

Abdominal Abscesses Caused by *Nocardia farcinica* in an Immunocompromised Patient: A Case Report and Literature Review

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Abstract: Nocardiosis is mainly an opportunistic infection that affects immunosuppressed individuals, with the most common manifestation being the pulmonary infection and cerebral abscesses. Abdominal abscesses caused by *Nocardia* is rare in diabetes patients. Here, we report a rare case of abdominal abscesses caused by *Nocardia farcinica* (*N. farcinica*) in a 56-year-old man with poorly controlled type 2 diabetes and prolonged use of corticosteroids for the treatment of secondary adrenal insufficiency. Abdominal CT suggested abdominal abscesses, and the culture of the abscess puncture fluid identified it as *N. farcinica* by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Treatment with a combination of trimethoprim-sulfamethoxazole (TMP-SMX) and imipenem/cilastatin (IPM/CS), along with surgical drainage and reduction in corticosteroid dosage, achieved successful outcomes in treating disseminated abdominal abscesses. Immunocompromised patients with unexplained fever, abdominal pain, and abdominal abscess should be suspected of *Nocardia* infection.

Keywords: abdominal nocardiosis, *Nocardia farcinica*, abdominal abscesses, diabetes, corticosteroid

Introduction

Nocardia is an aerobic Gram positive actinomycete, commonly considered an opportunistic pathogen. *Nocardia* infections are typically caused by traumatic bacterial invasion or inhalation, with the latter more common in immunocompromised patients, such as those on long-term corticosteroid or HIV/AIDS patients, or organ transplant recipients, and can lead to pulmonary infections.^{1,2} *Nocardia* can also cause infections in various extrapulmonary sites, with extrapulmonary infections typically resulting from hematogenous dissemination from primary lung lesions. The central nervous system (CNS) is the second most frequently involved organ (2–26%),^{2,3} but it can also lead to rare infections in the cornea,⁴ abdomen,⁵ heart,⁶ joints,⁷ and bones.⁸ Clinically, *Nocardia spp.* were proved to differ in virulence. *N. farcinica* is distinct from others *Nocardia spp.* by its high degree of antibiotic resistance and virulence. *N. farcinica* is more prone to cause disseminated infection involving multiple organs, especially the brain abscess.^{5,9} *N. brasiliensis* is the more aggressive than *N. caviae*, and *N. asteroides*.¹⁰ As already reported, the *Nocardia* species were closely correlated with infection sites, *N. farcinica* was more likely isolated in blood cultures (54%) and central nervous system (44.2%), respectively.¹¹ Moreover, *N. brasiliensis* was related predominately to skin and soft tissue infections (72.2%).¹¹ *N. nova* complex, *N. cyriacigeorgica*, and *N. farcinica* were the most common clinical isolates in pulmonary nocardiosis.¹² Difficulty in early diagnosis and delayed treatment of *Nocardia* can result in dissemination and high fatality rates, and the overall prognosis of disseminated nocardiosis patients is unsatisfactory.¹³ Currently, the diagnosis of nocardiosis relies mainly on direct microscopic examination and bacterial culture, although molecular methods have

been shown to be more accurate, sensitive, and specific in identifying *Nocardia* species.¹⁴ In this case report, we describe a rare occurrence of abdominal abscesses caused by *N. farcinica* in a 56-year-old man with poorly controlled type 2 diabetes and prolonged use of corticosteroids for the treatment of secondary adrenal insufficiency.

