A fatal case of disseminated nocardiosis due to *Nocardia otitidiscaviarum* resistant to trimethoprim–sulfamethoxazole: case report and literature review

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**Abstract**

**Background:** Disseminated nocardiosis still causes significant morbidity and mortality and is often caused by *Nocardia asteroides*, *N. basiliensis*, and *N. farcinica* and are often treated with trimethoprim–sulfamethoxazole (TMP–SMX). *Nocardia otitidiscaviarum* (*N. otitidiscaviarum*) rarely causes disseminated disease and resistance to TMP–SMX is even more rare.

**Case presentation:** A 37-year-old woman with metastatic breast cancer and right ear deafness with recent occupational gardening and manipulating soil, presented to the hospital with first time seizure and multiple skin nodules. Magnetic resonance imaging (MRI) showed ring enhancing lesions, biopsy of the skin and brain lesions grew *N. otitidiscaviarum*. She was empirically treated with TMP–SMX and Imipenem–Cilastatin, however, almost three weeks into therapy, susceptibility results revealed it to be resistant to both antimicrobials, she was subsequently changed to Amikacin, Linezolid, Moxifloxacin, and Doxycycline but ultimately died.

**Conclusions:** This case report highlights the importance of suspecting a rare *Nocardia* species in patients at risk with proper occupational exposure, moreover, TMP–SMX resistance should be suspected with lack of clinical response, this may have important implications on clinical practice when facing similar infections.

**Keywords:** Nocardiosis, *Nocardia otitidiscaviarum*, Trimethoprim–sulfamethoxazole (TMP–SMX)

**Background**

Disseminated nocardiosis is a rare disease that can be fatal and is often attributed to the three more commonly known species: *Nocardia asteroides*, *N. basiliensis*, and *N. farcinica* [1]. *N. otitidiscaviarum* was first isolated from the mid-ear of a guinea pig and hence its name, it was then isolated from humans as well [2, 3].

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preceding one month she had noticed multiple nodules under her skin on the right leg, and over her abdomen. They were mildly painful, eventually the overlying skin developed dark discoloration. There was no drainage, and she did not have similar skin lesions in the past. She is a known case of stage 4 invasive ductal carcinoma of the breast with metastasis to the liver, bone, and lungs that was diagnosed two years prior to the current presentation. She was recently on carboplatin/paclitaxel for a total of 8 weeks with the last dose given 3 weeks prior to this presentation. She has not been on corticosteroids in the preceding three months. Furthermore, over the past months prior to her current illness, she had been caring for domestic canaries and gardening frequently without the use of personal protective equipment nor gloves, reporting handling dirt and soil with her bare hands with frequent touching of her face.

On arrival the patient's vital signs were normal (Table 1), and her neurological examination was unremarkable. There were multiple nodules in the extensor area of the right leg and on the surface of her abdomen measuring 1 × 1 cm in size, they were firm, non-mobile with an erythematous base and overlying dark discoloration, they were mildly tender without any drainage (Fig. 1).

Blood results revealed elevated erythrocyte sedimentation rate (Table 1).

Computed tomography (CT) of the chest showed right lower lobe consolidation with cavity containing air-fluid level, with bibasilar atelectatic bands (Fig. 2).

CT brain showed left parietal–temporal hypodensities. Cerebrospinal fluid (CSF) analysis showed no signs of inflammation and microbiological evaluation including Mycobacterium tuberculosis PCR did not reveal any pathogen. Magnetic resonance imaging (MRI) of the Brain showed multiple ring enhancing lesions in the left frontoparietal region, bilateral frontal regions,

