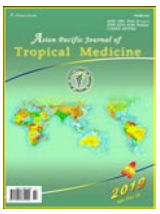

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Disseminated nocardiosis due to *Nocardia otitidiscaviarum*: A case report and literature review

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ABSTRACT

Rationale: Disseminated nocardiosis due to *Nocardia otitidiscaviarum* is rarely reported in immunocompetent hosts.

Patient concerns: A 59 year old male patient complained of painful soft tissue swellings and fever for two days.

Diagnosis: Disseminated nocardiosis due to *Nocardia otitidiscaviarum*.

Interventions: Initial antimicrobial therapy with imipenem and trimethoprim/sulfamethoxazole was switched to 6 weeks of trimethoprim/sulfamethoxazole, linezolid and tigecycline after sensitivity test results were available. Thereafter, the patient was switched to maintenance trimethoprim/sulfamethoxazole and moxifloxacin. Prednisolone was gradually tapered.

Outcomes: Soft tissue swelling and pain disappeared and the patient was discharged uneventfully.

Lessons: Disseminated nocardiosis due to *Nocardia otitidiscaviarum* should be suspected in immunocompetent hosts with risk factors such as medication with prednisolone. Early identification of the causative species and susceptibility results is crucial given the diverse resistance patterns amongst various *Nocardia* species.

1. Introduction

Nocardia spp. is a Gram-positive, weakly acid-fast microorganism that is ubiquitous in the environment with a worldwide distribution. Common factors include long term corticosteroid use, malignancy, human immunodeficiency virus infection and chronic obstructive pulmonary predisposing to Nocardia infectionsdisease[1]. Various *Nocardia* species differ in their pathogenicity, geographical distribution and antimicrobial susceptibility. Historically, before the advent of molecular techniques and mass spectrometry, biochemical methods were used in the identification of *Nocardia* species, resulting in only a few known *Nocardia* species[2]. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) has emerged as a useful tool for the accurate identification of *Nocardia* species[2-4].

First recognized in 1924 from a guinea pig with ear disease, *Nocardia otitidiscaviarum* (*N. otitidiscaviarum*) has been described as an opportunistic pathogen causing local and disseminated infection in both immunocompetent and immunocompromised hosts[1]. Herein, we describe a case of disseminated *N. otitidiscaviarum* predisposed by corticosteroid use and a literature review of published case reports and case series of *N. otitiscaviarum* infections.

2. Case report

This case report was approved by the local ethics committee of

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the author's affiliated institution. The patient provided consent to the use of photographs in the report. Identifying information of the patient was removed.

A 59-year-old man presented with an acute history of painful soft tissue swellings and fever. Upon further questioning, he denied any history of trauma and had been perfectly well 2 d before. He had no cough, hemoptysis, or chest pain. He had a history of hypertension, dyslipidemia, and stage Ⅳ chronic kidney disease (baseline serum creatinine ranging 284-313 μmol/L, reference range, 54-101 μmol/L), secondary to presumptive glomerulonephritis. Two months ago, he had been started on a prednisolone dose of 60 mg daily by his nephrologist for suspected immune-mediated glomerulonephritis. Clinical examination revealed a febrile middle-aged man with discreet tender, warm, and erythematous swellings over his left elbow (Figure 1), right thigh, and right buttock, consistent with cutaneous abscesses. There was no palpable lymphadenopathy. Cardiorespiratory and abdominal examination was unremarkable. He had no focal neurological deficit.

Laboratory findings included the following: serum sodium 140 mmol/L (reference range, 136-146 mmol/L), serum potassium 4.5 mmol/L (reference range, 3.6-5.0 mmol/L), serum bicarbonate 24.6 mmol/L (reference range, 19.0-29.0 mmol/L), serum creatinine 332 umol/L, haemoglobin 12.5 g/dL (reference range, 14.0-18.0 g/dL), white blood cell count 15.02×10^9/L (reference range, 4.0-10.0$\times10^9$/L), C-reactive protein 86.6 mg/L (reference range, 0.2-9.1 mg/L), serum albumin 31 g/L (reference range, 40-51 g/L), bilirubin 5 μmol/L (reference range, 7-32 μmol/L), alkaline phosphatase 51 U/L (reference range, 39-99 U/L), alanine aminotransferase 6 U/L (reference range, 6-66 U/L), and aspartate aminotransferase 17 U/L (reference range, 12-42 U/L). Blood cultures were non-yielding.

A chest radiograph showed a left upper lobe opacity, which was new compared to a previous radiograph taken three months before (Figure 2A-2B). A computed tomography scan of his thorax revealed a spiculated left upper lobe mass (Figure 2C) corresponding to the opacity detected on the chest radiograph.

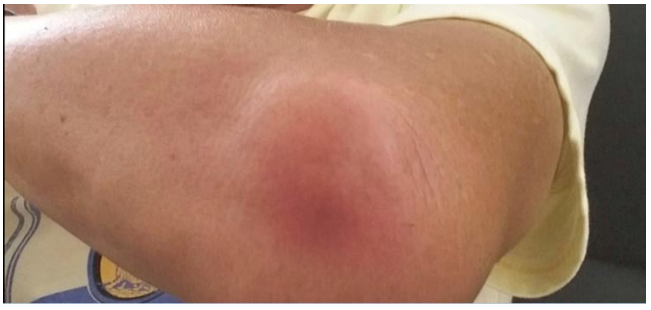

Figure 1. A cutaneous abscess seen over the left elbow of a febrile 59-year old man with disseminated nocardiosis.

