

Case Report

Primary cutaneous nocardiosis in children

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Introduction: Reports of paediatric cases of primary cutaneous nocardiosis are rare in Japan. We report the case of a 5-year-old immunocompetent boy with primary cutaneous nocardiosis.

Case presentation: One week after injuring his left knee, the boy presented with fever, pain in the left hip joint and gait disturbance. Oral administration of cephalosporin proved ineffective, and he was not able to stand due to pain in the inguinal region. On admission, swelling of the left inguinal lymph nodes and abscess with microsatellite pustules in the left knee were found. Gram-positive bacilli with branching filaments grew in the culture from the drained pustule. They were partially acid fast on Ziehl–Neelsen staining. His symptoms improved after initiating treatment with sulbactam/cefoperazon and sulfamethoxazole/trimethoprim (TMP-SMX). *Nocardia brasiliensis* was identified from 16S rRNA gene sequencing. TMP-SMX was administered for 5 weeks, and no relapses have occurred as of the 1-year follow-up.

Conclusion: *N. brasiliensis* lives in soil and is the major cause of primary lymphocutaneous nocardiosis. A cutaneous abscess with surrounding microsatellite lesions and lymphadenopathy suggest the possibility of cutaneous nocardiosis. Because growth of *Nocardia* spp. is very slow, adequate incubation time is necessary.

Keywords: Child; cutaneous nocardiosis; *Nocardia*; *Nocardia brasiliensis*.

Received 26 January 2015

Accepted 26 July 2015

Introduction

Most nocardial infections (nocardiosis) occur in immunosuppressed and immunodeficiency individuals (Biscione *et al.*, 2005; Roberts *et al.*, 2000; Santos *et al.*, 2002; Torres *et al.*, 2002). *Nocardia* spp. are found in soil, decomposing vegetation and other organic matter, as well as in fresh and salt water. Pulmonary nocardiosis is the most common clinical presentation, because inhalation is the primary route of bacterial exposure, and this infection may spread to any area of the body. Brain abscess is seen in 15–40 % of pulmonary nocardiosis cases (Jacobs & Schutze, 2011). Secondary cutaneous nocardiosis occurs by bloodstream infection from other organs. In contrast, primary cutaneous nocardiosis results from traumatic injury with soil contamination. Primary cutaneous nocardiosis can be further divided into the following three major subtypes: lymphocutaneous type, localized type and nocardial mycetoma

(Hiruma *et al.*, 1992). Japanese paediatric cases of primary cutaneous nocardiosis are seldom seen in the English literature. To the best of our knowledge, there have only been 16 described paediatric cases of primary cutaneous nocardiosis but most have been described in Japanese (Fukuda *et al.*, 2008). *Nocardia brasiliensis* was isolated as the causative organism in each of these Japanese cases (Taguchi *et al.*, 2011). Here, we report a 5-year-old immunocompetent boy with primary cutaneous nocardiosis.

Case report

A 5-year-old Japanese boy was admitted to our hospital with a 5-day history of hip joint pain, gait disturbance and high-grade fever. His past and family histories were unremarkable. He had bruised his left knee 7 days prior to symptom onset. At his first visit to a local hospital, a blood examination showed that his white blood cell count was increased to $17.7 \times 10^3 \mu\text{l}^{-1}$ and his C-reactive protein (CRP) level was elevated to 1.8 mg dl^{-1} . Despite administration of ceftoram pivoxil, his symptoms progressed and he became unable to stand due to pain in

Abbreviations: CRP, C-reactive protein; SBT-CPZ, sulbactam-cefoperazone; TMP-SMX, sulfamethoxazole/trimethoprim.



Fig. 1. (a) Erythematous swelling of the left knee, accompanied by white maceration and erosions with shallow ulcers and satellite pustules. (b) Gram-positive bacilli with distinguishing filaments grown from the drained pus. Gram staining; magnification $\times 400$.

the left inguinal region. A physical examination showed a body temperature of 38.5°C and painful swellings in the left inguinal lymph nodes with cellulitis. Erythematous swelling of the left knee was noted, accompanied by white maceration and erosions with shallow ulcers and satellite pustules (Fig. 1a). Another blood examination showed the following: white blood cell count of $18.9 \times 10^3 \mu\text{l}^{-1}$ (65.9 % neutrophils, 22.7 % lymphocytes) and serum CRP of 5.4 mg dl^{-1} . The levels of serum immunoglobulins and complements were all normal. Blood culture yielded negative results. Ultrasonography showed several swollen lymph nodes in the left inguinal region. Magnetic resonance imaging also showed inguinal lymphadenopathy with subcutaneous oedema.

