, dental infections, and immune dysfunction are the main risk factors for brain abscess, but the possibility of infection without obvious causes cannot be ruled out [14]. Oral bacteria such as *Streptococcus anginosus*, *Fusobacterium species* and *Aggregatibacter species* are the most common bacteria that cause brain abscess. Brain abscess caused by *Staphylococcus aureus* and other Gram-negative bacteria are relatively rare but have a poor prognosis for patients. *Mycobacterium tuberculosis* has regional prevalence, while brain abscesses caused by other fungi, parasites, and *Nocardia* are more common in immunocompromised patients [15].

Nocardia was first described as a saprophyte and innocuous species widely distributed in soil, water, and decaying plants. In recent years, more and more clinical data showed that some *Nocardia species* might cause life-threatening infections with varying pathogenicity, antibiotic resistance and prevalence. *Nocardia abscessus*, *Nocardia cyriacigeorgica*, *Nocardia farcinica*, and *Nocardia nova* commonly caused pulmonary infections, while *Nocardia brasiliensis* was often associated with cutaneous infections [16, 17]. Infections in other sites were typically caused by traumatic inoculation and hematogenous spread from primary foci [16]. Currently,

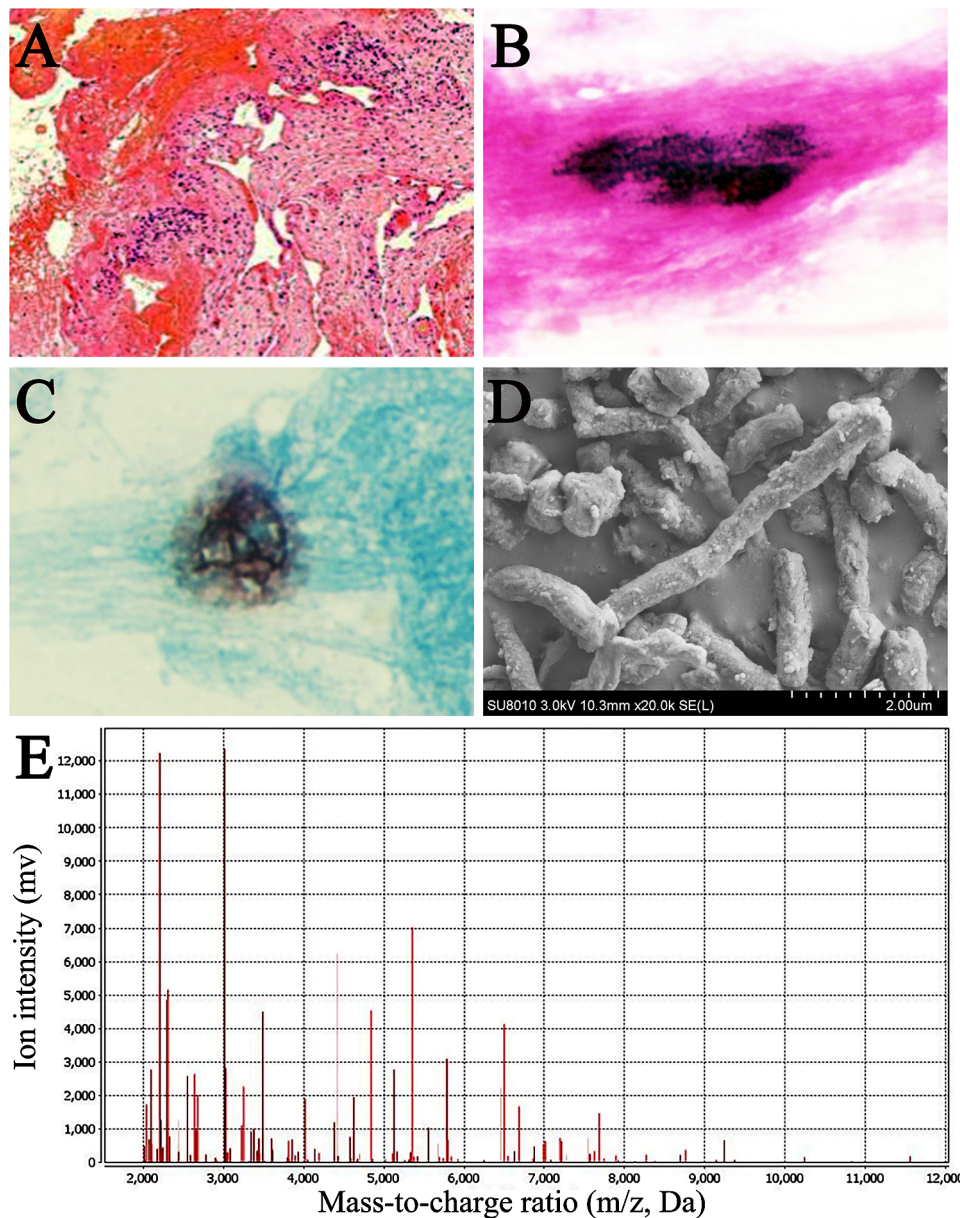


Fig. 2 Patient's etiological results. (A) HE staining section of the patient's abscess tissue showed inflammatory infiltration. (B) Gram staining of abscess tissue revealed purple bacterial clusters. (C) The abscess tissue was positive for acid fast staining, with visible red hyphae. (D) Under the electron microscope, slender bacterial bodies could be seen in *N. beijingensis* ZJSRMY1. (E) Identification peak diagram of *N. beijingensis* ZJSRMY1 by mass spectrometry

there is extremely limited information on the epidemiology of *N. beijingensis* infection. According to the literature collected by *N. beijingensis* on Pubmed retrieval platform and the nucleic acid sequence source of *N. beijingensis* isolates published on Genbank, it has a global popularity with higher prevalence in Japan, USA, France, Mexico, Costa Rica, KSA, China, Thailand, Italy, Israel, Colombia, Australia. Worryingly, the number of

immunocompetent patients with *N. beijingensis* is as high as 35.71% (10/28). A total of 28 cases of *N. beijingensis* infection were reported in the world, including 18 cases in immunocompromised patients (3 cases with diabetes, 1 case with smoking, 8 cases with HIV, 3 cases with solid organ transplantation, 6 cases with immunosuppressive drug, 2 cases with autoimmune diseases, and 1 case with malignant tumor), and 10 cases in immunocompetent

