CASE REPORT

First report of *Nocardia fusca* isolated in humans

María Ercibengoa Arana, José María Marimón Ortiz de Zarate

University Hospital Donostia, Donostia, Gipuzkoa, Spain

Correspondence to
Dr María Ercibengoa Arana, mercara@alumni.unav.es

Accepted 5 May 2015

SUMMARY

Nocardia fusca was first described in 1983; however, to date, no report of human infection has been done. In this work, we report the first case of *N. fusca* isolation during an episode of acute exacerbation in a patient with chronic obstructive pulmonary disease. The extent of the role of *N. fusca* as human pathogen still has to be determined.

BACKGROUND

Nocardia spp are found worldwide ubiquitous in the environment, forming part of the usual microbiota of soil and water as saprophytes, their main function being to degrade organic matter. Up-to-date, the National Center for Biotechnology Information (NCBI) recognises more than 100 *Nocardia* different species but there are only around 30 described as causing human infections. In the last few years, the number of *Nocardia* spp described as causing human disease is increasing, in part thanks to the development of molecular techniques for the species identification.

The first reference in literature to *Nocardia fusca* was done by Liu *et al*[1] in 1983. In this description *N. fusca* was isolated from the soil of a Chinese region but not from human beings. The articles on *N. fusca* published later by Xie *et al*[2 3] in Japan did not show any human episodes either.

The aim of this work was to describe the first human isolation of *N. fusca* in the bronchial secretion of a patient with a clinical episode of acute exacerbation of chronic obstructive pulmonary disease (COPD).

CASE PRESENTATION

N. fusca isolation was obtained from the bronchial secretion sample obtained after spontaneous expectoration from 77-year-old man with a medical history of mild COPD. The patient had right pachypleuritis as sequel of previous tuberculosis, peripheral bronchiectasis in the middle lobe with an area of subsegmental atelectasis, mild-to-moderate obstructive sleep apnoea, hypopnoea syndrome, and bad controlled arterial hypertension.

INVESTIGATIONS

In mid-December 2013 the patient attended his reference Hospital due to a worsening of his previous chronic bronchopneumopathy. An *Escherichia coli* respiratory infection was diagnosed and treated subsequently (cefditoren 400 mg orally two times per day for a week, corticosteroids and bronchodilator therapy). After a brief improvement, a second COPD exacerbation occurred on 14 January and because a heavy growth of *Pseudomonas aeruginosa* was obtained, the patient was treated with ciprofloxacin 500 mg orally two times per day for 3 weeks and inhaled steroids.

After a week of ciprofloxacin treatment, the patient remained without clear improvement so another sputum specimen was obtained. The sputum collected on 21 January, in which the *N. fusca* was isolated together with a poor growth of *P. aeruginosa* and *E. coli* in mixed culture, was of good microbiological quality: more than 25 polymorphonuclear leucocytes and less than 10 squamous epithelial cells per low (×10 magnification) power field. After 10 days, arterial blood gases were pO_2 of 54 mm Hg with O_2 saturation of 97.5% and pCO_2 of 46 mm Hg.

DIFFERENTIAL DIAGNOSIS

After 48 h incubation at 35°C on blood agar *N. fusca* showed a good growth of dry white colonies formed by Gram-positive branching bacilli that developed an orange pigmentation after 7–10 days of incubation. The catalase test was positive.

The identification of the *N. fusca* isolate was performed by sequencing a 1881 bp fragment of the 16S ribosomal RNA gene,[4] of 401 bp of the *hsp65* using the primers described by Telenti *et al*,[5] of 400 bp of the *rpoB*[6] and of 445 bp of the *secA1*.[7] The sequences of the four genes of the two isolates showed 100% similarity with the sequences of the *N. fusca* reference isolates of databases of the NCBI, leBIBI, the ribosomal database project and also with the sequences of the reference strains disposable at the National Center for Emerging and Zoonotic Infectious Disease of Centers for Disease Control and Prevention (Atlanta).

TREATMENT

N. fusca antimicrobial susceptibility testing was performed by the broth microdilution method using the Clinical and Laboratory Standards Institute guidelines[8] being susceptible to ampicillin (MIC=2 µg/mL), cefotaxime (minimum inhibitory concentration=4 µg/mL), ceftriaxone (MIC=4 µg/mL), cefepime (MIC=4 µg/mL), imipenem (MIC=2 µg/mL), tobramycin (MIC≤1 µg/mL), amikacin (MIC=4 µg/mL), ciprofloxacin (MIC=0.5 µg/mL), levofloxacin (MIC≤1 µg/mL), tigecycline (MIC≤0.25 µg/mL), linezolid (MIC≤2 µg/mL) and trimetoprim-sulfametoxazol (SXT) (≤2/38). However, *N. fusca* was non-susceptible to amoxicillin-clavulanic acid (MIC≥16 µg/mL). Ciprofloxacin MIC of 0.5 µg/mL by broth microdilution was confirmed by E test performed according to manufacturers' recommendations.

The patient was not specifically treated for the *Nocardia* isolated and continued with his ciprofloxacin treatment until 3 weeks of treatment were completed.

To cite: Ercibengoa Arana M, Marimón Ortiz de Zarate JM. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2015-209538

OUTCOME AND FOLLOW-UP

After finishing ciprofloxacin treatment, the patient returned on 10 February to his general practitioner because his COPD stable status had worsened due to a catarrhal process with symptoms of persistent cough with whitish sputum. A new sputum was collected, in which a *Streptomyces* spp were isolated but not the *N. fusca*, the *P. aeruginosa* nor the *E. coli*. The patient was treated with prednisone 30 mg/day during 7 days and short-acting bronchodilators (salbutamol) and no antibiotics. No more microbiological samples were obtained in the next month.