He initially declined surgical drainage. Magnetic resonance imaging (MRI) to delineate the soft tissue abscesses and revealed subcutaneous collections over the left elbow joint, right gluteus maximus, and was right sartorius and iliacus muscle, together with an intramuscular abscess within the right gracilis muscle (Figure 3A-3H).

He did subsequently undergo a diagnostic transthoracic needle aspiration of the lung lesion as well as an incision and drainage of the multiple subcutaneous abscesses. Histology of the lung specimen showed acute-on-chronic pneumonitis with microabscess formation. No granulomas or infective organisms were identified and there was no evidence of malignancy. Gram stain, fungal microscopy, acid-fast bacilli stain, and nucleic acid amplification test for *Mycobacterium tuberculosis* complex were negative.

Eventually, chalky colonies were seen on the blood agar plate several days later (Figure 4A) from both the lung and subcutaneous tissue specimens. On microscopy, beaded Gram-positive rods were seen (Figure 4B), suspicious for nocardiosis. Antimicrobial therapy was empirically switched to a combination of imipenem and trimethoprim/sulfamethoxazole. The causative microorganism was identified to be *N. otitidiscaviarum* by the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.

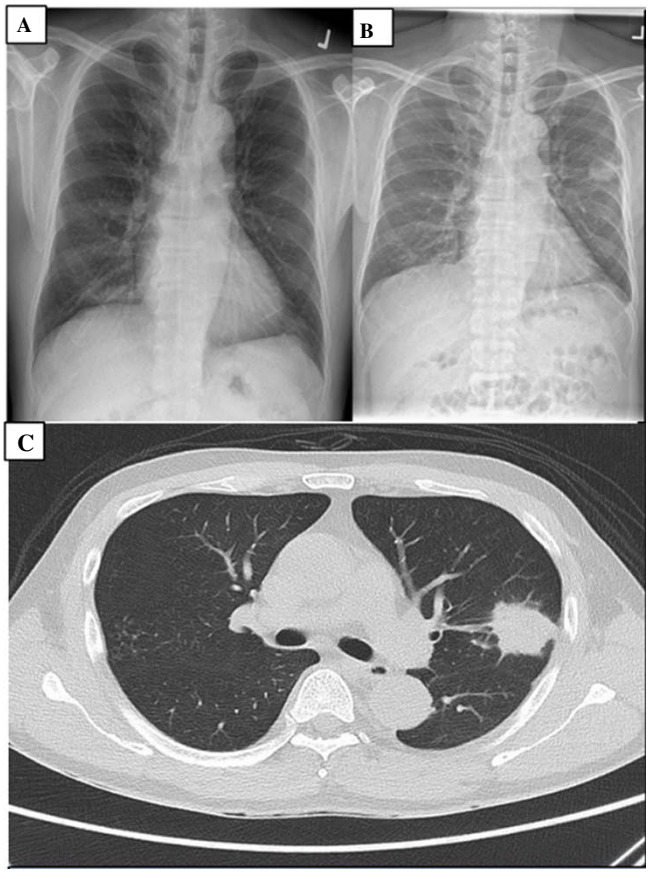

Figure 2. Radiographic images including previous and presenting chest radiographs, as well as a coronal view on CT scan of the pulmonary Nocardial lesion of the febrile middle-aged man. A: Chest radiograph 3 months prior to presentation, prior to commencement of corticosteroids. B: Left middle zone opacification at presentation. C: Spiculated mass in the left upper lobe corresponding to the opacity detected on chest radiograph.