Table 2 Drug sensitivity results of the *N. beijingensis* ZJSRMYY1

Antibiotic	Method	Result	Break	Sensitivity level
Imipenem	Etest	0.25 µg/mL	1–4	S
Amoxicillin-clavulanate	Etest	16 µg /mL	8–32	I
Ceftriaxone	KB	36 mm	19–23	S
Vancomycin	Etest	128 µg/mL	4–32	R
linezolid	Etest	2 µg/mL	4–8	S
Levofloxacin	Etest	1 µg/mL	0.5-2	I
Meropenem	Etest	0.5 µg/mL	1–4	S
TMP-SMZ	Etest	0.0032/0.0608 µg/ mL	2–4	S

E-test: Epsilon meter test; KB: Kirby-Bauer method; TMP-SMZ: Compound sulfamethoxazole. S: Sensitive; I: intermediate; R: Resistant

individuals (Table 3). The average age of cases of *N. beijingensis* nocardiosis was 52-years-old, with a higher prevalence in males than females. Neurological infections accounted for 11 cases (39%), followed by pulmonary infections in 10 cases (36%), skin infections in 2 cases (7%), and 1 case each in other sites (including thoracic cavity, kidneys, heart, and the erector spinae muscle) (4%). Regarding *N. beijingensis*, based on existing case reports, despite variations in the site of infection, these cases share a common feature - the formation of abscesses at the lesion site [18, 19]. This appears to be a distinguishing characteristic of *N. beijingensis* infection.

The patient we report here had a previously healthy constitution and no smoking history. However, based on the pulmonary CT findings revealing inflammatory infiltrates and multiple small nodules, we suspected that the patient had a pulmonary infection that subsequently disseminated to the central nervous system, causing intracranial infection. Although diabetes, HIV, autoimmune diseases and smoking have been identified as risk factors for *N. beijingensis* infection, this patient had no documented risk factors, nor any history of immunosuppressive medication [20, 21]. Therefore, prevention of *N. beijingensis* infection should not be limited to immunocompromised or susceptible individuals. Once patients exhibit clinical manifestations of infection, the possibility of *N. beijingensis* infection should be considered. In 2014, Crozier et al. reported the first case of *N. beijingensis*

infection in an immunocompetent patient in the United States [22]. Since then, an increasing number of reports have emerged in immunocompetent patients, predominantly involving the lungs and central nervous system [18]. Here we report the first case of brain abscess caused by *Nocardia beijingensis* infection in China, which develops an awareness of disseminated nocardiosis in immunocompetent individuals.

