# Multiple nocardial abscesses secondary to anti-neutrophil cytoplasmic antibody-associated vasculitis in an elderly patient: A case report and literature review

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**Abstract.** A nocardial abscess is a relatively rare opportunistic infection that typically occurs after immunosuppressive treatment and is a clinical challenge. In the present study, the case of a 69-year-old patient with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, and lung and kidney involvement, was reported. The patient received systemic glucocorticoid and cyclophosphamide treatment for 6 months, after which a large encapsulated abscess appeared on magnetic resonance imaging and CT in the subcutaneous tissue of the left hip and lung, respectively, and the pus culture showed *Nocardia*. Orthopedic abscess incision and ultrasound-guided thoracic puncture drainage were performed, and the lesion was completely absorbed after 1 month of treatment with linezolid and compound sulfamethoxazole. Tests for ANCA were negative, and renal function and urine tests were completely normal after 1 year of follow-up. Furthermore, a literature review performed for the present study retrieved a few reports of successful treatment of multiple nocardial abscesses secondary to ANCA-associated vasculitis in elderly patients in a short period of time. Therefore, the present case report and literature review have been reported to improve awareness of this rare disease, so as to facilitate its early diagnosis and treatment.

## Introduction

Nocardiosis is a rare but severe suppurative infection, most commonly seen in susceptible patients with underlying chronic diseases, such as those undergoing tumor chemotherapy, those suffering from alcoholism, or those with endogenous or iatrogenic immunosuppression (1,2). It has been reported that patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis become infected with *Nocardia* after immunosuppressive therapy, with high mortality rates due to ineffective treatment (3-5). For such patients, it was necessary to control the target organ damage caused by the primary vasculitis, as well as to actively treat the opportunistic nocardial abscesses, which makes the clinical treatment very challenging. In the present study, the case of an elderly patient presenting with typical multiple large nocardial abscesses with ANCA-associated vasculitis and renal insufficiency, who was treated with glucocorticoid and cyclophosphamide, is reported. After medical and surgical therapy, the abscesses were completely absorbed, the patient became negative for ANCA and renal function was completely recovered after 1 year of follow-up. In addition, the present study reviews the literature with regard to the age, clinical characteristics, specific treatment options and treatment outcomes of patients with this rare infection caused by nephropathy and immunosuppressive therapy, in order to improve the outcome of this life-threatening infection.

## Case report

A 69-year-old male patient was admitted to the Department of Geriatrics of the Affiliated Hospital of Nantong University (Nantong, China) in September 2020 due to recurrent lower abdominal pain for 1 month. On admission, the patient presented with persistent dull pain in the lower abdomen accompanied by poor appetite and fatigue, without any other complaints of discomfort. The patient was previously healthy. Physical examination showed that temperature, pulse, respiration and blood pressure were normal. Emaciation and anemia were also observed. The breath sounds from both lungs were coarse, but no rales were detected. The whole abdomen was soft, with mild tenderness around the umbilicus and lower abdomen, without rebound pain and muscle tension, and with mild edema in the bilateral lower extremities. Cardiovascular and nervous systems were normal. Blood test results after admission showed the following results: Hemoglobin, 77 g/l (normal range, 120-160 g/l); serum albumin, 28 g/l (normal range, 35-55 g/l); serum creatinine, 242 $\mu$mol/l (normal range, 64-104 $\mu$mol/l); erythrocyte sedimentation rate, 108 mm/h (normal range, 0-10 mm/h); C-reactive protein (CRP), 105 mg/l (normal range, 0-8 mg/l); and 24-h urine