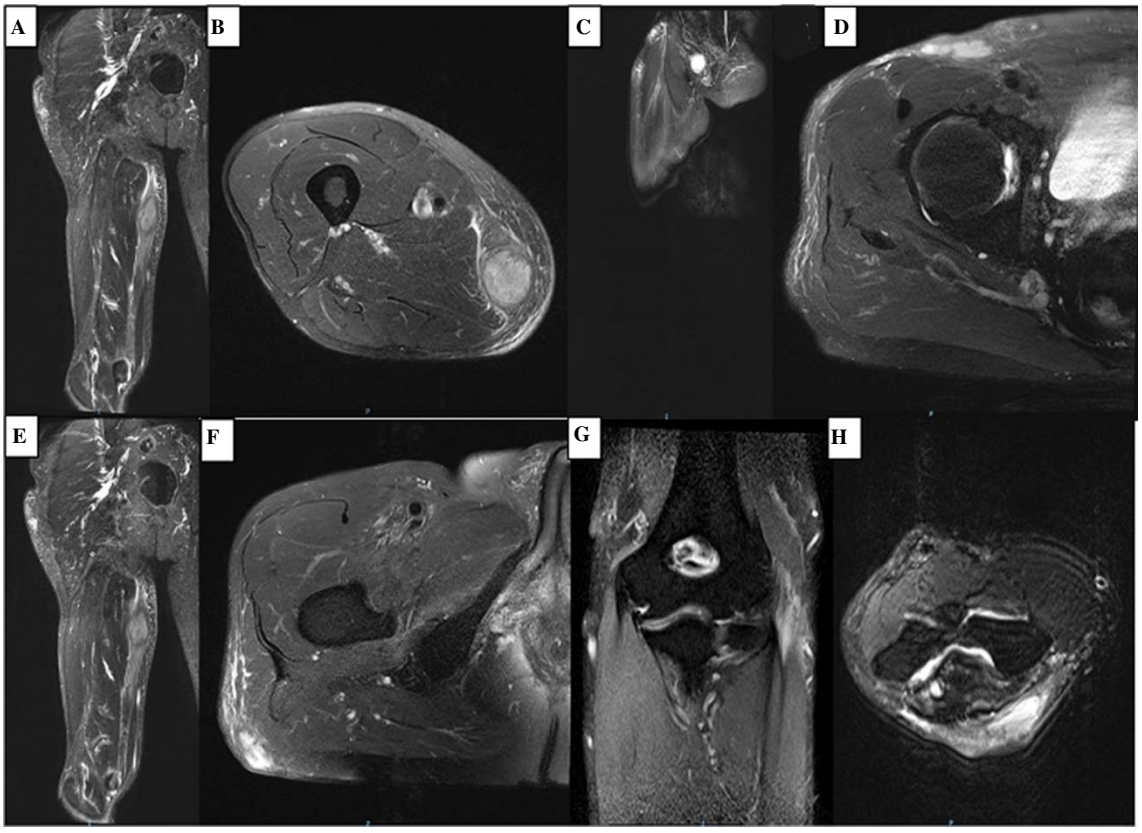

Figure 3. Skin and soft tissue abscesses at the right thigh, groin, buttock and the left elbow demonstrated on MRI on the febrile middle-aged man with disseminated nocardiosis. A/B: An 4 intramuscular abscess collection within the right gracilis muscle with surrounding edema. C/D: Small collection is noted within the subcutaneous fat overlying the right sartorius and iliacus muscle at the right groin region. E/F: A small collection within the subcutaneous fat overlying the postero-lateral aspect of the right gluteus maximus. G/H: Extensive area of subcutaneous hyperintense theta signal seen in the posterior aspect of the elbow joint; focal thick wall fluid collection with layering noted in the subcutaneous layers.

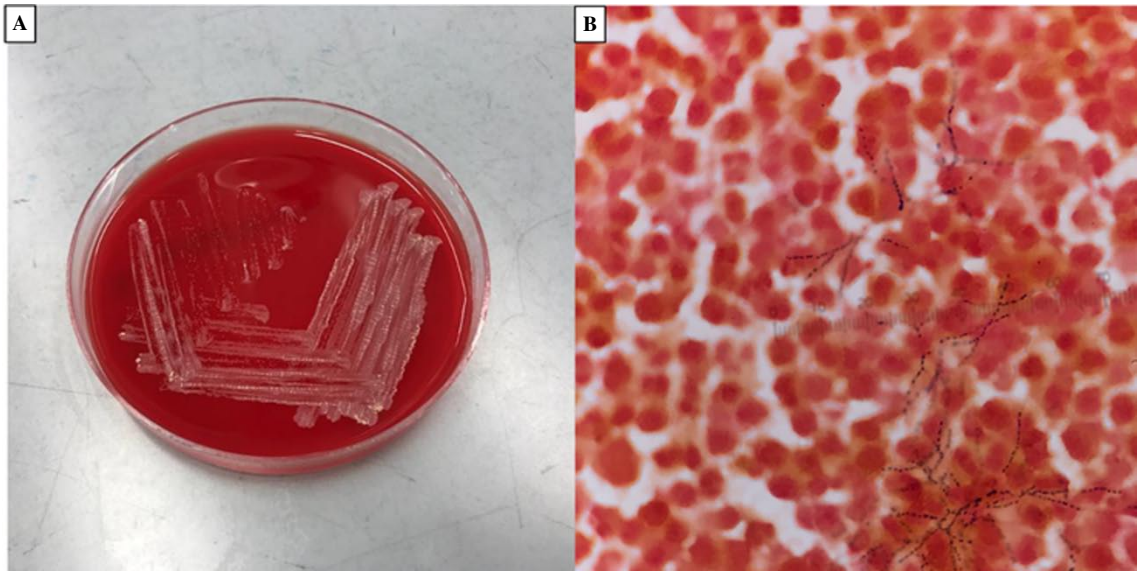

Figure 4. Culture morphology and microscopic (magnified at 40×) images of the *Nocardia* spp. isolates cultured from the patient. A: Chalky white colonies on blood agar plate. B: Microscopy slides of beaded Gram positive bacilli of *Nocardia* spp.