We reviewed all reported cases of *N. beijingensis* infection. Given that *N. beijingensis* infections often lead to the formation of abscesses at the site of infection, surgical intervention and antimicrobial therapy are necessary. Furthermore, susceptibility testing for *N. beijingensis* is indispensable. Currently, most reports indicate that *N. beijingensis* is susceptible to TMP-SMX, carbapenems, amikacin, and/or third-generation cephalosporins [22] but resistant to amoxicillin-clavulanic acid and ciprofloxacin according to the reported antimicrobial sensitivity results of *N. beijingensis* (Table 4), unlike *N. transvaalensis* is resistant to amikacin and *N. abscessus* is resistant to imipenem.

Our susceptibility results showed that the *N. beijingensis* ZJSRMYY1 strain was sensitive to TMP-SMX, linezolid and amoxicillin-clavulanate, intermediate to levofloxacin, but resistant to vancomycin, which explained the initial ineffectiveness of vancomycin treatment. Following the issuance of susceptibility results, we promptly switched to TMP-SMX and linezolid for treatment. Therefore, susceptibility testing played a crucial role in guiding the choice of antibiotics for *Nocardia* infections.

In conclusion, we report the first case of an immunocompetent individual who developed a brain abscess due to *N. beijingensis* infection in China. Abscess formation appears to be a common manifestation of *N. beijingensis* infection, and *N. beijingensis* has become an emerging pathogen in immunocompetent individuals. When patients present with symptoms such as headache, particular attention should be given to the possibility of intracranial infection of *N. beijingensis*. Susceptibility of *N. beijingensis* is uncertain to amoxicillin-clavulanic acid, ciprofloxacin and levofloxacin, therefore susceptibility testing is necessary in guiding the choice of antibiotics.