![Fig. 1 Nodular skin lesion overlying patient's abdomen (left) and leg (right)](image)

| Laboratory variable                  | Measurements | Normal value   | Clinical variable       | Measurements |
|--------------------------------------|--------------|----------------|-------------------------|--------------|
| WBC                                  | 9 × 10⁹/L    | 3.5–12.0 × 10⁹/L| Glasgow coma scale      | 15/15        |
| Haemoglobin                          | 125 g/L      | 120–160 g/L    | Temperature             | 37 °C        |
| Haemaocrit %                         | 38%          | 37–47%         | Blood pressure          | 110/64 mmHg  |
| Platelets                            | 144 × 10⁹/L  | 140–450 × 10⁹/L| Respiratory rate        | 20 Breaths/minute |
| International normalized ratio (INR) | 0.93 s       | 0.8–1.3 s      | Heart rate              | 88 Beats/minute |
| Erythrocyte sedimentation rate (ESR) | 120 mm/h     | 0–29 mm/h      | Oxygen saturation       | 99%          |
| C-reactive protein                   | 2.9 mg/L     | < 10 mg/L      |                         |              |
| Creatinine                           | 55 µmol/L    | 53–115 µmol/L  |                         |              |
right parietal lobe and vermis, while T2 weighted image showed cortical and subcortical cystic lesions (Fig. 3).

A left parietal mini-craniotomy was performed and frank pus was drained with necrotic tissue. The histopathology showed no evidence for malignancy (metastasis) but histological features consistent with brain abscess and no granulomas. A modified Kinyoun stain showed branching bacilli (Fig. 4). The skin lesion punch biopsy modified Kinyoun stain showed similar result.

Tissue samples from the patient’s brain and skin lesions were cultured onto different media including sheep blood agar, chocolate agar, MacConkey agar and Sabouraud Dextrose Agar (Saudi Prepared Media Laboratory Company Ltd, Riyadh, Saudi Arabia). Initial growth was observed from both samples after 2 days of incubation on blood, chocolate and Sabouraud agars. There was only one colony type observed, the isolate was found to be catalase positive, the colony Gram showed beaded branching Gram-positive bacilli, acid fast stain was negative, and modified Kinyoun stain was positive. The organism was identified using Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) (bioMerieux, Marcy-l’Etoile, France) with 99.9% confidence value as Nocardia otitidiscaviarum. This was done through an extraction process using the Vitek MS Mycobacterium/Nocardia kit (bioMerieux, Marcy-l’Etoile, France). Susceptibility testing was referred out and performed using the Sensititre™ RAPMYCOI panel (Thermo Fisher Scientific, Massachusetts, United States) and interpreted using Clinical and Laboratory Standards Institute interpretive breakpoints (CLSI M24: Clinical and Laboratory Standards Institute standard M24—Susceptibility Testing of Mycobacteria, Nocardia spp., and Other Aerobic Actinomycetes).

Upon presentation she was started on Imipenem-Cilastatin 500 mg IV every 6 h and trimethoprim–sulfamethoxazole (TMP–SMX) 15 mg/kg/day of TMP component IV divided every 8 h, on day 14 of hospital stay she developed a new skin lesion in the abdomen, Amikacin 30/kg/day IV was added. On day 22 of hospital stay, the susceptibility results returned from the outside referred lab showing TMP-SMX and Imipenem resistance (Table 2).

**Discussion and conclusion**

In this report, we describe a rare fatal case of disseminated nocardiosis due to *N. otitidiscaviarum* resistant to TMP–SMX in a lady with advanced cancer.

The most common clinical presentation of nocardial disease is pulmonary due to inhalation of mycelial fragments or via contact with the bacteria by a cut or abraded skin which may lead to extrapulmonary dissemination [1]. In our case, the patient’s risk factor was gardening.

*N. otitidiscaviarum*, formerly called *N. caviae*, was first reported in humans in the mid-1960s [2]. It was previously reported in 1924 after the organism was isolated from a guinea pigs middle ear [3]. Infections with *Nocardia* are being increasingly recognized, however, infections due to *N. otitidiscaviarum* are reported in only 0.3–2.9% of all *Nocardia* infections and remains infrequently reported [4]. In one review only 10 cases of 347 patients infected with *Nocardia* in the United States were identified as *N. otitidiscaviarum* [5]. In a Japanese...
report of more than 303 pathogenic *Nocardia* isolated from infected patients between 1992 and 2001, only 14 cases were due to *N. otitidiscaviarum* [6]. More recently, Chen Liu et al. described a fatal case of severe pneumonia due to *N. otitidiscaviarum* in an immunocompetent cotton farmer [7], while Ranjit Sah et al. reported successful treatment of a patient under steroid therapy with disseminated *N. otitidiscaviarum* [8]. Moreover, it was reported to cause disease in both immunocompetent and immunocompromised hosts in the forms of pulmonary, cutaneous, central nervous system and lymphocutaneous infections [4].