Case Presentation

A 56-year-old male patient presented to the emergency department of the People's Hospital of Guangxi Zhuang Autonomous Region, China, due to cough, fever and abdominal pain. The patient was diagnosed with abdominal infection and received intravenous injection of ceftriaxone for treatment. After 4 days, his condition was steadily deteriorated and he was admitted to the Department of Gastroenterology at our hospital. The patient had a history of poorly controlled type 2 diabetes and abuse of corticosteroids for the treatment of his reiterative gouty arthritis for 10 years, which resulted in secondary adrenal insufficiency. Currently, he takes prednisone acetate 20mg/d for the treatment of secondary adrenal insufficiency. A month ago, he inhaled air particles that had been contaminated during house renovation activities. The laboratory examination revealed leukocytosis ($28.56 \times 10^9/L$), neutrophil ratio of 90.3%, C-reactive protein of >200 mg/L (normal values 0–5 mg/L), procalcitonin of 1.60 ng/mL (normal values 0–0.05 ng/mL), and poor glycemic control (Glu 8.95mmol/L, HbA1c 11.5%). The patient had recurrent fever with a maximum temperature of 39.1°C and a palpable mass in the lower abdomen. Pulmonary CT showed bilateral pneumonia, tracheal diverticulum, multiple bilateral rib old fractures and a small amount of pericardial effusion (Figure 1A). Abdominal CT indicated irregular nodular or slightly low-density shadows with multiple soft tissue densities in the right renal hilum, right retroperitoneal space, and right pelvic extraperitoneal space, with the largest of those locating in front of the right iliac muscle, measuring about 52mm $\times$ 38mm, suggesting infectious lesions and encapsulated effusion (Figure 1B). Brain CT demonstrated no abnormalities. Treatment included empirical anti-infection, active blood glucose control, oxygen therapy, and fluid replacement. Due to the seriousness of the patient's infection and the uncertainty regarding the presence of multi-drug resistant bacterial infection, imipenem/cilastatin (IPM/CS) was used without determination of a clear infectious etiology. Next day, the patient underwent invasive puncture drainage of the largest abscess located in front of the right iliac muscle under CT-guidance, and punctured milky yellow green pus was sent to microbiological examination. Meanwhile, blood cultures were taken. Gram staining of the puncture fluid showed elongated, branching Gram-positive bacteria, with beaded filamentous structures (Figure 2A), which was suspected actinomycosis. However, the modified acid-fast staining showed acid-fast thin branching bacterium, which highly suspected the presence of *Nocardia* infection (Figure 2B). Small, dry, wrinkled, pale yellow colonies appeared on the blood agar (Figure 2C) and examination of the colonies under a 10x objective lens showed abundant aerial hyphae on agar medium (Figure 2D), which was further identified as *N. farcinica* by MALDI-TOF MS (Bruker, France, reference database version is V10 9607MSPs). The treatment plan was modified to include combination therapy with TMP-SMX (3 pieces every 8 hours, each piece containing 80 mg of trimethoprim and 400mg of sulfamethoxazole) and IPM/CS (1 g, every 8 hours), along with continuous drainage of the abdominal abscesses, and reduction the dosage of glucocorticoids. During

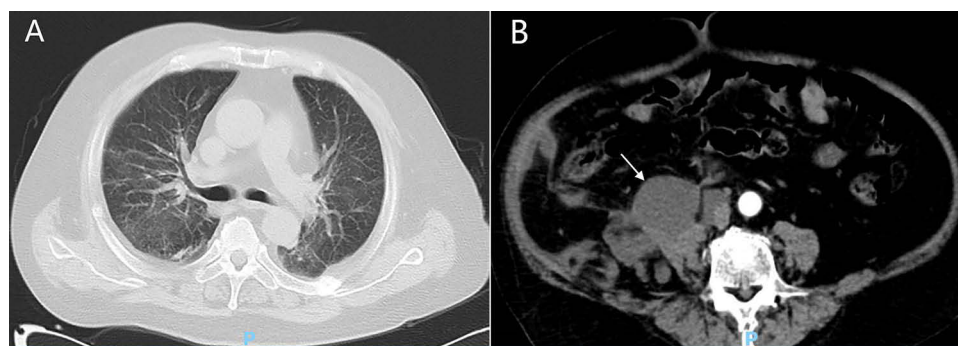


Figure 1 (A) Pulmonary CT showed bilateral pneumonia; (B) Abdominal CT indicated irregular nodular or slightly low-density shadows with multiple soft tissue densities in the right renal hilum, right retroperitoneal space, and right pelvic extraperitoneal space, with the largest of those locating in front of the right iliac muscle (white Arrow), measuring about 52mm $\times$ 38mm, suggesting infectious lesions and encapsulated effusion.