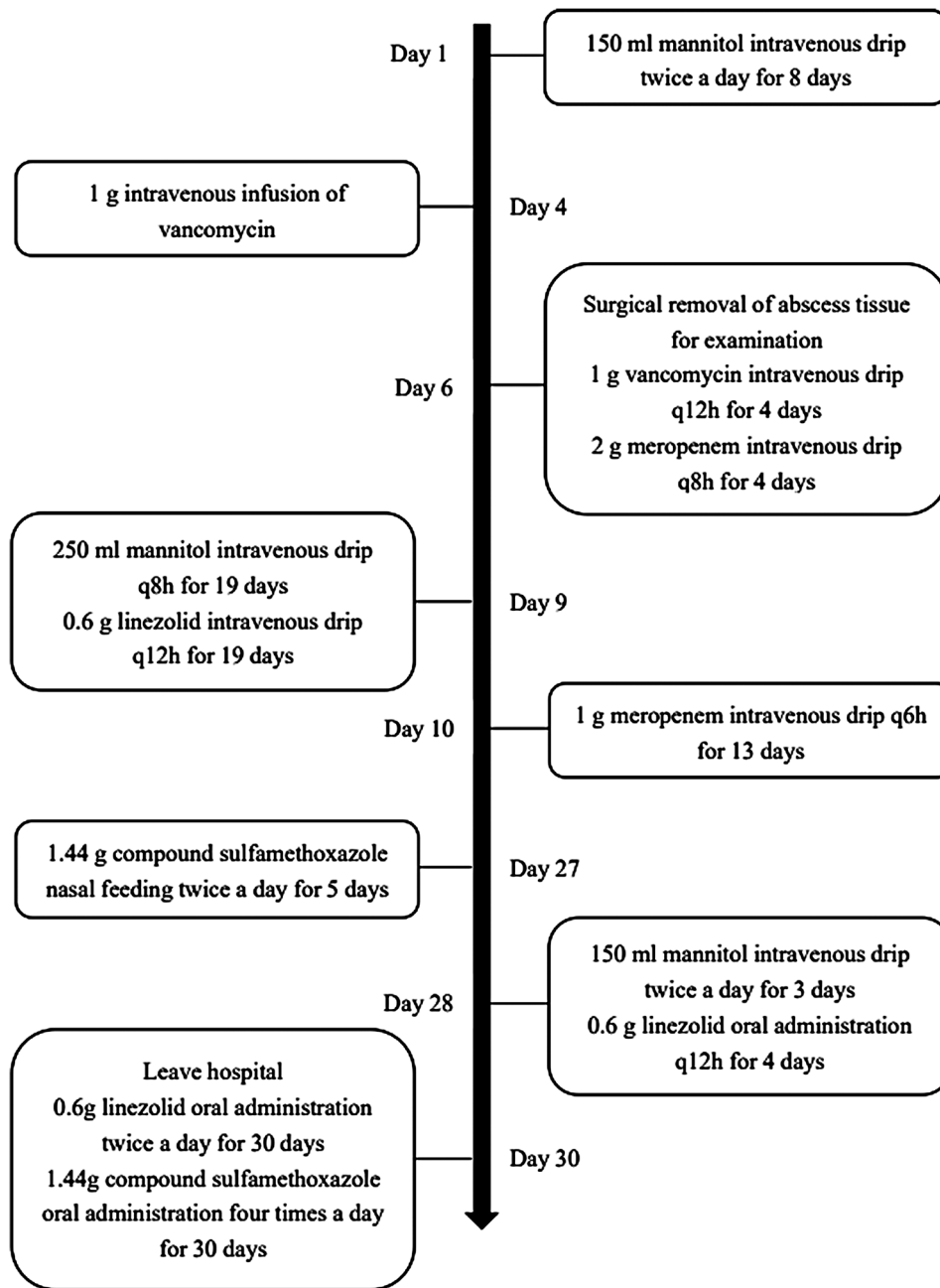


Fig. 3 Treatment timeline

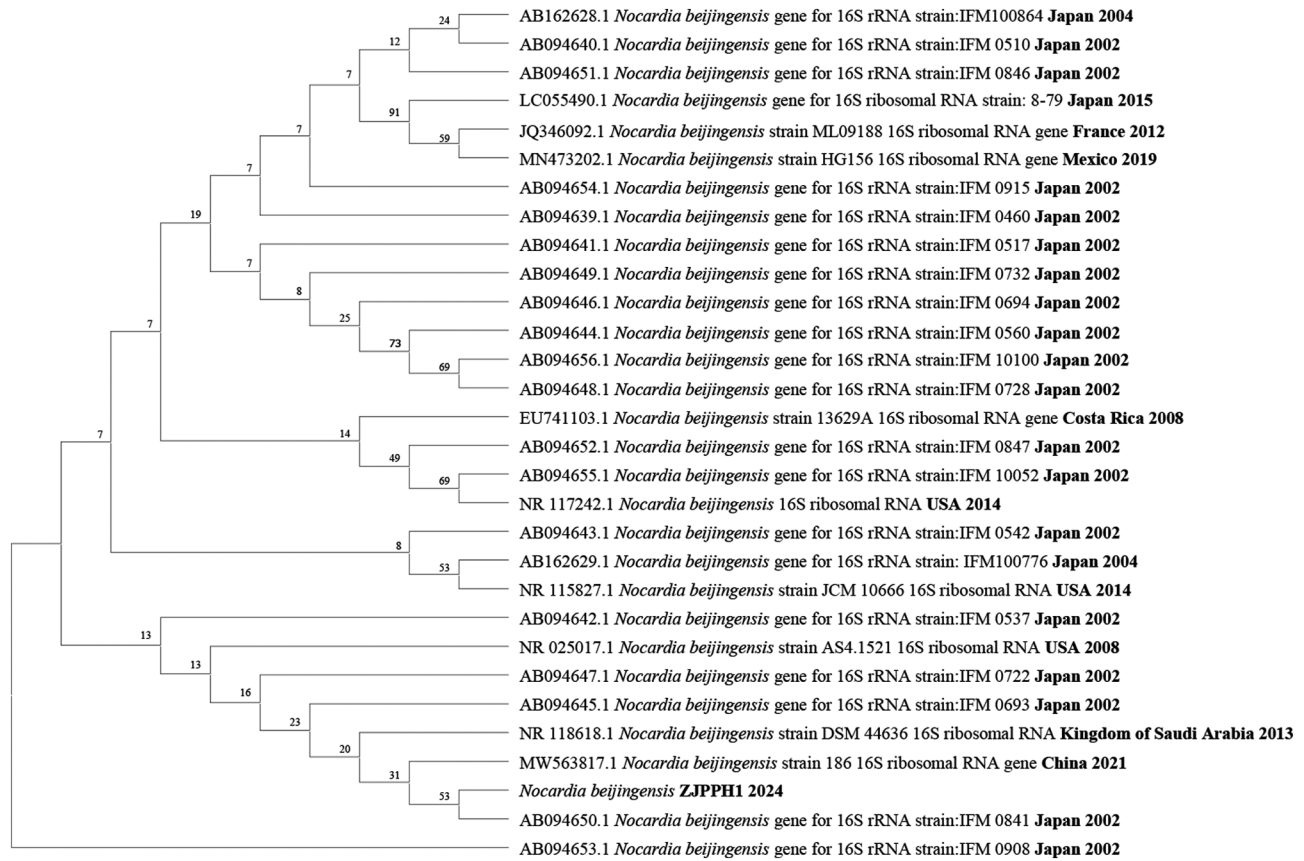


Fig. 4 Phylogenetic tree of *N. beijingensis* ZJPPH1

Table 3 Reported cases of *N. beijingensis* in immunocompetent and immunocompromised patients

Year	Country	Age	Gender	Organ involved	Immunodeficiency factors	Treatment	Outcome	Reference
2020	USA	57	Female	Intracranial	-	TMP/SMX, intravenous injection/15 mg/kg/8 h/6 weeks; TMP/SMX oral/160/800 mg/8 h/12 months	Rehabilitation	Roy et al. [23]
2021	USA	47	Male	Lung	-	Imipenem/cilastin and TMP/SMX, intravenous; TMP/SMX and doxycycline, oral	Rehabilitation	Raslan et al. [24]
2023	China	57	Female	Chest	-	Surgical removal of abscess; TMP/SMX, 15 months	Rehabilitation	Qi et al. [25]
2020	Japan	68	Male	Intracranial	-	Meropenem and TMP/SMX; TMP/SMX, 7 months	Relieve symptoms and transfer to long-term care	Tanaka et al. [26]
2015	Italy	75	-	Spinal	-	Imipenem and amikacin, 3 weeks; TMP/SMX, 3 months	Rehabilitation	Rigotti et al. [27]
2015	Israel	55	Female	Lung	-	Prednisone 30 mg daily, 21 days; TMP/SMX, oral/3 months; Ceftriaxone, intravenous/1 month	Rehabilitation	Abdel-Rahman et al. [28]
2021	USA	58	Male	Intracranial	-	TMP-SMX and ceftriaxone, intravenous/8 weeks; TMP-SMX and azithromycin, oral/1 year	Septicemia leading to death	Diioia et al. [29]

Table 3 (continued)

