

# ***Nocardia abscessus* Cutaneous Abscess: A Case Report and Review of the Literature**

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We describe a cutaneous abscess caused by *Nocardia abscessus* in a previously healthy woman. A 74-year-old woman presented with recurrent bullae on her left forearm that developed 1 week prior and was initially suspected to be a cutaneous infection with *Mycobacteria* or *Tinea corporis*. Histopathologically, the skin lesion formed an abscess. A smear revealed a few branched Gram-positive filamentous microorganisms that formed a creamy white colony on a blood agar plate after incubation for 3 days. The colony tested negative on acid-fast bacilli (AFB) staining, but was positive on modified AFB staining. The

isolate was confirmed to be *N. abscessus* by 16S rRNA sequencing analysis. The isolate was susceptible to trimethoprim-sulfamethoxazole, amikacin, cefotaxime and erythromycin but resistant to penicillin. The patient was treated with clarithromycin but subsequently lost to follow-up. To the best of our knowledge, this is the first report of a human cutaneous infection with *N. abscessus* in Korea. (**Ann Clin Microbiol** 2018;21:64-67)

**Key Words:** Cutaneous abscess, *Nocardia abscessus*, 16S rRNA sequence

## **INTRODUCTION**

*Nocardia* are aerobic, branched, Gram-positive bacteria that are ubiquitous in the soil, and that cause various forms of disease in humans, including pulmonary, systemic, extra-pulmonary, cutaneous, and central nervous system nocardiosis [1]. Infection with *Nocardia* species usually occurs through inhalation or direct cutaneous inoculation of the organism. Cutaneous infection acquired by direct inoculation typically presents as a localized nodular process in immunocompetent hosts [2]. However, systemic infection is frequently observed in immunocompromised hosts and is associated with a high mortality rate. *Nocardia abscessus*, previously known as *Nocardia asteroides* type 1, reportedly causes human pulmonary infection, brain abscess [3], pericarditis and soft tissue infection [4]. To the best of our knowledge, only one case of human infection in a 29-year-old female having infected with *N. asteroides* type I isolated from her lung abscess has been reported in Korea [5]. However, no cutaneous infection by *N. abscessus* has been reported in Korea.

We describe a forearm abscess due to *N. abscessus* in immunocompetent patient, which was initially suspected to be cutaneous infection with *Mycobacterium* or *Tinea corporis*.

## **CASE REPORT**

A previously healthy 74-year-old woman presented with recurrent forearm bullae that had developed 1 week prior. Her vital signs were stable, with the exception of her body temperature (37.2°C). Laboratory data tests indicated a white blood cell count of 7,910/ $\mu$ L with 82.3% neutrophil, a hemoglobin level of 8.4 g/dL, and a platelet count of 223,000/ $\mu$ L. The level of C-reactive protein (CRP) was 0.28 mg/dL. Renal and liver blood chemistry tests were within reference ranges. Her chest radiography revealed no active lesion.

The culture for bacteria and fungi and skin biopsy at the lesion site in left forearm were carried out. Histopathologically, an abscess had formed, but staining results (Gram, periodic acid-Schiff, and acid-fast-bacilli [AFB]) did not indicate the