In nature, *N. otitidiscaviarum* is found in soil, decomposing vegetation, and other organic matter, as well as in fresh and saltwater [9]. A survey of 504 soil samples in India revealed that *N. otitidiscaviarum* had a much lower prevalence compared to other *Nocardia* which may indicate the reason for its low incidence in clinical practice [10]. In addition, it was noted to be less pathogenic in humans when compared to other *Nocardia*.

Being described as an opportunistic pathogen, individuals with weakened immune system, such as patients suffering from diabetes mellitus, chronic obstructive pulmonary disease, mixed connective tissue disorder, ulcerative colitis, cirrhosis, human immunodeficiency virus (HIV) infection, malignancies, those receiving long-term or large doses of corticosteroid therapy, and stem cell or solid organ transplant recipients are at higher risk for infections due to *N. otitidiscaviarum* [11], similarly, our case had stage 4 invasive ductal carcinoma of the breast and was on chemotherapy for eight weeks with the last dose given three weeks before her presentation.

In a review of the database for *N. otitidiscaviarum*, 25 cases had been reported between 1997 and 2018 [7, 12–30]. More than half of those cases were reported in immunocompromised patients. Prolonged use of corticosteroids was a major risk factor in the majority [12, 13, 16, 20, 21, 23, 30, 31]. In other cases, organ transplant recipients [32], endocrine disorders [26], HIV and rheumatic heart disease were identified as risk factors [18, 20, 25]. On the other spectrum, eight cases were reported in immunocompetent patients. Four of those were engaged in gardening or farming and were exposed to dust inhalation similarly to our patient [7, 15, 19, 22]. Only one case
reported no underlying immunocompromised state nor any occupational risk factors like farming [13].

It may be challenging to diagnose such patients who present with many possible differential diagnoses. Conventional evaluation of specimens including wound drainage, skin and brain lesions biopsies, CSF analysis and cultures along with imaging studies, all remain the principal diagnostic methods. In the present report, the species was determined using MALDI-TOF MS. Although the gold standard for Nocardia species identification is molecular biology with amplification and sequencing of one or two gene(s) among rrs (i.e. the gene coding for 16S rRNA), hsp65, secA1 and sodA, MALDI-TOF MS is increasingly being used for identifying Nocardia species. MALDI-TOF MS adequately identifies frequent species in 95–100% of cases, however for cases of a low identification score molecular biology-based identification remains important [33]. The isolate in the current study had a 99.9% confidence value, hence no molecular sequencing was performed.

Most N. otitidiscaviarum isolates are reported to be resistant to beta-lactams while usually being susceptible to Amikacin, Fluoroquinolones [12, 34], and trimethoprim–sulfamethoxazole, hence, Sulfonamides remain the standard agents for treatment [12]. Meanwhile, some studies reported N. otitidiscaviarum susceptibility to Linezolid in-vitro; however, data from in-vivo studies are still lacking and the risk of haematological toxicity with prolonged Linezolid therapy is high, hindering its clinical use [35, 36]. A study that assessed 552 clinical isolates of Nocardia from six major laboratories in the USA, found sulfonamide resistance to be only 2%, which is lower than previously shown [37, 38]. The authors hypothesized that these discrepancies may be associated with difficulty in the laboratory interpretation of in vitro MICs for TMP-SMX and SMX and the lack of quality controls for Nocardia for these agents [39]. The isolate in the current study showed MIC of ≥8/152 for TMP/SMX respectively, which indicates it to be a realistic phenomenon. However, Imipenem resistance has been more commonly described [34]. Typical in-vitro antimicrobial susceptibility patterns of various Nocardia species indicates that N. otitidiscaviarum is usually susceptible to TMP–SMX (Table 3).