Year	Country	Age	Gender	Organ involved	Immunodeficiency factors	Treatment	Outcome	Reference
2019	Colombia	58	Male	Intracranial	-	1 g meropenem and 15 mg/kg TMP-SMX /amikacin every 8 h	Death from multiple infections	Solano-Varela et al. [30]
2012	France	42	Male	Lower left leg anterior skin	-	TMP/SMX oral/160/800 mg/ six times daily	Skin lesions subsided; Not followed up	Derancourt et al. [31]
2014	USA	48	Male	Lung	-	Surgical removal of lesion site; Ceftriaxone, 6 weeks; TMP/SMX, 6 months	Rehabilitation	Crozier et al. [22]
2016	Thailand	59	Male	Intracranial	HIV	TMP/SMX	Rehabilitation	Phoom-poung et al. [32]
2022	USA	57	Male	Left adrenal	Type 2 diabetes	Surgical removal of lesion site; Linezolid 3 months; TMP-SMX for 7 months	Rehabilitation	Pender et al. [18]
2017	Thailand	32	Male	Heart	HIV	TMP/SMX; Imipenem/cilastatin	Infectious shock leading to death	Laksananun et al. [33]
2017	USA	50	Male	Intracranial	HIV	TMP-SMX and meropenem, 1 year	Take a turn for the better	Keenan et al. [34]
2023	Mexico	37	Male	Intracranial	HIV	Surgical removal of lesion site; TMP-SMX, and vancomycin, 8 days	Take a turn for the better	Nieves et al. [4]
2022	Mexico	49	Male	Intracranial	HIV	Imipenem and TMP/SMX intravenously 2 weeks; linezolid and TMP/SMX intravenously 3 weeks; Amoxicillin/clavulanic acid and TMP/SMX 1 year	Rehabilitation	Leon-Tavares et al. [35]
2020	USA	45	Male	Intracranial	HIV	TMP/SMX, imipenem, and amikacin 2 weeks; Oral minocycline and TMP/SMX	Take a turn for the better	Bertrán-López et al. [36]
2014	USA	50	Female	Lung	Type 1 diabetes, solid organ transplantation, immunosuppressant	TMP/SMX 6 months	Take a turn for the better	Aragaki-Nakahodo et al. [37]
2017	USA	50	Female	Lung	Autoimmune disease, immunosuppressant, smoke	Meropenem 4 weeks	Take a turn for the better	Sheikh-Taha et al. [38]
2011	Japan	48	Male	Lung	Solid organ transplantation, immunosuppressant	Imipenem/cilastatin 30 days; Ceftriaxone 12 days; Minocycline 3 months	Take a turn for the better	Ogawa et al. [39]
2016	USA	52	Female	Eyes	Immunosuppressant	TMP/SMX, amikacin and b/trimethoprim	Take a turn for the better	Gonzalez et al. [40]
2011	France	47	Male	Lung	HIV	Imipenem and amikacin 3 weeks; TMP/SMX 3 months	Rehabilitation	Martinaud et al. [19]
2015	Australia	80	Male	Intracranial	Type 2 diabetes	Meropenem, ceftriaxone and TMP/SMX 1 week; Amikacin	Take a turn for the better	Angela et al. [41]
2015	Thailand	58	Male	Psoas muscle	Solid organ transplantation	TMP/SMX and imipenem 2 weeks; TMP/SMX 4 weeks	Take a turn for the better	Palavutitotai et al. [42]
2011	Japan	79	Male	Skin of left forearm	Malignancy	Garenoxacin 2 weeks	Rehabilitation	Ohmori et al. [43]
2008	China	13	Female	Lung	SLE, immunosuppressant	Meropenem 4 weeks; TMP/SMX 1 year	Rehabilitation	Chu et al. [44]
2008	Japan	60	Female	Lung	Immunosuppressant	TMP/SMX, meropenem and levofloxacin	Died of respiratory failure	Takayanagi et al. [45]
2021	Thailand	35	Female	Lung	HIV	TMP/SMX 3 weeks	Rehabilitation	Kiatsuranon et al. [46]

Table 4 Summary of reported drug sensitivity results of *N. beijingensis*

Reported strains	1 [25]		2 [39]		3 [29]		4 [22]	
	MIC (µg/mL)	S/I/R	MIC (µg/mL)	S/I/R	MIC (µg/mL)	S/I/R	MIC (µg/mL)	S/I/R
Antibiotic								
Amikacin	< 1	S	-	-	≤ 1	S	≤ 1	S
Amoxicillin-clavulanic acid	≥ 64/32	R	-	-	64	R	> 64	R
Ceftriaxone	< 4	S	0.5	S	≤ 4	S	≤ 4	S
Ciprofloxacin	≥ 4	R	-	-	4	R	4	R
Clarithromycin	0.5	S	-	-	0.5	S	8	R
Imipenem	< 2	S	0.5	S	≤ 2	S	≤ 2	S
Linezolid	< 1	S	-	-	≤ 1	S	2	I
Minocycline	< 1	S	2	I	2	I	≤ 1	S
Trimethoprim/sulfamethoxazole	< 0.25/4.75	S	1/19	S	≤ 0.25	S	≤ 0.25/0.1	S
Tobramycin	< 1	S	-	-	≤ 1	S	≤ 1	S
Doxycycline	< 0.12	S	-	-	4	I	8	R
Moxifloxacin	≥ 8	R	-	-	≤ 0.25	S	1	I

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Author contributions

Lihong Jin and Weiqun Zhang analyzed data and draft articles. Fang Su collected clinical data. Youqi J and Yumei Ge modified the article. All authors reviewed the manuscript.

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Data availability

Data available on request from the corresponding author.

Declarations**Ethics approval and consent to participate**

This study was supported by the Ethics Committee of Zhejiang People's Hospital (Ethics Committee Approval of Biomedical Research Involving Humans, Approval No.: 2022JS008) and was carried out in accordance with the ethical standards of the Declaration of Helsinki.

Consent for publication

Written and informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests

The authors declare no competing interests.

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