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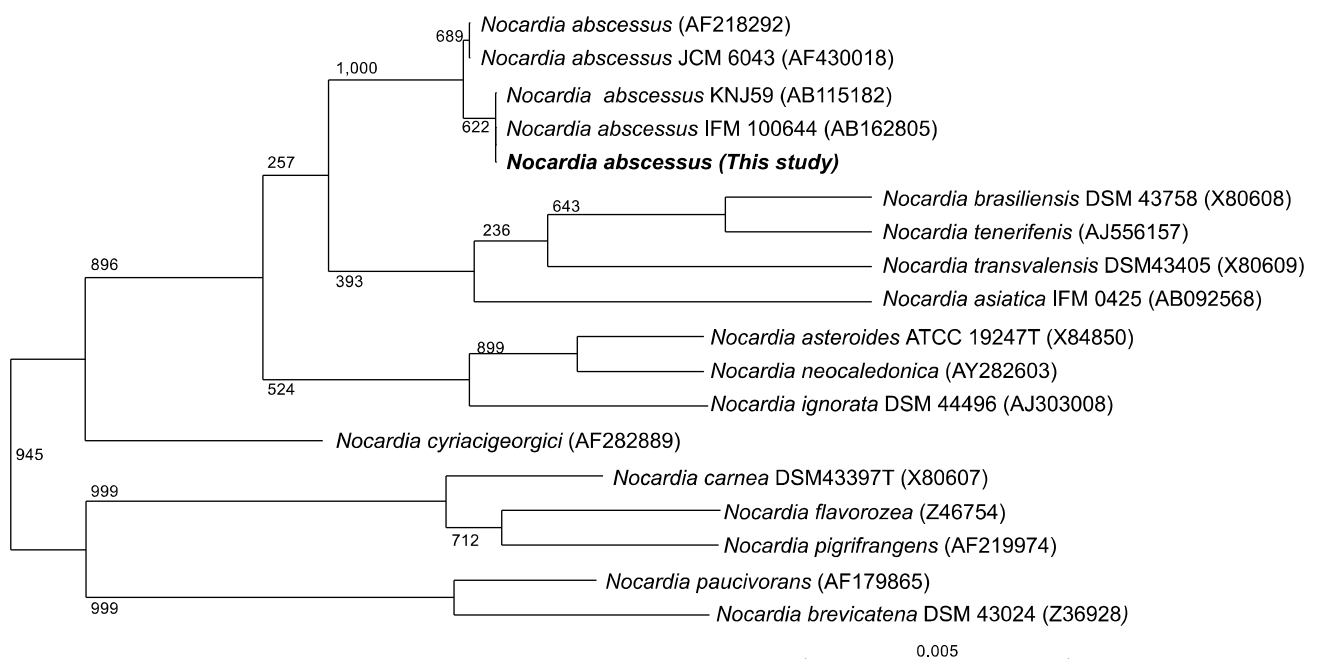
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presence of microorganisms. However, microscopic examination of the smear revealed filamentous to rod-shaped bacteria stained with gram-positive bacteria; these stained partially positive in modified Ziehl-Neelson acid-fast staining. Creamy white colonies with white aerial hyphae developed after incubation on Blood Agar Plate (BAP) agar for 3 days. This suggested the presence of *Nocardia* species. To identify the microorganism to species level, we carried out 16S rRNA sequencing (1,362 bp), which indicated 100% similarity with *N. abscessus* strains (GenBank accession number AB115182, AB162805). The phylogenetic relationships of isolate CBU 05/1969 with other related *Nocardia* strains based on 16S rRNA sequence (27F: AGA GTT TGA TCM TGG CTC AG, 1492R: TAC GGY TAC CTT GTT ACG ACT T) are shown in Fig. 1. The minimal inhibitory concentration was 1.5  $\mu\text{g/mL}$  for trimethoprim/sulfamethoxazole (SXT), 0.125  $\mu\text{g/mL}$  for amikacin, 1.5  $\mu\text{g/mL}$  for cefotaxime, 0.25  $\mu\text{g/mL}$  for erythromycin, 0.032  $\mu\text{g/mL}$  for imipenem [6], 1  $\mu\text{g/mL}$  for penicillin, 24  $\mu\text{g/mL}$  for vancomycin as determined in E-test (bioMérieux Inc., Durham, NC, USA). The patient was initially treated with clarithromycin and subsequently lost to follow-up.

## DISCUSSION

*Nocardia* species are aerosolized in dust; consequently, the respiratory tract is the main portal of entry [7]. However, direct inoculation of the skin and subcutaneous tissues can cause primary cutaneous infection, which typically presents as a localized nodular process with abscess formation. The course of infection is closely related to the immune competence of the host; infections in immunocompetent hosts are mostly chronic and localized to a single organ or region. Primary cutaneous nocardiosis usually occurs following traumatic introduction into the skin by a thorn, puncture wound, or animal scratch [1]. The cause of the infection was not clear in this case, but direct inoculation by traumatic introduction such as garden or farm work likely caused the infection. Although a few cutaneous infections by *N. asteroides*, *Nocardia otitidiscaviarum*, and *N. abscessus* have been reported, most cases are caused by *Nocardia brasiliensis*. In Korea, a few cases of cutaneous infections by *N. asteroides* or *N. brasiliensis*, but none by *N. abscessus*, have been reported (Table 1) [8-14]. Cutaneous nocardiosis is underdiagnosed because of the relatively slow growth of the organism, leading to failure of isolation [1]. Moreover, *N. abscessus* was only recently classified in the year 2000 [15], and cutaneous infection by this organism may be rare. Indeed, primary



**Fig. 1.** Phylogenetic tree of the current isolate (CBU 05/1969; 1,362 bp) and *Nocardia* species. The 16S rRNA gene sequences of *Nocardia* species available in GenBank were aligned using CLUSTAL V and the phylogenetic tree was generated by the neighbor-joining method. Bootstrap values (%) are shown near their corresponding branches; '0.1' indicates 0.1 nucleotide substitutions per site.