Similarly, in our case combined drug therapy with Imipenem and TMP-SMX were used for a total of 22 days until the susceptibility result showed resistance to both agents and treatment with Linezolid, Ceftriaxone, moxifloxacin, doxycycline was used in addition to Amikacin that was added earlier due to the appearance of new skin lesions. The delay in obtaining susceptibility results from the outside lab clearly had a negative

| Drug                  | N. abscessus | N. brasiliensis | N. brevicatena and N. paucivorans | N. cyriacegeorgica | N. farcinica | N. nova complex | N. otitidiscaviarum | N. pseudobrasiliensis | N. transvalensis complex |
|-----------------------|--------------|----------------|----------------------------------|-------------------|-------------|---------------|-------------------|-----------------------|--------------------------|
| Amoxicillin–Clavulanic Acid | S            | S              | –                                | –                 | R           | R             | S                 | –                     | R                       |
| Amikacin              | S            | –              | S                                | S                 | S           | –             | –                 | –                     | S                       |
| Ceftriaxone           | S            | –              | S                                | R                 | S           | R             | –                 | –                     | S                       |
| Ciprofloxacin         | R            | R              | R                                | S                 | S           | –             | –                 | S                     | –                       |
| Clarithromycin        | R            | R              | R                                | R                 | S           | –             | S                 | S                     | –                       |
| Gentamicin            | –            | –              | R                                | –                 | –           | S             | –                 | –                     | S                       |
| Imipenem              | R            | –              | R                                | S                 | S           | R             | –                 | S                     | –                       |
| Linezolid             | S            | S              | –                                | –                 | S           | S             | S                 | S                     | S                       |
| Minocycline           | –            | –              | S                                | –                 | –           | –             | –                 | –                     | R                       |
| Sulfamethoxazole      | –            | –              | –                                | –                 | –           | –             | S                 | –                     | S                       |
| Tobramycin            | –            | –              | –                                | –                 | –           | –             | R                 | –                     | –                       |

S susceptible, R Resistant

The optimal antimicrobial management for N. otitidiscaviarum is still not clearly defined, however, combined treatment is suggested for disseminated and severe disease. In our case, the isolated N. otitidiscaviarum was susceptible to Linezolid and Amikacin and was resistant to TMP-SMX, Ciprofloxacin, Imipenem, Cefepime, Cefoxitin, Amoxicillin-Clavulanic acid, Clarithromycin and Tobramycin. Seven cases were similarly reported with resistance to TMP-SMX [17, 19, 21, 24, 28, 30] with four cases reported in immunocompetent patients [17, 19, 24], and one infecting a farmer [19], details of these studies are described in Table 4.
| References       | Years | Age/gender | Immune Status                        | Drug Susceptibility                                                                 | Treatment                                      | Outcome       |
|------------------|-------|------------|---------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------|---------------|
| Matsu et al. [19] | 2000  | 74M        | Immunocompetent (Farmer)              | Resistant to: TMP-SMX, Penicillin, Piperacillin, Imipenem, Ceftazidime. Susceptible| TMP-SMX à Clarithromycin + Amikacin           | Recovered     |
|                  |       |            |                                       | to: Amikacin, Minocycline, Clarithromycin                                            |                                               |               |
| Yoshida et al. [30] | 2004  | 69M        | On Corticosteroid therapy             | Resistant to: Ampicillin, Piperacillin, Cefazolin, Imipenem, minocycline, Vancomycin, TMP-SMX, Erythromycin. Susceptible to: Levoflaxacin, Gentamicin and Levoflaxacin | Imipenem + TMP-SMX à TMP-SMX + Gentamicin     | Recovered     |
| Mahgoub et al. [17] | 2016  | 41F        | Immunocompetent                        | Resistant to: Azithromycin, Ceftazidime, Penicillin, Rifampicin and TMP-SMX. Susceptible to: Amikacin, Ciprofloxacin, Meropenem and Streptomycin | TMP-SMX + Amikacin + Imipenem à Ceftriaxone + Amikacin + Ciprofloxacin | Recovered     |
| Candel et al. [13] | 2017  | 79M        | On Corticosteroid therapy             | Resistant to: TMP-SMX. Susceptible to Aminoglycosides, Beta-lactams and Carbapenem  | Levoflaxacin + Vancomycin + Tobramycin        | Died          |
| Princess et al. [21] | 2018  | 51F        | On Corticosteroid therapy             | Resistant to: TMP-SMX, Amoxicillin, Clavulanate. Susceptible to: Amikacin, Ciprofloxacin, Linezolid, Imipenem and Ceftriaxone | Azithromycin + Doxycycline à TMP-SMX + Imipenem | Died          |
| Saksena et al. [24] | 2020  | 74M        | Immunocompetent                        | Resistant to: Ampicillin, Amoxicillin-Clavulanate, Erythromycin, TMP-SMX and imipenem. Susceptible To: Amikacin, Linezolid, Ciprofloxacin, and Gentamicin | Amoxicillin-Clavulanate + Azithromycin à TMP-SMX | Died          |
| Saksena et al. [24] | 2020  | 74F        | Immunocompetent                        | Resistant to: Ampicillin, Amoxicillin-Clavulanate, Erythromycin, TMP-SMX and imipenem. Susceptible To: Amikacin, Linezolid, Ciprofloxacin, and Gentamicin | Meropenem + Colistin à TMP-SMX added          | Died          |