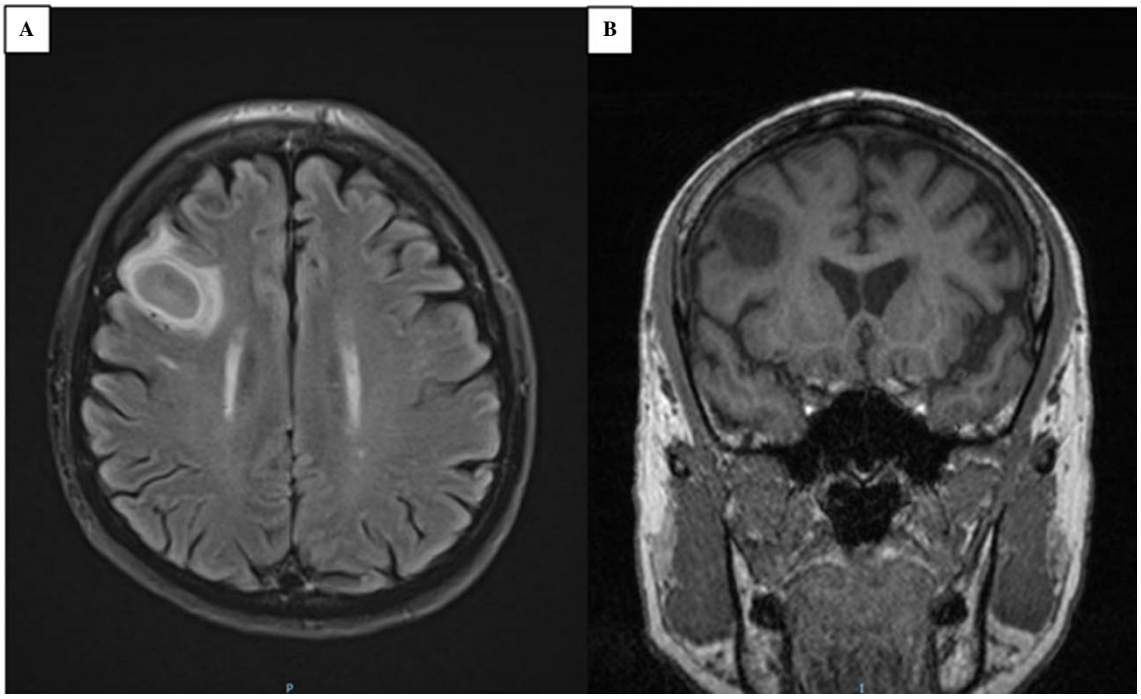

Figure 5. MRI brain images demonstrating presumptive Nocardial brain abscess at the right frontal lobe on coronal and sagittal views. A: Coronal view of MRI brain showing 2.3 cm×2.1 cm×1.3 cm solitary, well-circumscribed, lesion demonstrating restricted diffusion, T2-weighted hyperintensity and T1-weighted hypointensity that is consistent with a cerebral abscess. Mild surrounding vasogenic edema without significant mass effect is seen. B: Sagittal view showing the same lesion in the frontal lobe.

An MRI of his brain showed a solitary lesion in the right frontal lobe, consistent with a cerebral abscess (Figure 5A-5B). Hence, this patient has disseminated nocardiosis resulting in subcutaneous,intramuscular, lung and brain abscesses, predisposed by cortico steroids.

Susceptibility testing using the broth microdilution method suggested that this isolate was susceptible to amikacin [minimum inhibition concentration (MIC)≤8 μg/mL], tobramycin (MIC≤4 μg/mL), trimethoprim/sulfamethoxazole (MIC≤2/38 μg/mL), and linezolid (MIC≤8 μg/mL), intermediate to moxifloxacin (MIC=2 μg/mL), doxycycline (MIC=2 μg/mL), and minocycline (MIC=2 μg/mL), and resistant to amoxicillin/clavulanic acid (MIC≥32/16 μg/mL), ceftriaxone (MIC≥64 μg/mL), cefepime (MIC≥32 μg/mL), imipenem (MIC≥16 μg/mL), ciprofloxacin (MIC≥4 μg/mL), and clarithromycin (MIC≥8 μg/mL). Tigecycline MIC was tested to be 0.5 μg/mL but without interpretive criteria from the Clinical&Laboratory Standards Institute. Antimicrobial therapy was further switched to trimethoprim/sulfamethoxazole, linezolid and tigecycline. Aminoglycosides were not used in view of his underlying renal disease. He completed 6 weeks of this combination therapy before switching to maintenance trimethoprim/sulfamethoxazole and moxifloxacin. His prednisolone was gradually tapered and ceased and all his cutaneous lesions were drained surgically. A summary of his clinical progress is shown in Figure 6.

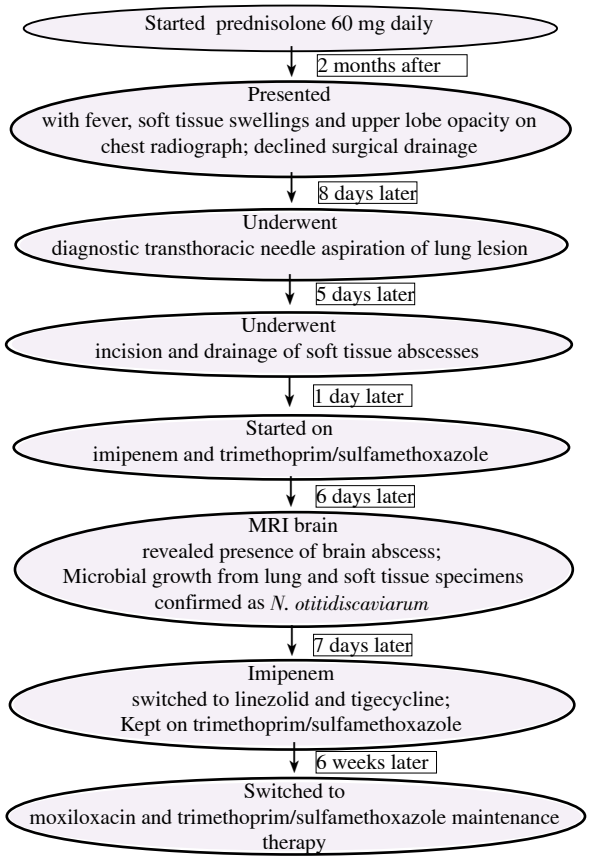

Figure 6. Timeline of clinical events summarizing the progress of this patient from immunosuppression, presentation to eventual treatment regimen.