**Table 1.** Clinical characteristics and diagnostic tools for the patients with primary cutaneous Nocardiosis in Korea

Pathogen	Age/ sex	Subtype	Predisposing factors	Underlying disease	Diagnostic tools	Treatment regimen
<i>N. asteroides</i> [8]	42/F	LC	Traumatic injury	No	Biochemical	TMP/SXT, 6 m
<i>N. brasiliensis</i> [9]	64/M	SC	Chemotherapy	Thymoma	16S rRNA	TMP/SXT+IMP+AMK
<i>N. brasiliensis</i> [10]	68/M	SC	Traumatic injury	Cardiomyopathy	16S rRNA	TMP/SXT, 6 m
<i>N. brasiliensis</i> [11]	68/M	SC	Steroid injection	Cushing syndrome	16S rRNA	TMP/SXT+CRO, 3 m
<i>N. brasiliensis</i> [12]	56/M	LC	Prednisolone/chemotherapy	Lung cancer	16S rRNA	TMP/SXT, 6 m
<i>N. farcinica</i> [13]	67/M	Mycetoma	Not described	DM	16S rRNA	CPD, 4 w+Surgery
<i>N. nova</i> [14]	51/M	LC	Immunosuppressive agents	ESRD	16S rRNA+secA1	CRO, 9 w & TMP/SXT, 4 m
<i>N. abscessus</i> *	74/F	SC		Unknown	16S rRNA	CLM 2 w+Cryoth

Abbreviations: M, male; F, female; LC, lymphocutaneous; SC, superficial cutaneous; DM, diabetes mellitus; ESRD, end stage of renal disease; 16S rRNA, 16S ribosomal RNA sequencing analysis; secA1, secA1 sequence; TMP/SXT, trimethoprim/sulfamethoxazole; IMP, imipenem; AMK, amikacin; CRO, ceftriaxone; CPD, cefpodoxime; CLM, clarithromycin; Cryoth, Cryotherapy; m, month; w, week.

\*Present study.

cutaneous nocardiosis is likely considerably more common than is generally appreciated [1].

The clinical findings of nocardiosis, including cutaneous cases, are nonspecific, and cases may be mistaken for other bacterial infections including actinomycosis and tuberculosis as well as fungal infections and malignancies that affect multiple systems. Awareness of the possibility of nocardiosis can expedite the diagnostic work-up, particularly in patients with predisposing factors or who are immunocompromised. Modified acid-fast and Gram staining are particularly important for a rapid presumptive diagnosis [16]. Most *Nocardia* species are Gram-positive branched rods that stain positive in acid-fast tests if a weak acid is used. Mycobacteria do not stain well with gram stain and modified acid-fast stain. Similarly, *Actinomyces* are not stained by modified acid-fast stains. Typical colonies are usually seen after 3 to 5 days and have a chalky white or cotton ball appearance because of the abundant aerial filaments [17]. Initial species identification can be performed based on biochemical reactions but this is not useful for differentiating *Nocardia* species. In some cases, species must be confirmed using a molecular technique such as 16S rRNA sequencing or PCR, which may change the initial biochemical identification. Identification of *Nocardia* to the species level is important for adjusting the antibiotic therapy, as resistance profiles differ among species [18].

As nocardiosis is rare, the most appropriate therapeutic agent, administration route, and treatment duration are unclear, but sulfonamide has been the agent of choice for more than 60 years [2]. For patients with disseminated or severe nocardiosis, combination therapy with two or more active agents (e.g., ceftriaxone, imipenem, amikacin) is usually used [2]. In primary cutaneous

nocardiosis, SXT monotherapy may be adequate or used in combination with a fluoroquinolone for deep infection or mycetoma [19]. The duration of therapy depends on the site of the lesion and the patient's immune status. Primary cutaneous nocardiosis should be treated for 1-3 months. However, cases with pulmonary and CNS involvement should be treated for  $\geq 6$  months due to the risk of recurrence [17].

In conclusion, we described a cutaneous abscess due to *N. abscessus* infection in an immunocompetent patient, which was initially suspected to be due to cutaneous *Mycobacterium* or *T. corporis* infection. To the best of our knowledge, this is first report of a human infection by *N. abscessus* in Korea. 16S rRNA sequencing is essential for identification of *Nocardia* to the species level. Accurate diagnosis may facilitate development of an effective treatment for infections by *Nocardia* species.

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=국문초록=

## *Nocardia abscessus*에 의해 발생한 피부 궤양: 증례보고 및 문헌고찰

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저자들은 이전에 건강하였던 74세 여자환자에서 *Nocardia abscessus*에 의해 발생한 피부감염을 국내에서 최초로 보고하고자 한다. 환자는 1주일 전부터 왼쪽 전완부에 반복적인 수포가 발생하여 마이코박테리아에 의한 감염 또는 체부백선을 의심하였다. 피부 병변의 조직검사에서 궤양의 형태를 보였으며 도말검사에서 사상형 그람양성균이 관찰되었다. 3일 후 우유 빛의 백색 균집락이 관찰되었으며 AFB 염색에 음성이었으나 modified AFB에 양성 결과를 나타냈다. 16S rRNA 염기서열 검사에서 *N. abscessus*와 일치하였으며 trimethoprim-sulfamethoxazole, amikacin, cefotaxime, erythromycin에 감수성이었다. Clarithromycin으로 치료를 시작하였으나 이후 본 병원을 방문하지 않았다. 저자의 확인에 의하면 이 보고는 *N. abscessus*에 의한 사람에서 피부감염의 국내 최초의 예이다. [Ann Clin Microbiol 2018;21:64-67]

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