M, male; F, female; TMP-SMX, trimethoprim-sulfamethoxazole; GCS, Glasgow coma scale
impact on patient outcome, such words would advocate for wider availability of such testing and higher turn-round time.

Mortality due to disseminated Nocardiosis is high, therefore early diagnosis and initiation of therapy are of vital importance in Nocardial infections. In our case, the patient was started on empirical treatment for Nocardiosis that was later adjusted according to the susceptibility results, however, the delay in administering proper antimicrobials and her pre-existing advanced malignancy may have attributed to her mortality.

In conclusion, *N. otitidiscaviarum* infection though rare may have considerable mortality; early diagnosis and susceptibility testing are crucial in avoiding similar devastating outcomes. In addition, surveillance for emerging TMP-SMX resistance should be closely monitored.

Abbreviations

TMP-SMX: Trimethoprim-sulfamethoxazole; WBC: White blood cells; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; CT: Computed tomography; CSF: Cerebrospinal fluid; AFB: Acid-fast bacilli; M. tb: Mycobacterium tuberculosis; PCR: Polymerase chain reaction; MRI: Magnetic resonance imaging; GMS: Grocott methenamine silver; PAS: Periodic acid–Schiff; MALDI-TOF MS: Matrix-assisted laser desorption ionization-time of flight mass spectrometry; MIC: Minimum inhibitory concentration; CLSI M24: Clinical and Laboratory Standards Institute standard M24—Susceptibility Testing of Mycobacteria, Nocardia spp, and Other Aerobic Actinomycetes, HIV: Human immunodeficiency virus.

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Author contributions

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Availability of data and materials

All the data for this study will be made available upon reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by King Saud University IRB No. 21-1509E. Next of kin consented to the publication of this report.

Competing interests

None declared.