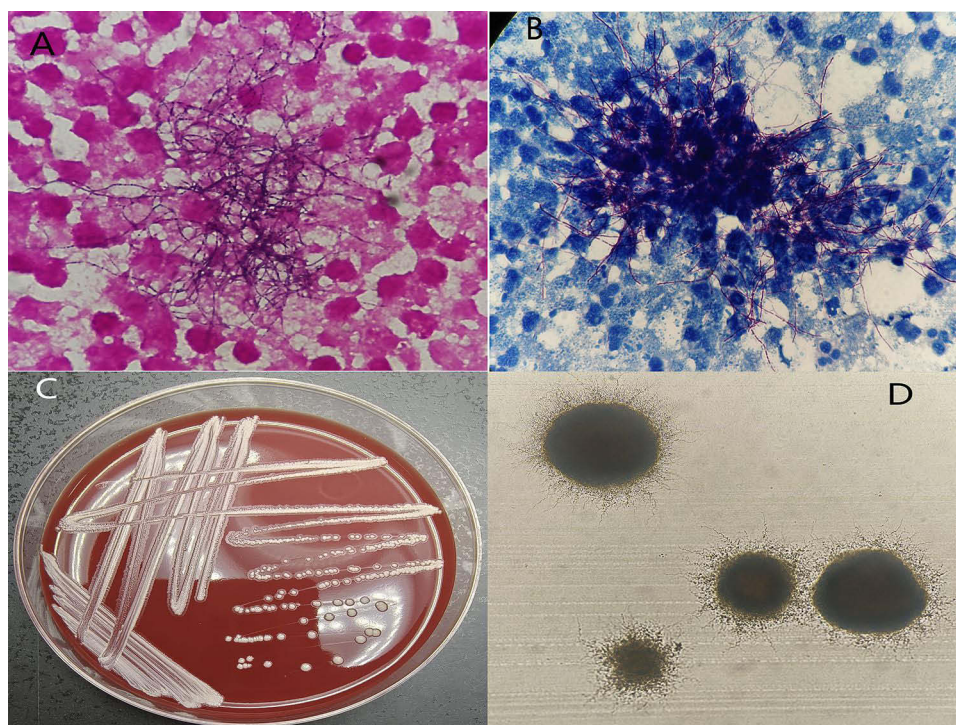


Figure 2 (A) Gram staining of the puncture fluid showed elongated, branching Gram- positive bacteria, with beaded filamentous structures; (B) The modified acid-fast staining showed acid-fast thin branching bacterium; (C) Small, dry, wrinkled pale yellow colonies appeared on the blood agar; (D) Examination of the colonies under a 10x objective lens showed abundant aerial hyphae on agar medium.

hospitalization, no pathogens were found in blood and sputum cultures. After 27 days of treatment, the patient's temperature returned to normal, inflammatory markers significantly decreased (Figure 3A–D), and the abdominal abscesses were notably absorbed (Figure 3E), indicating improvement in the condition and the patient can be discharged. We advised the patient to continue oral TMP-SMX 3 pieces three times a day for 6–12 months.

Discussion and Literature Review

Nocardiosis is a neglected tropical disease and a potentially life-threatening infection that requires timely diagnosis and appropriate treatment due to its significant morbidity and mortality. Invasive *Nocardia* infections primarily affect patients with cellular immunodeficiency (solid organ or hematopoietic stem cell transplant recipients and those receiving corticosteroids or immunosuppressants) because T-cell-mediated immunity and pulmonary macrophages play crucial roles in the local control of *Nocardia*.^{15,16} Corticosteroids inhibit the influx of neutrophils, thereby promoting the spread of *Nocardia*.¹⁷ Diabetes, chronic kidney disease and cirrhosis are generally considered as risk factors for invasive nocardiosis.¹²

Direct microscopic examination and bacterial culture are still the main methods for diagnosing nocardiosis, which rely on close cooperation between clinicians and microbiologists. Gram staining and modified acid-fast staining are helpful for early suspicion of nocardiosis. Gram staining is characterized by elongated, branching Gram- positive bacilli, with beaded filamentous structures, which can also be seen in other actinomycetes, such as *Streptomyces*. However, the modified acid-fast staining showed a positive result, which can distinguish *Nocardia* from *Streptomyces*. *Nocardia* culture grows slowly, and mixed bacterial infections can further mask the identification results, leading to false negatives. Given these difficulties in culture methods, PCR method, MALDI-TOF, and mNGS have become the promising methods for identifying *Nocardia* to the species level. Although the PCR method exhibits high sensitivity and specificity in detecting *Nocardia*, recent studies have shown that PCR detection in respiratory samples may only reflect airway colonization, so positive results should be interpreted with caution.¹⁸ mNGS is a new approach to the identification of difficult and atypical infectious diseases. However, the main drawback of mNGS is the expensive cost, which may be