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protein, 1.38 g/day (normal range, 0-0.15 g/day). Chest CT showed interstitial inflammation in the bilateral inferior lungs (Fig. 1A). The titer of myeloperoxidase-anti-neutrophil cytoplasmic antibody (MPO-ANCA) was 1,573 AU/ml (normal range, <100 AU/ml) using the AtheNA Multi-Lyte® Autoimmune Vasculitis Plus Test System (cat. no. 22020054; Zeus Scientific, Inc.). Thereafter, the patient was transferred to the Department of Nephrology. The patient refused a renal biopsy, and the diagnosis was ANCA-associated vasculitis, renal insufficiency, interstitial pneumonia and moderate anemia. After 5 days of an intravenous infusion of 40 mg methylprednisolone, the treatment was changed to oral prednisone acetate (15 mg three times a day), and 0.6 g cyclophosphamide (CTX) was intravenously administered once. The patient was discharged at 16 days post-admission, and instead was prescribed oral prednisone and monthly intravenous CTX medication, and the dose of corticosteroid was gradually tapered. After 6 months of treatment, the dosage of prednisone acetate was tapered to 25 mg once a day, and the total CTX dosage in 7 months was 4.2 g.

In April 2021, the patient developed swelling and pain in the left hip. After 6 days, the patient was readmitted to the Affiliated Hospital of Nantong University. The vital signs of the patient were stable and normal, but there was a 15x10-cm mass on the left hip. The local skin temperature was increased, with tenderness and swelling, but there was no obvious redness. There was moderate edema in the bilateral lower extremities. A routine blood test showed the following results: White blood cell count, $8.0x10^9$/l ($4.0\text{-}10.0x10^9$/l); neutrophils, 79.8% (40-75%); hemoglobin, 82 g/l; urine protein, negative; plasma albumin, 28.8 g/l; serum creatinine, 76 $\mu$mol/l; MPO, negative; and serum hypersensitive CRP, 27.5 mg/l. Serum markers of HIV, syphilis and hepatitis were negative. The tuberculin test was also negative. A chest CT scan revealed new left encapsulated pleural effusion and new anterior mediastinal nodules (Fig. 1B). Magnetic resonance imaging (MRI) of the left femur indicated encapsulated fluid signals in the proximal subcutaneous part of the left thigh. The mass measured 132x77x44 mm, with internal separation, peripheral soft-tissue swelling and edema, and was considered to be an infectious lesion accompanied by abscess formation (Fig. 2A). After admission, moxifloxacin sodium chloride (0.4 g/day) was intravenously administered for anti-infection purposes, while the dose of oral prednisone acetate was reduced to 10 mg per day and CTX treatment was discontinued. The patient initially refused surgery and asked for conservative treatment. Therefore, under the guidance of ultrasound, 30 ml was extracted from the subcutaneous abscess at the lateral edge of the left thigh, and the puncture pus was collected for bacterial culture and drug sensitivity testing. A metronidazole sodium chloride injection (5 mg/ml) was applied locally for repeated washing. In addition, 10 g of human albumin was intravenously provided on a daily basis as supportive care. After 5 days of treatment, the mass of the left hip did not improve, the discomfort worsened and the patient agreed to surgical intervention. A local subcutaneous abscess incision and aspiration were performed after orthopedic consultation. During the operation, subcutaneous tissue necrosis and a large amount of pus were observed and removed. Furthermore, closed negative pressure drainage was performed on the wound surface after surgery. Weak acid-fast staining (Fig. 2B) and Gram-positive staining (Fig. 2C) (performed at room temperature for ~20 min) of the aspirated pus showed filamentous *Nocardia* using a light microscope (Olympus Corporation). Accordingly, the antibiotic was adjusted to linezolid glucose injection, 0.6 g by intravenous drip, twice a day. After 12 days, a repeated chest CT scan revealed a small amount of bilateral pleural effusion, and the left region was encapsulated slightly more than before. The anterior mediastinal nodules were similar to 12 days ago (Fig. 1C). The adjustment of the antibiotic to linezolid glucose injection was not observed to be associated with increased pleural effusion of polyserositis. Based on these results, ultrasound-guided puncture and drainage was performed in the left pleural cavity, which extracted 15 ml of pus, and then a metronidazole sodium chloride injection (5 mg/ml) was applied locally for repeated washing. At 2 days after the drainage procedure (April 2021), the patient insisted on being discharged from the hospital due to financial reasons. After discharge, the patient was provided with linezolid tablets (0.6 g orally, every 12 h) and compound trimethoprim-sulfamethoxazole (TMP-SMX) tablets (0.48 g orally, twice a day) for continuous anti-bacterial treatment, as well as prednisone (10 mg daily) orally for maintenance therapy. Subsequent outpatient review of renal function showed a creatinine level of 120 $\mu$mol/l, while there was a negative result for MPO and a repeated chest CT scan indicated that the lung abscess had completely disappeared 11 days after discharge (Fig. 1D). No MRI was performed after discharge due to financial reasons. Thereafter, all antibiotics were discontinued, and prednisone was discontinued after 6 months. The condition