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References

1. Ambrosioni J, Lew D, Garbino J. Nocardiosis: Updated Clinical Review and Experience at a Tertiary Center. Infection. 2010;38:89–97.
2. Hemmersbach-miller M, Martel AC, Benitez AB, Sosa AO. Brain abscess due to *Nocardia otitidiscaviarum*: report of a case and review. Scan J Infect Dis. 2004;36:381–4.
3. Clark NM, Braun DK, Pasternak A, Chenoweth CE. Primary cutaneous *Nocardia otitidiscaviarum* infection: case report and review. Clin Infect Dis. 1995;20:1266–70.
4. Ishihara M, Takada D, Sugimoto K, Oghro H, Gonoi T, Akiyama Y, et al. Primary brain abscess caused by *Nocardia otitidiscaviarum*. Intern Med. 2014;53:2007–12.
5. Beaman BL, Burnside J, Edwards B, Causey W. Nocardial infections in the United States, 1972–1974. J Infect Dis. 1976;134:286–9.
6. Kageyama A, Yazawa K, Ishikawa J, Hotta K, Nishimura K, Mikami Y. Nocardial infections in Japan from 1992 to 2001, including the first report of infection by *Nocardia transvalensis*. Eur J Epidemiol. 2004;19:383–9.
7. Liu C, Feng M, Zhu J, Tao Y, Kang M, Chen L. Severe pneumonia due to *Nocardia otitidiscaviarum* identified by mass spectroscopy in a cotton farmer: a case report and literature review. Medicine (Baltimore). 2017;96:e6526.
8. Sah R, Khadka S, Neupane S, Nepal G, Singla S, Kumari P, et al. Disseminated infection with *Nocardia otitidiscaviarum* in a patient under steroid therapy. Clin Case Rep. 2020;8:369–73.
9. Lerner PI. Nocardiosis. Clin Infect Dis. 1996;22:891–905.
10. Kurup PV, Randhawa HS, Sandhu RS. A survey of *Nocardia asteroides*, *N. caviae* and *N. brasiliensis* occurring in soil in India. Sabouraudia. 1968;6:260–6.
11. Corti ME, Villafaña-Fioti MF. Nocardiosis: a review. Int J Infect Dis. 2003;7:243–50.
12. Betrán A, Villuendas MC, Rezusta A, Molés B, Rubio MC, Revillo MJ, et al. Cavitary pneumonia caused by *Nocardia otitidiscaviarum*. Braz J Microbiol. 2010;41:329–32.
13. Candel FJ, González J, Mateszcz M, Cinza R, Clas R, Candel I, et al. [Bacteremic infection due to *Nocardia otitidiscaviarum*: case report and review]. An Med Interna. 2005;22:489–92.
14. Deepa R, Banu ST, Jayalakshmi G, Parveen JD. Pulmonary nodular infection due to *Nocardia otitidiscaviarum* in a debilitated host. Indian J Pathol Microbiol. 2016;59:240–2.
15. Dikensoy O, Filiz A, Bayram N, Balci I, Zer Y, Celik G, et al. First report of pulmonary *Nocardia otitidiscaviarum* infection in an immunocompetent patient from Turkey. Int J Clin Pract. 2004;58:210–3.
16. Huang CH, Hsuheh PR, Chen YH. Empyema thoracis due to *Nocardia otitidiscaviarum*. J Microbiol Immunol Infect. 2015;48:580–1.
17. Mahgoub A, Gumaa SA, Joseph MR, Saleh MS, Elsheikh AH, Elkhafila AI, et al. Pulmonary nocardiosis caused by *Nocardia otitidiscaviarum* in an adult asthmatic female patient: the presence of acid-fast branching filaments is always significant. S Afr Med J. 2016;107:43–5.
18. Mari B, Montón C, Manscal D, Luán M, Sala M, Domingo C. Pulmonary nocardiosis: clinical experience in ten cases. Respiration. 2001;68:382–8.
19. Matsuoka T, Takeuchi M, Kawai T, Nako M, Okamoto M, Tada S, et al. [Pulmonary *Nocardia otitidiscaviarum* infection in an immunocompetent host]. Nihon Kokyuki Gakkai Zassi. 2000;38:844–9.
20. Pelea Al, Garcia-Suarez Mdel M, Manteca A, Melon O, Aranan C, Cimadevilla R, et al. A fatal case of *Nocardia otitidiscaviarum* pulmonary infection and brain abscess: taxonomic characterization by molecular techniques. Ann Clin Microbiol Antimicrob. 2009;8:11.
21. Princess I, Ebenezer R, Ramakrishnan N, Nandini S. Pulmonary Nocardiosis and Scrub Typhus in an Immunocompromised Host. J Glob Infect Dis. 2018;10:108–11.

22. Ramamoorthy K, Pruthvi BC, Rao NR, Belle J, Chawla K. Pulmonary nocardiosis due to Nocardia otitidiscaviarum in an immunocompetent host—a rare case report. Asian Pac J Trop Med. 2011;4:414–6.

23. Sadamatsu H, Takahashi K, Tashiro H, Komiya K, Nakamura T, Sueoka-Aragane N. Successful treatment of pulmonary nocardiosis with fluoroquinolone in bronchial asthma and bronchiectasis. Respir Care Rep. 2017;5:e00229.

24. Saksena R, Ryenga D, Rajan S, Gaird R, Dawar R, Sardana R, et al. Fatal pulmonary infection by trimethoprim–sulphamethoxazole resistant Nocardia otitidiscaviarum: report of two cases and review. J Infect Dev Ctries. 2020;14:214–22.