Cefazolin was initially administered intravenously on the assumption of staphylococcal or streptococcal cellulitis. On hospital day 2, the pustules on the left knee were drained and irrigated with normal saline. His fever sub-

sided to 37.4°C , but pain in the left inguinal region continued and the serum CRP level showed no significant change. Gram-positive bacilli with distinguishing filaments were grown from the drained pus, indicating actinomycetes (Fig. 1b). The bacilli showed β -lactamase production and were partially acid fast on Ziehl–Neelsen staining using 3 % hydrochloric acid alcohol as a decolorizer. As empirical pharmacotherapy, oral sulfamethoxazole-trimethoprim (TMP-SMX) and intravenous sulbactam-cefoperazone (SBT/CPZ) were started on hospital day 4. His fever subsequently subsided, the left hip joint pain disappeared and the pustules on his left knee also improved. On hospital day 7, characteristic white colonies were identified on blood agar cultures, which were covered eventually by white aerial mycelium. The bacilli did not grow under anaerobic conditions in blood agar. The patient was then discharged. After 5 weeks of treatment with TMP-SMX, the pustules on the left knee were completely resolved. No recurrence has been seen as of the 1-year follow-up. *N. brasiliensis* (IFM 11662) was identified from 16S rRNA gene sequencing (Fig. 2). The 16S rRNA gene was amplified by PCR using primers 8F (5'-AGAGTTT-GATCCTGGCTCAG-3') and 1542R (5'-ACAAAGGAGGT-GATC-3'), and sequenced using the universal primer pairs 8F (5'-AGAGTTT-GATCCTGGCTCAG-3') and 691R (5'-ACCGCTACACCAGGA-3'), 520F (5'-CAGCAGCCGCGG-TAATAC-3') and 1100R (5'-GGGTTGCGCTCGTTG-3'), and 926F (5'-AAACTCAAAGGAATTGACGG-3') and 1542R (5'-ACAAAGGAGGTGATC-3') in three separate reactions. PCR was performed with a DNA thermal cycler (TaKaRa) using 35 cycles of denaturation at 94°C for 60 s, primer annealing at 60°C for 60 s and primer extension at 72°C for 120 s (Kageyama *et al.*, 2004). The cultures from the patient showed susceptibility to both TMP-SMX and SBT/CPZ in an antibiogram test using disk diffusion.

Discussion

The genus *Nocardia* belongs to the order *Actinomycetales*, which includes Gram-positive filamentous bacteria such as *Actinomyces*, *Streptomyces* and mycobacteria (Jacobs & Schutze, 2011). The genus *Nocardia* includes 104 species (<https://www.dsmz.de/>), and *N. brasiliensis* is the major cause of localized and lymphocutaneous nocardiosis in immunocompetent children, as well as a potential cause of systemic disease in immunocompromised hosts.

Primary cutaneous nocardiosis resembles soft-tissue infections by *Staphylococcus aureus* or streptococci, and non-tuberculous acid-fast bacterial disease, but this form of *Nocardia* disease usually follows a more indolent course (Futei, 2013). Trauma usually precedes symptom onset by about 1–3 weeks. Invasive *Nocardia* grows in a localized region and then spreads to regional lymph nodes. In more advanced cases, mycetoma can develop through sinus tract development.

Colonies usually appear as waxy, folded or heaped colonies at the edges within 1–2 weeks of incubation. With further incubation, the colonies develop aerial hyphae showing