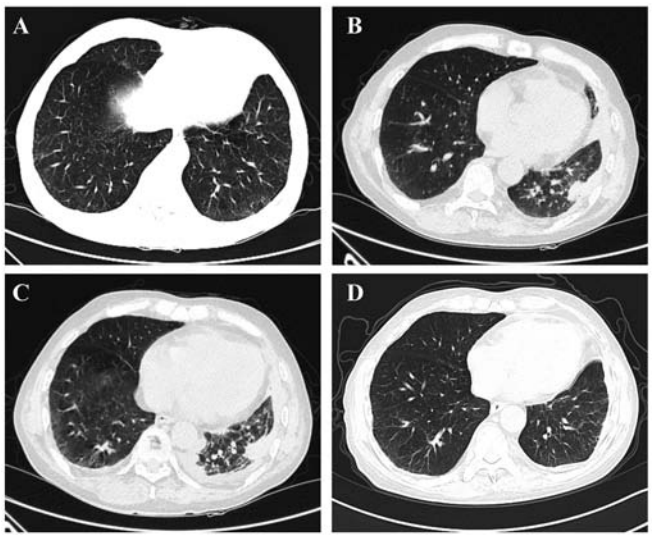


Figure 1. *Nocardia* infection and chest CT scan results before and after treatment. (A) In September 2020, when the patient was initially diagnosed with anti-neutrophil cytoplasmic antibody-related vasculitis, the chest CT scan showed interstitial inflammation in both inferior lungs. (B) In April 2021, the patient developed pain in the left hip, and a plain chest CT scan on the first day of admission indicated a new left encapsulated pleural effusion. (C) At 12 days after admission, during the hospitalization for the diagnosis and treatment of *Nocardia* infection, a repeat plain chest CT scan indicated a small amount of bilateral pleural effusion, and the left region was encapsulated slightly more than before. (D) In May 2021, 11 days after the patient was discharged, a repeat plain chest CT scan indicated that the left encapsulated pleural effusion had completely disappeared.