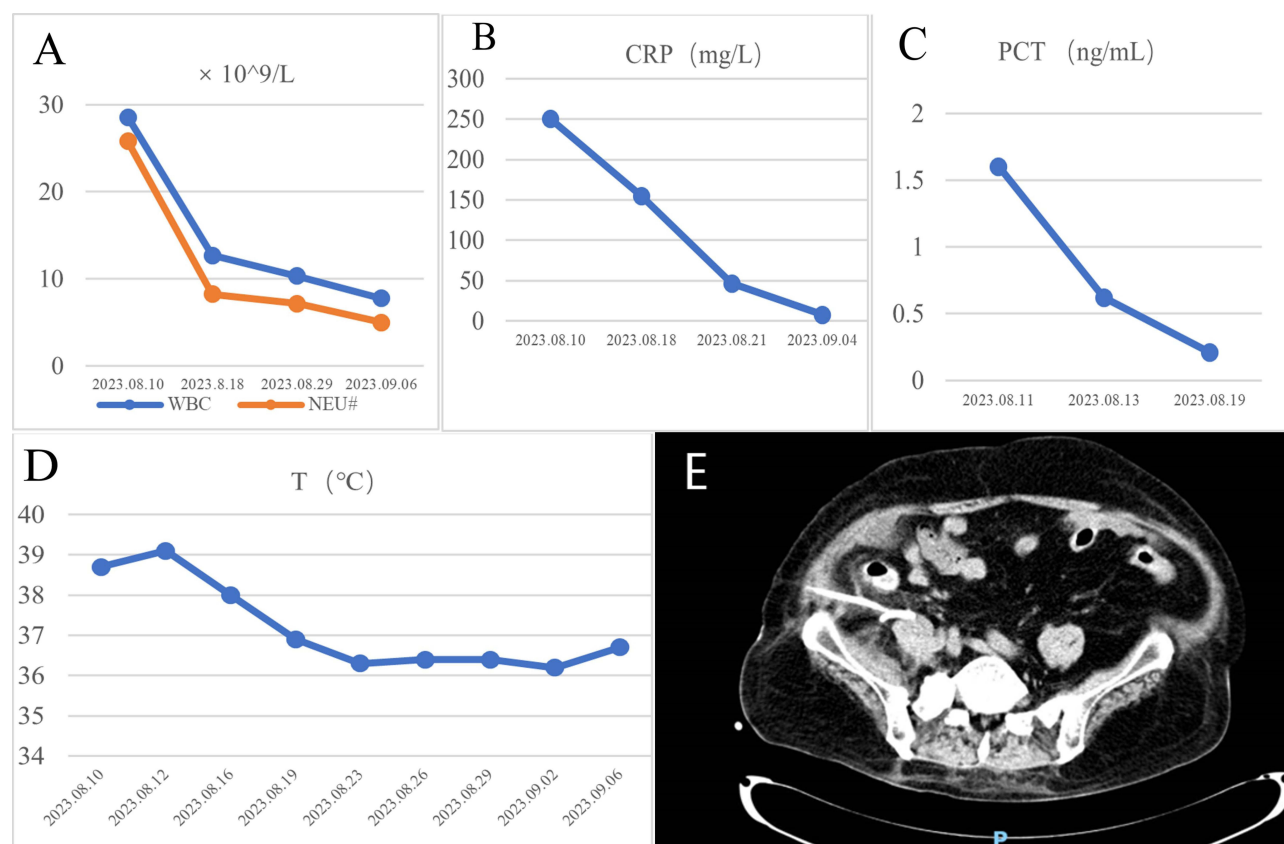


Figure 3 Dynamic changes of laboratory examination. (A) WBC, NEU significantly decreased; (B) CRP significantly decreased; (C) PCT significantly decreased; (D) Temperature returned to normal; (E) Abdominal abscesses has been notably absorbed.

a burden for some patients.¹⁹ In the past ten years, MALDI-TOF has been widely used for the identification of *Nocardia* due to its rapid and cost-efficient. Recent studies using improved databases found that MALDI-TOF MS has shown remarkable accuracy in correctly identifying the species in 100% of cases for *N. farcinica* and between 94% and 100% for *N. cyriacigeorgica*. However, when it comes to other clinically frequent species such as *N. nova* and *N. abscessus*, the ability of MALDI-TOF MS to differentiate between closely related species within their respective complexes is limited.²

We used the Web of Science and PubMed databases to review the existing literature written in English from 2010 to 2023 on abdominal nocardiosis. Search items included “nocardiosis”, “nocardia”, “abdominal”, “retroperitoneal”, “infection”, “abscesses”. There are a total of 21 eligible cases, including 10 cases of disseminated abdominal nocardiosis (Table 1) and 11 cases of isolated abdominal nocardiosis (Table 2). As summarized, the mortality disseminated abdominal nocardiosis significantly was higher than isolated abdominal nocardiosis (60% vs 18.2%). Among these cases, disseminated abdominal nocardiosis was found to invade and usually attack the lungs (9 cases, 90%) and brain (6 cases, 60%). *N. farcinica* (9 cases) represented the most common isolated species. In terms of underlying diseases, solid organ transplant was the most frequent (4 cases), and other underlying diseases included but not limited to use corticosteroids or/and immunosuppressants (4 cases), hematologic malignancy (2 cases), primary nephrotic syndrome (1case), diabetes mellitus (1case) among others.