3. Discussion

A computerized search for publications on *N. otitidiscaviarum* in the Medline database of the National Library of Medicine was conducted for the literature review. Only reports available in English, published in the last 25 years, were included. Articles were identified through screening of titles and their abstracts to determine final eligibility. Key words used include "*Nocardia otitidiscaviarum*".

The search terms yielded a total of 106 articles, in which 49 articles were included[5-53]. One article was excluded in view of inconsistently reported results. One article[43] was reviewed from its abstract only, as the full manuscript was not available. A total of 141 cases of *N. otitidiscaviarum* infections, including our case, were collated. Their clinical features and antimicrobial susceptibilities were shown in Table 1. The median age was 57 years, and 69.2% were males. The commonest risk factors reported included corticosteroids use (n=11), chronic lung disease (n=12), solid organ transplant (n=8), underlying human immunodeficiency virus (n=4) and solid organ malignancy (n=3). Eighteen patients did not appear to have any underlying medical conditions. Mortality occurred in 8 out of 49 cases reported (16.3%). Seventy-two cases had their sites of infection stated. The commonest clinical infective syndrome included pneumonia (n=35, 48.6%),

Table 1. Clinical and microbiological characteristics of patients with reported *Nocardia otitidiscaviarum*.

No.	Age	Gender	Significant medical history/ risk factor(s)	Site(s) of involvement	Death	Country	Modality of identification	Antimicrobial susceptibility testing				Treatment regimen	Ref
								Susceptible	Intermediate susceptibility	Resistance	Modality of testing		
1	59	Male	Chronic kidney disease	Skin and soft tissue abscess Muscle abscess Brain abscess	No	Singapore	MALDI-TOF MS	AMK, TOB, SXT, LZD	MOX, DOX, MIN	AMC, CRO, FEP, IMI, CIP, CLR	Broth microdilution	SXT + LZD + TIG → MOX + SXT	NA
2	51	Male	Asthma Corticosteroids	Pneumonia	Yes	India	MALDI-TOF MS	CRO, IMI, AMK, CIP, LZD		AMC, SXT	NM	IMI + SXT	[5]
3	65	Male	Nil	Pneumonia	No	India	MALDI-TOF MS, *16S RNA*	CRO, IMI, GEN, AMK, SXT, LZD		AMC	Vitek	SXT	[6]
4	58	Male	Nil	Pneumonia	Yes	China	MALDI-TOF MS	NM	NM	NM	NA	AMK + IMI + SXT	[7]
5	72	Female	Asthma; Bronchiectasis	Pneumonia	No	Japan	*16S RNA*	IMI, LEV, SXT, MIN		CRO	NM	SXT + MIN → MIN → LEV	[8]
6	41	Female	Asthma	Pneumonia Parapneumonic effusion	No	Sudan	*16S RNA*	MEP, AMK, STR, CIP		SXT, AZI, ERY, RIF	Disk diffusion	CRO + CIP	[9]
7	37	Male	Nil	Pneumonia Parapneumonic effusion Skin and soft tissue abscess	No	China	Not mentioned	NM	NM	NM	Disk diffusion	MIN + TMP/ SMX	[10]
8	14	Female	Rheumatic heart disease	Pneumonia Empyema	Yes	India	Molecular methods	IMI, GEN, AMK, CIP, SXT		AMC, CRO, CTX	Disk diffusion	Nil	[11]
9	69	Female	Nil	Brain abscess	No	Turkey	DNA sequence analysis	AMK, IMI, SXT, LZD		AMS, CTX	NM	Surgery+ MEP + AMK → MEP + SXT → SXT	[12]
10	79	Female	Nil	Brain abscess	No	Japan	*16S RNA*	GEN, AMK, SXT, LZD, MIN	TOB, CIP, DOX	AMC, CRO, CTX, FEP, IMI, CLR	NM	Surgery + SXT	[13]
11	42	Male	Liver cirrhosis; Corticosteroids	Empyema	No	Taiwan	*16S RNA*	NM	NM	NM	NM	Surgery + MEP + AMK + SXT → SXT	[14]
12	60	Male	COPD	Skin ulcers Lymphadenopathy	No	India	*16S RNA*	AMK, LZD, MIN			NM	AMK + LZD → LZD	[15]
13	45	Male	Nil	Cornea abscess	No	India	*16S RNA*	AMK, MOX, SXT	LZD	CRO, IMI	Etest	Local GEN + LEV	[16]
14	17	Female	Cystic fibrosis	Pneumonia	No	Qatar	*16S RNA*	AMK, MOX, SXT, LZD		CRO, IMI	Etest	SXT + CLR + MOX	
15	36	Female	Nil	Pneumonia	No	India	Not mentioned	NM	NM	NM	NM	SXT	[17]
16	57	Male	Corticosteroids DM	Pneumonia	NM	Spain	*16S RNA*	GEN, AMK, SXT		AMC, CTX, IMI, TOB, CIP			[18]
17	51	Male	Nil	Pneumonia	No	Taiwan	*16S RNA*	NM	NM	NM	NM	SXT	[19]
18	89	Male	Lung cancer COPD	Pneumonia	Yes			NM	NM	NM	NM	SXT	
19	79	Male	Nil	Cutaneous infection	NM			NM	NM	NM	NM	NM	
20	NM	NM	NM	Ocular infection	NM	India	*16S RNA*	AMK, TOB, CLR		GAT, AZI	Etest	NM	[20]
21	63	Male	Heart transplant Corticosteroids	Soft tissue infection	No	Spain	*16S RNA*	AMK, SXT, LZD, MIN			Broth microdilution	MEP → SXT	[21]