DISCUSSION

Respiratory infections are the most frequent clinical manifestation of nocardiosis, but *Nocardia* can also be found infecting the central nervous system, skin and other localisations.[9 10] Chronic lung diseases, specially COPD and cellular immunosuppression are among the most common underlying conditions for pulmonary nocardiosis (PN), corticosteroids therapy and other immunosuppressive therapies increasing the risk for PN.[10–12]

Clinically, PN as other respiratory infections, show unspecific clinical and radiological findings, fever, cough, expectoration and dyspnoea[11–13] being the most common clinical manifestations and alveolar infiltrates and nodules the typical radiological signs.[12–14] Besides, differentiate between colonisation and respiratory disease in PN is difficult to ascertain, especially in patients with COPD with mixed infections. *Nocardia* isolation in a respiratory specimen accompanied by clinical and radiological findings of respiratory infection is necessary, but do not always establish a diagnosis of PN.[12–14]

The patient described in the present work had COPD. The lack of eradication of *N. fusca* during the cycle of ciprofloxacin therapy despite its in vitro susceptibility is not surprising in a patient with COPD. A reduction in the blood supply in bronchial secretions and local alteration of alveolar surface, might justify the poor antimicrobial effect. The symptoms, physical examination and radiological findings of this patient were in concordance with the symptoms and findings of PN reported in the literature for patients with COPD.[10 14 15] However, we were unable to define the true value of this infection, hesitating over considering it a mere colonisation or the cause of exacerbation.

In conclusion, an infection by *N. fusca* was detected in a patient with COPD isolating the microorganism from his bronchial secretions. To the best of our knowledge, this is the first report of *N. fusca* outside Asia and also the first evidence in the literature of the isolation of *N. fusca* infecting humans, although the extent of its pathogenicity is still to be demonstrated.

Acknowledgements The authors would like to acknowledge Melissa Bell, PhD, on Public help of the CDC by the help in the confirmation of bacteria identification.

Learning points

- New molecular techniques made possible the identification of a new and clinically significant *Nocardia* spp.
- *Nocardia fusca* may act as opportunistic pathogen, although the extent of its pathogenicity is still to be demonstrated.
- The isolation of a microorganism from a non-sterile specimen does not necessarily guarantee its causative role in disease.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Liu Z, Ruan JS, Yan XC. The new species of Nocardia. *Acta Microbiol* 1983;23:298–304.
2 Xie SX, Ogawa J, Shimizu S. NAD+-dependent (S)-specific secondary alcohol dehydrogenase involved in stereoinversion of 3-pentyn-2-ol catalyzed by Nocardia fusca AKU 2123. *Biosci Biotechnol Biochem* 1999;63:1721–9.
3 Xie SX, Ogawa J, Shimizu S. Production of (R)-3-pentyn-2-ol through stereoinversion of racemic 3-pentyn-2-ol by Nocardia fusca AKU 2123. *Appl Microbiol Biotechnol* 1999;52:327–31.
4 Larruskain J, Idigoras P, Marimón JM, *et al*. Susceptibility of 186 *Nocardia* sp. isolates to 20 antimicrobial agents. *Antimicrob Agents Chemother* 2011;55:2995–8.
5 Telenti A, Marchesi F, Balz M, *et al*. Rapid identification of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. *J Clin Microbiol* 1993;31:175–8.
6 Carrasco G, Valdezate S, Garrido N, *et al*. Identification, typing, and phylogenetic relationships of the main clinical Nocardia species in Spain according to their *gyrB* and *rpoB* genes. *J Clin Microbiol* 2013;51:3602–8.
7 Conville PS, Zelazny AM, Witebsky FG. Analysis of *secA1* gene sequences for identification of Nocardia species. *J Clin Microbiol* 2006;44:2760–6.
8 National Committee for Clinical Laboratory Standards. *Susceptibility testing of mycobacteria, nocardiae, and other aerobic actinomycetes. Approved standard M24-A. National Committee for Clinical Laboratory Standards*. Wayne, PA, 2011.
9 Brown-Elliott BA, Brown JM, Conville PS, *et al*. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. *Clin Microbiol Rev* 2006;19:259–82.
10 Muñoz J, Mirelis B, Aragón LM, *et al*. Clinical and microbiological features of nocardiosis 1997–2003. *J Med Microbiol* 2007;56:545–50.
11 Martínez R, Reyes S, Menéndez R. Pulmonary nocardiosis: risk factors, clinical features, diagnosis and prognosis. *Curr Opin Pulm Med* 2008;14:219–27.
12 Chen J, Zhou H, Xu P, *et al*. Clinical and radiographic characteristics of pulmonary nocardiosis: clues to earlier diagnosis. *PLoS ONE* 2014;9:e90724.
13 Kurahara Y, Tachibana K, Tsuyuguchi K, *et al*. Pulmonary nocardiosis: a clinical analysis of 59 cases. *Respir Investig* 2014;52:160–6.
14 Minero MV, Marín M, Cercenado E, *et al*. Nocardiosis at the turn of the century. *Medicine (Baltimore)* 2009;88:250–61.
15 Garcia-Bellmunt L, Sibila O, Solanes I, *et al*. Pulmonary nocardiosis in patients with COPD: characteristics and prognostic factors. *Arch Bronconeumol* 2012;48:280–5.