25. Sandre RM, Summerbell RC. Disseminated Nocardia otitidiscaviarum in a patient with AIDS. Can J Infect Dis. 1997;8:347–50.

26. Sudou A, Hashimoto T, Nakamura H, Yegusu H, Sarashina G, Hatao E, et al. [Pulmonary Nocardia otitidis-caviarum infection in a patient with Cushings disease]. Nihon Kokyuki Gakkai Zasshi. 2001;39:210–4.

27. Taniguchi H, Mukae H, Ashitani J, Ihi T, Sakamoto A, Kohno S, et al. Pulmonary Nocardia otitidiscaviarum infection in a patient with chronic respiratory infection. Intern Med. 1998;37:872–6.

28. Thirouvengadame S, Mutthusamy S, Balaji WK, Easow JM. Unfolding of a Clinically Suspected Case of Pulmonary Tuberculosis. J Clin Diagn Res. 2017;11:1101–1103.

29. Tone A, Matsuo K, Watanabe Y, Tamaoki A, Hiramaki S. [Pulmonary Nocardia otitidis-caviarum infection in a patient with bronchiectasia]. Nihon Naika Gakkai Zasshi. 2002;91:3037–9.

30. Yoshida K, Bandoh S, Fujita J, Tokuda M, Negayama K, Ishida T. Pneumothorax caused by Nocardia otitidiscaviarum in a patient with rheumatoid vasculitis. Intern Med. 2004;43:615–9.

31. Parengal J, Alebbi SM, Alqatami HM, Ben Abid F. Disseminated life threatening Nocardia otitidiscaviarum infection in a young female with newly diagnosed systemic lupus erythematosus, case report and review of literature. IDCases. 2021;12:e01265.

32. Chawla K, Mukhopadhyay C, Payyanur P, Bairy I. Pulmonary nocardiosis from a tertiary care hospital in Southern India. Trop Doct. 2009;39:163–5.

33. Margalit I, Lebeaux D, Tishler O, Goldberg E, Bishara J, Yahav D, Coussem J. How do I manage nocardiosis? Clin Microbiol Infect. 2021;27(4):550–5. https://doi.org/10.1016/j.cmi.2020.12.019.

34. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ, Jr. Clinical and laboratory features of the Nocardia spp. based on current molecular taxonomy. Clin Microbiol Rev. 2006;19:259–82.

35. Jodlowski TZ, Melnychuk I, Conry J. Linezolid for the treatment of Nocardia spp. infections. Ann Pharmacother. 2007;41:1694–9.

36. Moylett EH, Pacheco SE, Brown-Elliott BA, Perry TR, Buescher ES, Birmingham MC, et al. Clinical experience with linezolid for the treatment of nocardia infection. Clin Infect Dis. 2003;36:313–8.

37. Lai CC, Liu WL, Ko WC, Chen YH, Tan HR, Huang YT, Hsieh PR. Multicenter study in Taiwan of the in vitro activities of tigecycline, doripenem, and other antimicrobial agents against clinical isolates of various Nocardia species. Antimicrob Agents Chemother. 2011 May;55(5):2084–9. doi: https://doi.org/10.1128/AAC.01808-10.

38. Lai CC, Liu WL, Ko WC, Chen YH, Tang HJ, Huang YT, Hsieh PR. Antimicrobial-resistant nocardia isolates, Taiwan, 1998–2009. Clin Infect Dis. 2011;52(8):833–5. https://doi.org/10.1093/cid/ciq265.

39. Brown-Elliott BA, Biehle J, Conville PS, Cohen S, Saubolle M, Sussland D, Wengenack N, Kriel K, Bridge L, McNulty S, Vasireddy R, Wallace RJ Jr. Sulfonamide resistance in isolates of Nocardia spp. from a US multicenter survey. J Clin Microbiol. 2012 Mar;50(3):670–2. doi: https://doi.org/10.1128/JCM.01243-11.

40. Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnock DW. Manual of clinical microbiology 10th edition, Washington, DC: ASM Press; 2011.