No.	Age	Gender	Significant medical history/ risk factor(s)	Site(s) of involvement	Death	Country	Modality of identification	Antimicrobial susceptibility testing				Treatment regimen	Ref
								Susceptible	Intermediate susceptibility	Resistance	Modality of testing		
22	57	Male	Heart transplant Corticosteroids	Pneumonia	No			AMK, SXT, LZD, MIN			Broth microdilution	MEP + AMK → SXT	
23	45	Male	HIV	Pneumonia	Yes			AMK, SXT, LZD, MIN			Broth microdilution	SXT	
24	78	Male	Pulmonary fibrosis	Pneumonia	Yes	Spain	*16S RNA*	AMK, SXT, LZD, MIN			Broth microdilution	SXT	
25	23	Male	Renal transplant	Pneumonia	No	India	Biochemical tests	NM	NM	NM	NM	FEP + SXT	[22]
26	17	Male	Renal transplant	Pneumonia	No			NM	NM	NM	NM	FEP + SXT	
27	62	Female	Bronchiectasis	Pneumonia	No			NM	NM	NM	NM	SXT	
28	36	Male	Nil	Pneumonia	No			NM	NM	NM	NM	AMK + SXT	
29	85	Female	COPD	Brain abscess	Yes	Spain	*16S RNA*	IMI, GEN, AMK, CIP, SXT, LZD		ERY	Etest	SXT + IMI → SXT + LZD → SXT	[23]
30	65	Female	Breast cancer Immunosuppressants	Cutaneous	No	Greece	*16S RNA*	GEN (4), AMK (4), TOB (4), SXT (2), MOX (4), LZD (4), DOX (4), MIN (4), TIG (4)		AMC (4), CRO (4), CTX (4), FEP (4), IMI (4), SXT (2), CIP (4), CLR (4)	Disk diffusion	LEV	[24]
31	47	Male	Renal transplant Immunosuppressants	Cutaneous	No							LZD	
32	82	Male	Nil	Cutaneous	No							MIN	
33	77	Male	Lung cancer Immunosuppressants	Pneumonia	No							CIP + LZD	
34	55	Male	Nil	Cutaneous abscess	No	Turkey	*16S RNA*	NM	NM	NM	NM	AMK + IMI → SXT	[25]
35	67	Female	Polyarteritis nodosa Corticosteroids	Pneumonia	No	Spain	*16S RNA*	GEN (2), AMK (2), TOB (1), CIP (2), SXT (2), LZD (2), MIN (2)		CRO (2), IMI (2), TOB (1)	Etest	SXT	[26]
36	72	Male	COPD	Pneumonia	No	Spain						SXT	
37	52	NM	NM	Bone, viscera	No	Mexico	Biochemical tests	NM	NM	NM	NM	SXT + AMK + dapsone	[27]
38	70	Male	Rheumatoid arthritis Infliximab Methotrexate Corticosteroids	Skin	No	France	NM	NM	NM	NM	NM	Ofloxacin + clindamycin	[28]
39	69	Male	Rheumatoid arthritis Corticosteroids	Epyema	No	Japan	Biochemical tests	GEN, LEV	SXT, ERY	IMI, MIN	Disk diffusion	Pleural drainage + SXT + LEV	[29]
40	44	Male	Renal transplant DM Corticosteroids Cyclosporine	Brain abscess Myositis	Yes	Spain	NM	GEN, CIP, SXT, DOX		CRO, CTX, IMI, TOB	NM	Surgery + SXT	[30]
41-54	NM	NM	NM	Pneumonia (6); Skin (6); Others (2)	NM	Japan	Biochemical tests	NM	NM	NM	NM	NM	[31]
55	36	Female	Sickle cell anaemia Dilated cardiomyopathy End stage renal failure	Pneumonia Bacteremia	No	United States	NM	GEN, AMK, TOB, CIP, GAT, SXT, CLR, LZD			Disk diffusion and broth microdilution	SXT → AMK + GAT → GAT	[32]
56	42	Female	Renal transplant	Subcutaneous abscess	No	India	Biochemical tests	AMC, CTX, IMI, GEN AMK, CIP, SXT			Disk diffusion	IMI + FEP + AMK	[33]
57	65	Male	Nil	Pneumonia Parapneumonic effusion	No	Turkey	NM	AMK, TOB, SXT	NM	NM	NM	SXT → IMI → SXT	[34]
58	60	Female	Nil	Cutaneous nodules Lymphangiitis	No	Japan	Biochemical tests	NM	NM	NM	NM	SXT	[35]
59	46	Male	HIV	Pneumonia	No	Spain	NM	NM	NM	NM	Broth microdilution	Tuberculosis treatment	[36]
60	50	Male	Nil	Skin Pneumonia Parapneumonic effusion	No	United Arab Emirates	NM	NM	NM	NM	NM	AMK + SXT + rifampicin	[37]
61	21	Male	Intravenous drug abuser	Brain abscess	No	France	Biochemical tests	CIP, SXT	IMI, MIN	ERY		IMI + SXT → SXT	[38]
62	50	Female	Renal transplant	Brain abscess	No	Norway	*16S RNA*	MEP, RIF			NM	MEP + RIF	[39]
63	76	Male	NIl	Pneumonia	No	Japan	Biochemical tests	TOB, SXT, MIN		IMI	Disk diffusion	MIN → TMP/SMX	[40]
64	59	Male	HIV	Pneumonia Lymphadenopathy Extraperitoneal mass	No	Canada	Biochemical tests	AMK, SXT		CTX, GEN, TOB, ERY, MIN	Disk diffusion	AMK + SXT + CTX → SXT	[41]