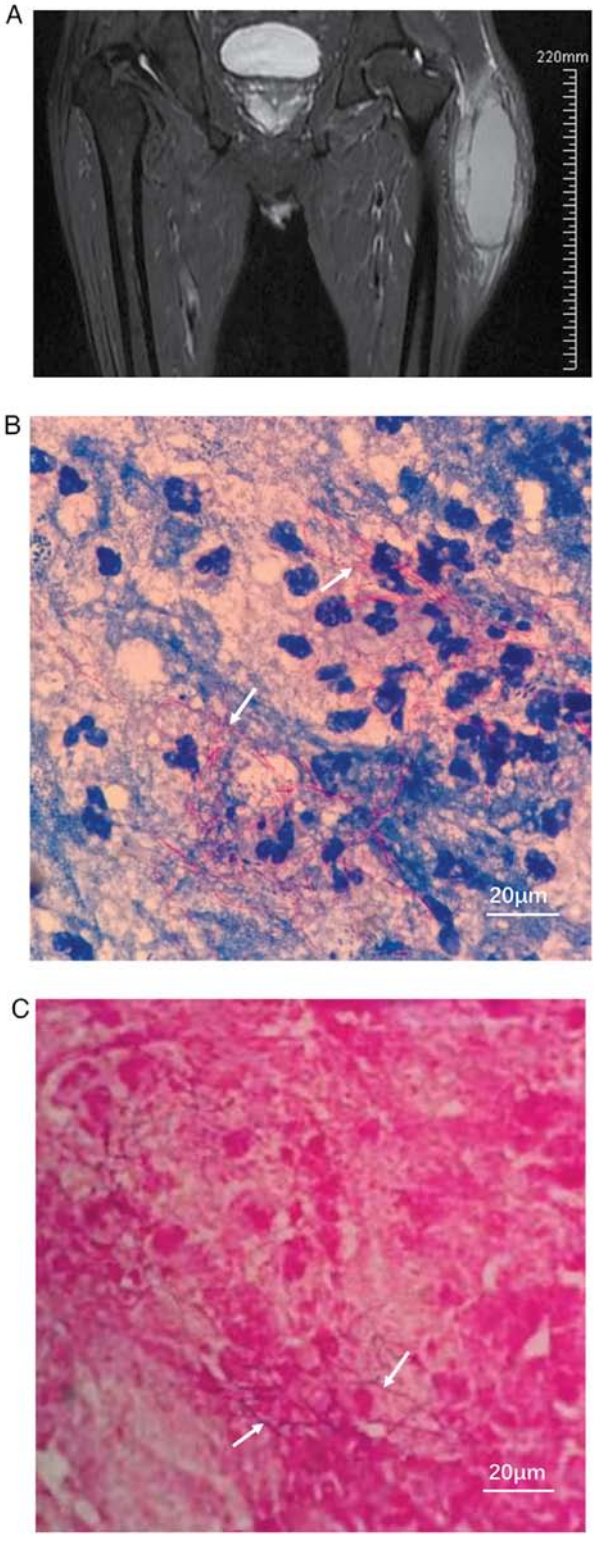


Figure 2. Results of the left femur. (A) Coronal MRI scan of the left femur showed encapsulated fluid under the skin of the proximal segment of the left thigh, and the surrounding soft tissue was swollen, with edema. (B) Weak acid-fast staining of the aspirated pus showed filamentous *Nocardia* (arrows) using a light microscope (magnification, x1,000). (C) Gram-positive staining of the pus also showed filamentous *Nocardia* (arrows) using a light microscope (magnification, x1,000).

of the patient was stable during the 1 year of follow-up after discharge, with MPO results remaining negative and renal function still normal (serum creatinine, 87 $\mu$mol/l) (Fig. 3).

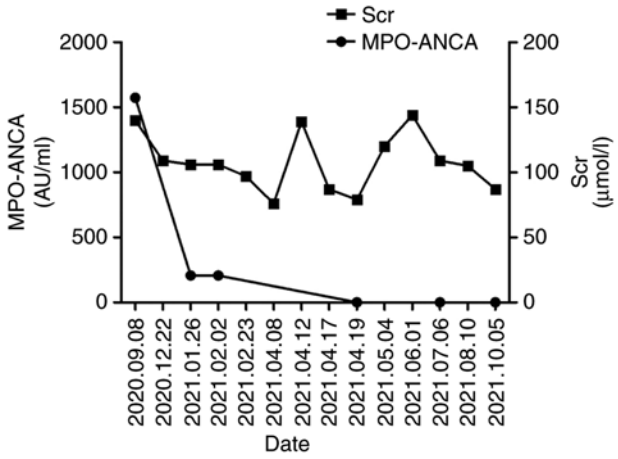


Figure 3. Changes in the serum creatinine and MPO-ANCA titer levels. After the diagnosis of nocardiosis infection was made, the patient's serum creatinine level showed dynamic changes and no relapse of ANCA-associated vasculitis occurred. MPO-ANCA, myeloperoxidase-anti-neutrophil cytoplasmic antibody; TMP-SMX, trimethoprim-sulfamethoxazole; Scr, serum creatinine.

The patient will have a good prognosis and will be followed up for the next 2 years.