Abdominal nocardiosis is often misdiagnosed as tuberculosis,^{20,21} or abdominal malignancies.^{22,23} This misidentification can occur due to the similarities in symptoms and imaging findings between these conditions and abdominal nocardiosis. Misdiagnosed can lead to incorrect treatment methods, including anti-tuberculous medications or unnecessary extensive surgeries.^{20,22,23} A published case (Table 2, Case 7) initially suspected primary renal cell carcinoma and underwent a right nephrectomy. However, postoperative biopsy not observed evidence of neoplasia; instead, eventually confirmed a diagnosis of *Nocardia* renal abscess.²² Another published case (Table 2, Case 11) suspected to have a uterine

Table 1 Clinical Characterizations of Disseminated Abdominal Nocardiosis During 2010–2023

Number	Year	Age/sex	Species	Site	Underlying Conditions	Treatment	Outcome
1	2010 ²⁵	66/F	<i>N. farcinica</i>	Brain, blood, lymph nodes, adrenal gland abscess	TNF- α therapy for psoriasis	TMP-SMX, linezolid	Dead
2	2010 ²⁶	61/F	<i>N. nova</i>	Skin, lung, brain, kidney, pancreas	Prednisone use for ulcerative colitis	TMP/SMX	Live
3	2011 ²⁷	42/M	<i>N. concava</i>	Lung, blood, liver	Polychondritis, use prednisone and immunosuppressive drugs	Sulphadiazine, Vancomycin, imipenem, Ciprofloxacin, amikacin	Dead
4	2012 ²⁸	68/F	<i>N. farcinica</i>	Brain abscesses, lung, kidney abscesses	Malnutrition	Cotrimoxazole, Amikacin, imipenem, ciprofloxacin	Dead
5	2014 ²⁹	75/F	<i>N. farcinica</i>	Brain, lung, kidney, pancreas, spleen	Immunocompetent	Meropenem, vancomycin, acyclovir, cefepime	Dead
6	2015 ³⁰	59/F	<i>N. cerradoensis</i>	Brain, skin, blood, lung, Peritoneum, retroperitoneum,	Renal transplant	Meropenem, amikacin, TMP/SMX	Live
7	2016 ³¹	37/M	<i>N. otitidiscaviarum</i>	Subcutaneous soft tissue, lungs, liver	Immunocompetent	Minocycline, TMP-SMZ	Live
8	2016 ³²	58/M	<i>N. nova complex</i>	Lung, blood, small bowel	Large B-cell non-Hodgkin lymphoma	TMP-SMZ, imipenem	Dead
9	2018 ³³	12/M	NR	Peritonitis, lung, kidney and brain abscesses	Immunocompetent	Piperacillin-tazobactam, amikacin	Dead
10	2021 ⁵	66/F	<i>N. farcinica</i>	Lung, brain, right kidney and abdomen	Primary nephrotic syndrome	Meropenem, TMP-SMX	Live

Table 2 Clinical Characterizations of Isolated Abdominal Nocardiosis During 2010–2023

Number	Year	Age/Sex	Species	Site	Underlying Conditions	Treatment	Outcome
1	2010 ³⁴	83/F	<i>N. veterana</i>	Bowel abscess	Colon carcinoma	Surgical drainage, cefazolin, metronidazole, TMP-SMX	Live
2	2012 ²⁸	59/F	<i>N. farcinica</i>	Right adrenal abscess	Ileal lymphoma, hemodialysis	Surgical drainage, Amikacin, cefuroxime, TMP-SMX	Dead
3	2012 ³⁵	54/F	NR	Colon	Immunocompetent	Surgical resection	Live
4	2013 ³⁶	30/F	NR	Adnexal collection	Immunocompetent	Amikacin, TMP-SMX	Live
5	2016 ³⁷	59/M	<i>N. farcinica</i>	Liver abscess	Post liver transplantation	Surgical drainage, TMP-SMX, amikacin, imipenem	Live
6	2016 ³⁸	58/F	<i>N. farcinica</i>	Blood, abdominal fluid	Crohn disease, (TNF- α) antagonist,	IPM/CS, amikacin, Bactrim	Live
7	2018 ²²	63/F	<i>N. paucivorans</i>	Renal abscess	Diabetes mellitus, post lung transplant	Surgical resection, imipenem, TMP-SMX	Live
8	2019 ²⁰	63/M	<i>N. farcinica</i>	Liver	Immunocompetent	Amikacin, TMP-SMX	Dead
9	2019 ³⁹	11/F	<i>N. farcinica</i>	Abdominal abscesses	Post renal transplant	TMP-SMX, meropenem, IPM/CS, linezolid	Live