No.	Age	Gender	Significant medical history/ risk factor(s)	Site(s) of involvement	Death	Country	Modality of identification	Antimicrobial susceptibility testing				Treatment regimen	Ref
								Susceptible	Intermediate susceptibility	Resistance	Modality of testing		
65	31	Male	Nil	Skin	No	France	Biochemical tests	IMI, AMK, SXT		GEN, TOB, ERY	Disk diffusion	IMI + SXT → SXT	[42]
66-67	NM	NM	NM	NM	NM	France	NM	NM	NM	NM	NM	NM	[43]
68-70	NM	NM	NM	Skin (1), Eye (1), Unknown (1)	NM	Thailand	Biochemical tests	NM	NM	NM	NM	NM	[44]
71	78	Female	Asthma Corticosteroids	Skin	No	Japan	Biochemical tests	MIN	AMK, SXT	IMI, MEP	Broth microdilution	MIN → ofloxacin + DOX	[45]
72	86	Male	Nil	Skin	No	United States	NM	SXT			NM	SXT	[46]
73	31	Male	HIV Intravenous drug abuse	Skin Brain abscess	No	Italy	Biochemical tests	NM	NM	NM	NM	SXT + netilmycin	[47]
76	NM	NM	NM	NM	NM	China	*16S RNA*	AMK, TOB, SXT, LZD	MIN	AMC, CRO, CTX, FEP, IMI, CIP, CLR	Broth microdilution	NM	[48]
77-80	NM	NM	NM	Joints (3) Skin (1)	NM	Saudi Arabia	NM	NM	NM	NM	NM	NM	[49]
81-86	NM	NM	NM	NM	NM	Canada	Multilocus sequence analysis	AMK (6), TOB (3), MOX (1), SXT (5), LZD (6), DOX (1), MIN (2)	AMC (6), CRO (6), FEP (6), IMI (6), TOB (3), CIP (6), MOX (5), SXT (1), DOX (5), MIN (4)		Broth microdilution	NM	[50]
87-94	NM	NM	NM	NM	NM	Taiwan	*16S RNA*	AMK (8), SXT (8), LZD (8)	CRO (1), CIP (3)	AMC (8), CRO (7), IMI (8), CIP (5)	Broth microdilution	NM	[51]
95-106	NM	NM	NM	NM	NM	Iran	*16S RNA*	CTX (2), FEP (4), GEN (6), AMK (12), TOB (12), CIP (2), MOX (3), SXT (12), CLR (4), LZD (12), DOX (1), MIN (1)	CRO (2), CTX (1), FEP (4), CIP (3), MOX (3), CLR (1), DOX (1), MIN (1)	AMC (12), CRO (10), CTX (9), FEP (4), IMI (12), GEN (6), CIP (7), MOX (6), CLR (7), DOX (10), MIN (10)	Broth microdilution	NM	[52]
107-141	NM	NM	NM	NM	NM	Spain	*16S RNA*	AMC (3), IMI (6), TOB (31), CIP (21), LZD (35), MIN (7)	AMK (34), SXT (30),	AMC (32), CTX (35), IMI (29), AMK (1), TOB (4), CIP (14), SXT (5), ERY (35), MIN (28)	Etest	NM	[53]

AMC: amoxicillin clavulanic acid; AMS: ampicillin/sulbactam; CRO: ceftriaxone; CTX: cefotaxime; FEP: cefepime; IMI: imipenem; MEP: meropenem; GEN: gentamicin; AMK: amikacin; TOB: tobramycin; STR: streptomycin; SXT: trimethoprim/sulfamethoxazole; GAT: gatifloxacin; MOX: moxifloxacin; LEV: levofloxacin; CIP: ciprofloxacin; CLR: clarithromycin; AZI: azithromycin; ERY: erythromycin; LZD: linezolid, DOX: doxycycline; MIN: minocycline, RIF: rifampin; TIG: tigecycline; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HIV: human immunodeficiency virus; NM: not mentioned.

Table 2. Antimicrobial susceptibility of *Nocardia otitidiscaviarum* reported in the literature.