## Discussion

*Nocardia* is an aerobic gram-positive bacterium, belonging to Mycobacteriaceae family, which can infect humans through skin trauma or respiratory inhalation (6). In different types of immunosuppressed populations, the overall incidence of Nocardiosis has been reported as ≤3.6%, while the associated mortality is as high as 77% (7-9). To the best of our knowledge, very few cases of *Nocardia* infection in elderly patients with ANCA-associated vasculitis have been reported as successfully treated in a short period of time (3-5). The most common site of *Nocardia* infection is the lung, followed by the skin and the brain (10). *Nocardia* infection is usually seen in susceptible patients with chronic diseases, or endogenous or iatrogenic immunosuppression (11). In a review of the literature, 15 published cases of *Nocardia* infection worldwide from the last two decades in patients with underlying renal diseases, such as systemic lupus erythematosus, membranous proliferative glomerulonephritis, nephrotic syndrome or kidney transplantation, were found (3-5,12-23; Table I). Among them, 3 cases were ANCA-associated vasculitis, and only 1 case was reported in China, but 1 case in Japan was successfully treated. The current study is the first case of successful treatment of *Nocardia* secondary infection with linezolid in an elderly patient with ANCA-associated vasculitis in China. In the present case, the patient was an immunosuppressed elderly male who received glucocorticoid therapy for ANCA-associated vasculitis. Renal insufficiency might also impair normal immune function (24). The risk of *Nocardia* infection may therefore be higher in older patients with renal insufficiency who are receiving immunosuppressive therapy. The reported patient had the three of the aforementioned risk factors for *Nocardia* infection. The lungs and skin were simultaneously involved, and the condition manifested as

Table I. Reported cases of *Nocardia* infection with underlying renal disease and receiving immunosuppressive therapy.

| First author, year | Country | Age, years | Sex | Type of kidney disease | Clinical syndrome | Immunosuppressive agents | Treatment | Outcome | (Refs.) |
|---|---|---|---|---|---|---|---|---|---|
| McNab *et al*, 2000 | Chile | 24 | F | Lupus nephritis | Pleuropneumonia and occipital abscess | Cyclophosphamide and prednisone | Cotrimoxazole and cefixime | Deceased | (12) |
| Lee *et al*, 2002 | South Korea | 37 | F | Lupus nephritis | Pleural effusion | Methylprednisolone and cyclophosphamide | TMP-SMX | Cured | (13) |
| Pottumarthy *et al*, 2003 | USA | 43 | F | SLE | Pulmonary infection | Cyclosporine and prednisone | TMP-SMX | Cured | (14) |
| Sonesson *et al*, 2004 | Sweden | 60 | M | ANCA-associated vasculitis | Pulmonary infection and brain abscess | Methylprednisolone and cyclophosphamide | Meropenem | Deceased | (3) |
| Elmaci *et al*, 2007 | Turkey | 49 | M | Nephrotic syndrome | Mass lesion in the left lower extremity and brain abscess | Prednisone and cyclophosphamide | TMP-SMX | Cured | (15) |
| Tilak *et al*, 2012 | India | 50 | M | Renal transplant | Brain abscess | Cyclosporine, azathioprine and prednisolone | TMP-SMX | Cured | (16) |
| Lee *et al*, 2012 | South Korea | 64 | M | Membranous glomerulopathy | Pulmonary infections and mass in the right upper arm | Prednisolone | TMP-SMX | Cured | (17) |
| Ates *et al*, 2013 | Turkey | 40 | F | Lupus nephritis | Subcutaneous and brain abscesses | Azathioprine and prednisolone | TMP-SMX and ceftriaxone | Cured | (18) |
| Patel *et al*, 2013 | India | 50 | M | Renal transplant | Pulmonary infection | Prednisolone, MMF and cyclosporine | Ceftriaxone and minocycline | Cured | (19) |
| Weerakkody *et al*, 2015 | Sri Lanka | 38 | M | Renal transplant | Brain abscess | Tacrolimus and MMF | Imipenem and levofloxacin | Cured | (20) |
| Grahammer and Fischer, 2015 | Germany | 71 | M | Membranous glomerulonephritis | Pulmonary and i ntramuscular abscesses | Prednisone and MMF | Imipenem, levofloxacin TMP-SMX and linezolid | Cured | (21) |
| Poisnel *et al*, 2015 | France | 51 | M | Peritoneal dialysis | Pulmonary and urinary tract infections | Methylprednisolone | TMP-SMX | Deceased | (22) |
| Hirayama *et al*, 2016 | Japan | 68 | M | ANCA-associated vasculitis | Pulmonary infection | Cyclophosphamide and prednisolone | TMP-SMX | Cured | (4) |
| Zhu *et al*, 2017 | China | 60 | M | Nephrotic syndrome | Pulmonary and cutaneous infections | Cyclophosphamide and methylprednisolone | TMP-SMX and ceftriaxone | Cured | (23) |