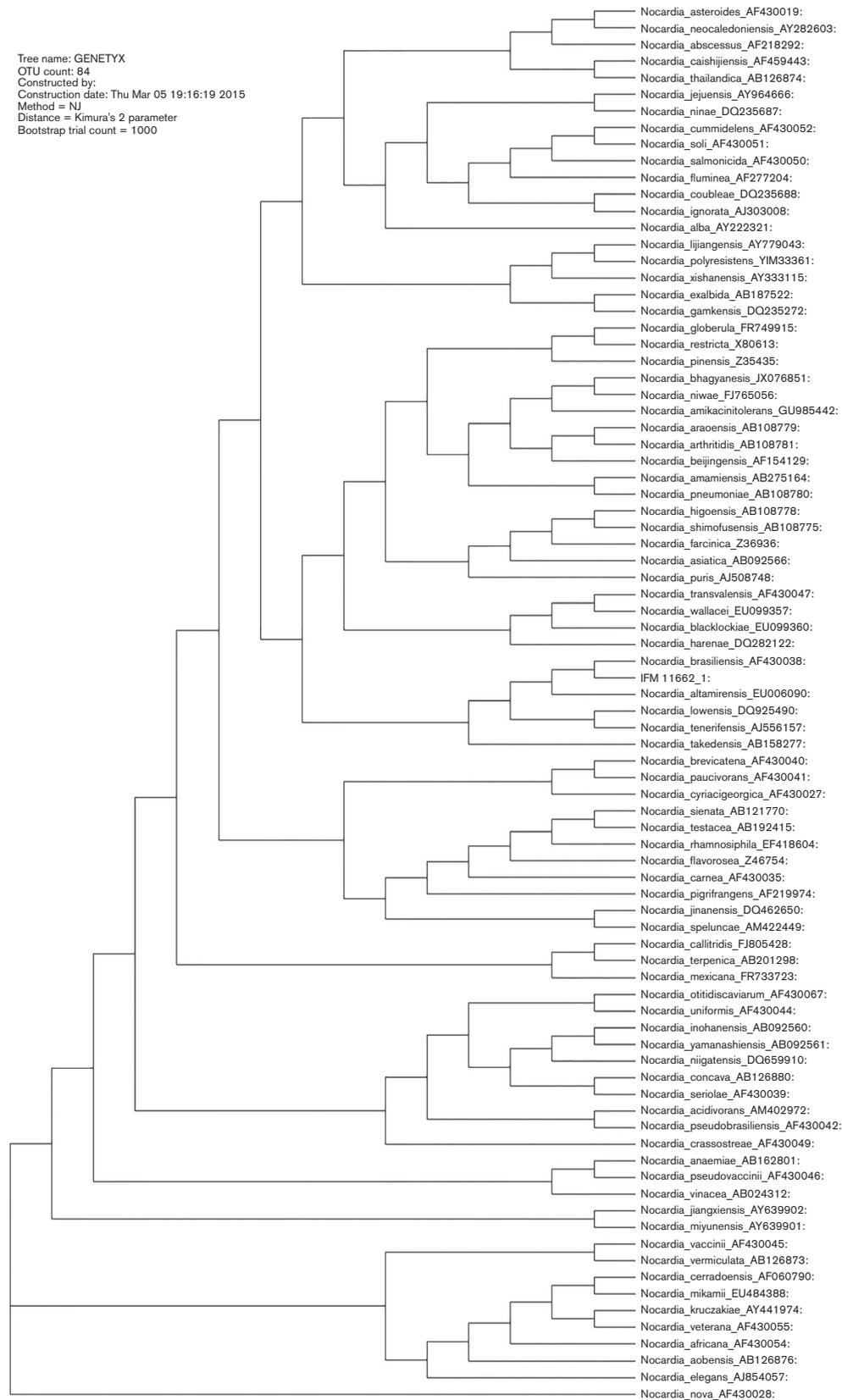


Fig. 2. Phylogenetic tree derived from 16S rRNA gene sequence analysis. The tree was recreated using the neighbour-joining method.

a white, chalky appearance (Jacobs & Schutze, 2011). *Nocardia* spp. form these characteristic colonies like other actinomycetes, but the incubation time should be prolonged because they grow very slowly (Lucas, 2005). Surgical drainage of abscesses is important in the treatment of cutaneous nocardiosis. TMP-SMX is the most commonly used pharmacotherapy but optimal antimicrobial treatment regimens have not been firmly established. *Nocardia* spp. display variability in their *in vitro* antimicrobial susceptibility patterns, and management of nocardial infections must be individualized. Superficial cutaneous infection is treated for at least 1–3 months to minimize the risk of disease relapse.

In conclusion, the possibility of cutaneous nocardiosis should be considered for cases showing abscess with satellite pustules and lymphadenopathy. Culture establishment is the basis of diagnosis and treatment decision making. We suggest an incubation time of at least 1 week, because *Nocardia* spp. grow very slowly.

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