Drug	AMC	CRO	CTX	IMI	GEN	AMK	TOB	SXT	LZD	MOX	CIP	DOX	MIN	CLR	ERY
Susceptible	1	2	3	7	21	55	26	53	47	10	10	7	17	6	0
Intermediate	0	3	1	1	0	1	1	2	0	4	7	3	3	1	1
Resistant	71	31	55	65	8	1	9	9	0	6	33	10	40	14	40
Total	72	36	59	73	29	57	36	64	47	20	50	20	60	21	41

AMC amoxicillin clavulanic acid; CRO ceftriaxone; CTX cefotaxime; IMI imipenem; GEN gentamicin; AMK amikacin; TOB tobramycin; SXT trimethoprim/sulfamethoxazole; MOX moxifloxacin; CIP ciprofloxacin; CLR clarithromycin; ERY erythromycin; LZD linezolid; DOX doxycycline; MIN minocycline.

skin and soft tissue infection (n=25, 34.7%), brain abscess (n=8, 11.1%), parapneumonic effusion/empyema (n=7, 9.72%), lymph nodal involvement (n=3, 4.17%), septic arthritis (n=3, 4.17%), ocular infection (n=3, 4.17%), osteomyelitis (n=1, 1.39%), extraperitoneal mass (n=1, 1.39%) and bacteremia (n=1, 1.39%). 7 patients (9.72%) presented with disseminated disease.

Table 2 shows the commonest antimicrobial agents tested. We included agents with at least 20 isolates tested, where susceptibilities were reported specifically to be sensitive, intermediate or resistant only. The most susceptible agents included linezolid (n=47, 100.0%), amikacin (n=55, 96.5%), trimethoprim/sulfamethoxazole (n=53, 82.8%), gentamicin (n=21, 72.4%) and tobramycin (n=26, 72.2%). Beta-lactam antimicrobial agents exhibited high rates of resistance against this species, with

98.6% for amoxicillin clavulanic acid, 93.2% for cefotaxime, 89.0% for imipenem and 86.1% for ceftriaxone.

In one of the largest retrospective study of nocardiosis with 113 patients proven with Nocardial infections, the commonest implicated species included *Nocardia brasilensis* (*n*=54, 47.8%), *Nocardia asteroides* (*n*=36, 31.8%), *Nocardia farcinica* (*n*=7, 6.2%), *Nocardia flavorosea* (*n*=4, 3.5%), and *N. otitidiscaviarum* (*n*=3, 2.7%). Cutaneous infection was the commonest presentation in 64 patients (56.6%), followed by pulmonary infection in 38 (33.6%) and brain abscesses in 7 patients (6.2%). Eight patients (7.1%) presented with disseminated infection, with 5 secondary to *Nocardia asteroides* and 3 secondary to *Nocardia farcinica*. Mortality in this series was 8.0%[19]. We report the largest series of cases of *N. otitidiscaviarum* infection reported over the course of 25 years, in which pulmonary involvement appear the commonest. The case fatality rate in our series appears much higher at 16.3%, likely due to more cases of pneumonia and brain abscesses reported. Indeed, amongst the eight cases of mortality in our series, six patients had pulmonary involvement only and two had brain abscesses.

Based on a Spanish series of 35 strains of *N. otitidiscaviarum*, beta-lactam resistance rates appeared to be high, which is consistent with our series. Among three beta-lactams tested, including amoxicillin/clavulanate, cefotaxime, and imipenem, resistance ranged from 82.9% to 100.0%. This contrasts with other commoner Nocardial species that are relatively more beta-lactam susceptible. For example, *Nocardia cyriacigeorgica*, which is the commonest Nocardial isolate in this series, exhibits resistance to cefotaxime and imipenem in only 2.8% of the cases[53]. Given the significant associated morbidity and mortality, and that susceptibility results take time to return, early identification of the causative Nocardial species plays a huge role in targeting an appropriate initial empiric therapy. In general, the treatment of disseminated nocardiosis entails a combination systemic antimicrobial therapy for a protracted duration. Currently, no prospective trials are available to guide effective therapy. For severe infections secondary to *N. otitidiscaviarum*, we suggest initial combination therapy with linezolid, amikacin and trimethoprim/sulfamethoxazole until susceptibility results return.

There are current no interpretative breakpoints from the Clinical &Laboratory Standards Institute for the use of tigecycline for nocardiosis. In a case series of fifteen cases of nocardiosis reported by Maraki *et al*[24] the minimal inhibitory concentration (MIC_{90}) range of all isolates are at most 0.19 g/mL, including four isolates of *N. otitidiscaviarum*. In Lai *et al*'s study, tigecycline appears most effective for *Nocardia brasiliensis* and *Nocardia puris*, with MIC values of ⩽8 μg/mL against all of the tested isolates[51]. Our patient received tigecycline together with linezolid and trimethoprim/sulfamethoxazole as part of a combination therapy for disseminated nocardiosis with clinico-radiological improvement. These emerging data potentially suggests tigecycline as a possible option in the treatment of nocardiosis.

We present an interesting case of disseminated nocardiosis secondary to a rare species of *Nocardia*, treated with combination tigecycline, linezolid and trimethoprim/sulfamethoxazole. Awareness of the possible risk factors for this infection is crucial to suspecting this disease, which can present in a widely diverse manner, virtually involving any organ. Early identification of the causative species and susceptibility results is crucial given the diverse resistance patterns amongst various *Nocardia* species.

Conflict of interest statement

We declare that we have no conflict of interest.

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