(Continued)

Table 2 (Continued).

Number	Year	Age/ Sex	Species	Site	Underlying Conditions	Treatment	Outcome
10	2020 ⁴⁰	81/M	<i>N. paucivorans</i>	Retroperitoneal abscess	Large B-cell lymphoma	Surgical drainage, TMP-SMX, amikacin, ceftriaxone, minocycline	Live
11	2022 ²³	66/F	NR	Uterus, ureter, colon	Immunocompetent	Surgical resection, imipenem, doxycycline	Live

Abbreviation: NR, not reported.

tumor and invaded the ureter and colon and performed hysterectomy, bilateral adnexectomy, colectomy, and partial left ureter resection. The final pathology showed Xanthogranulomatous inflammation caused by *Nocardia*.²³

Surgical debridement and drainage are crucial for the prognosis of abscess caused by *Nocardia*, as aspiration or resection can control the source. Some patients with abscesses may require repeated aspiration or resection, due to abscess may reduce the permeability of antibiotics.²⁴ In terms of isolated abdominal nocardiosis, 7 cases (63.6%) emphasized the role of surgical resection and drainage in promoting prognosis.

In vitro drug sensitivity testing of *Nocardia* can be used to guide antibacterial therapy, but there are some technical difficulties in vitro drug sensitivity testing, including method selection, bacterial suspension preparation, as well as the reading and interpretation of results. Therefore, microbiological laboratories do not routinely conduct in vitro drug sensitivity tests, and most of them rely on empirical anti-infection treatment. Due to the specific antibiotic sensitivity patterns associated with each species of *Nocardia*, it is crucial for clinical microbiology laboratories to provide reliable species identification to guide the selection of initial antimicrobial therapy. The most significant difference between *Nocardia* species is their different susceptibility to β -lactam antibiotics. It is worth noting that if species identification or antibiotic sensitivity testing cannot be conducted, β -lactam antibiotics should not be used as a single therapy for initial antibiotic treatment. A study on the distribution of *Nocardia* species and drug resistance in China showed that TMP-SMX was the most active drug against *Nocardia* isolated in China, and it could be used as the primary drug for treating *Nocardia* infections even without species identification or antibiotic susceptibility testing.⁴¹ Linezolid and amikacin are also effective drugs against most *Nocardia* species, with activity of 99.5% and 96.0%, respectively.⁴¹ Imipenem has varying sensitivity to various species of *Nocardia*, with a good sensitivity rate of 90.1% to *N. cyriacigeorgica*, while it showed a relatively low sensitivity rate to *N. farcinica* (45.5%).⁴¹ For immunocompetent patients, a 6-month course of antibacterial treatment is generally recommended, whereas immunosuppressed patients or those with disseminated CNS lesions typically require at least 6–12 months of treatment.⁵ The continuous presence or recurrence of *Nocardia* infection is often attributed to the use of insensitive antibiotics or inadequate treatment.

Conclusion

Poorly controlled diabetes and prolonged use of corticosteroids are the risk factors for disseminated abdominal abscesses in this patient. Antibiotic therapy, combination with surgical interventions and a gradual dosage reduction of glucocorticoids contribute to the management of *N. farcinica* disseminated abdominal abscesses.

Abbreviations

MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; TMP-SMX, trimethoprim-sulfamethoxazole. IPM/CS, imipenem/cilastatin; CNS, central nervous system.

Data Sharing Statement

All the data are fully available without restriction.

Ethics Approval and Patient Consent

Written informed consent was obtained from the patient for the publication of the case details. The study was approved by the medical ethics committee of The People's Hospital of Guangxi Zhuang Autonomous Region.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflict of interest in this work.

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