Table I. Continued.

| First author, year | Country | Age, years | Sex | Type of kidney disease | Clinical syndrome | Immunosuppressive agents | Treatment | Outcome | (Refs.) |
|---|---|---|---|---|---|---|---|---|---|
| Wang *et al*, 2019 | China | 53 | F | ANCA-associated renal vasculitis | Brain abscess | Methylprednisolone | Meropenem + voriconazole → piperacillin sodium/tazobactam → sodium + voriconazole cefoperazone/ sulbactam + micafungin | Deceased | (5) |
| Present study | China | 69 | M | ANCA-associated vasculitis | Pulmonary and intramuscular abscesses | Cyclophosphamide and prednisone | Linezolid and TMP-SMX | Cured | - |

TMP-SMX, trimethoprim-sulfamethoxazole; SLE, systemic lupus erythematosus; MMF, mycophenolate mofetil; ANCA, anti-neutrophil cytoplasmic antibody; M, male; F, female; →, therapy updated.

multiple sites of suppurative necrosis and abscess formation, which are typical characteristics of nocardiosis. However, clinical recovery was finally achieved after comprehensive treatment.

Linezolid is a synthetic antibacterial agent of the novel antibiotic oxazolidinone, which is active against most Gram-positive bacteria (25). Linezolid has been reported as a novel second-line drug for *Nocardia* infection, and is generally well tolerated (26). In the present case, the patient was clinically cured after receiving linezolid treatment for 2 weeks, and no serious adverse drug reactions, such as hematological side effects, lactic acidosis or peripheral neuropathy, were observed, possibly due to the short-term nature of the treatment. Despite the development of various new drugs, including linezolid, in recent decades, sulfonamides remain the first-line therapy against *Nocardia* infection (27,28), the most representative drug being TMP-SMX; however, drug-resistance has increased over time (29). In the present case, the renal function of the patient was impaired at the time of admission. After treatment of the primary disease with immunosuppressants, and anti-infection treatment with linezolid during hospitalization, the renal function of the patient returned to normal. A therapeutic dose (0.48 g, twice a day) of oral TMP-SMX was added after discharge. During the follow-up, renal function fluctuated in a short period of time, but returned to normal after the TMP-SMX was discontinued. During a year of follow-up, the laboratory test results of the patient were normal.

The present typical case and the related published literature indicate that rare opportunistic infections are not entirely uncommon in immunocompromised patients. Clinicians should be aware of possible *Nocardia* infection and its tendency to spread when patients present with clinical manifestations of systemic dissemination or locally encapsulated effusion (pus). An early diagnosis of *Nocardia* infection, and the precise and rational use of sensitive antibiotics can significantly improve the prognosis of this high mortality-associated infection.

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**Availability of data and materials**

All data generated and/or analyzed during this study are included in this published article.

**Authors' contributions**

XC and YZ contributed to the conceptualization and design of the study, the collection of clinical information and the drafting of the manuscript. YF analyzed medical images (MRI and CT scans) and patient data, and advised on patient treatment. YF and YZ contributed to critical revisions of

the intellectual content and confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

**Ethics approval and consent to participate**

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Affiliated Hospital of Nantong University (Nantong, China; approval no. #2020-K029).

**Patient consent for publication**

Written informed consent was obtained from the patient for the publication of the data and images included in the present case report.

**Competing interests**

The authors declare that they have no competing interests.

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