Clin. Lab. 2019;65:XXX-XXX

CASE REPORT

Positive Serum Beta-D-glucan by G Test and Aspergillus Fumigatus Sputum Culture Mimic Invasive Pulmonary Aspergillosis in a Pulmonary Nocardia Patient: a Case Report and Literature Review

Yan L. Ge [1], Xiao Y. Zhu [1], Kun Hu [2], Qian Zhang [1], Wen Q. Li [1], Ci Zhang [1], Dong F. Shao [1], Ling Wang [1], Hai F. Zhang [1], Cong H. Liu [3], Yi Chen [1], Qian C. Chen [1], Jing J. Jin [1], Tian T. Xu [1], Ai S. Fu [1]

[1] *Department of Respiratory Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China*
[2] *Department of Clinical Medicine, North China University of Science and Technology, Tangshan, Hebei, China*
[3] *Department of Internal Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China*

SUMMARY

Background: **Invasive pulmonary aspergillosis and nocardia overlap in clinical and radiological presentations, so differentiating between nocardia and invasive pulmonary aspergillosis is confusing.**
Though sputum culture could distinguish between nocardia and aspergillus fumigatus, but for the ultimate diagnosis, sputum culture provided limited help. Here we report a case of a patient with positive G test and aspergillus fumigatus sputum culture mimic invasive pulmonary aspergillosis ultimately diagnosed as nocardia through bronchoalveolar lavage culture combined metagenomic next-generation sequencing (NGS).
Methods: **Bronchoalveolar lavage culture combined metagenomic NGS for infectious diseases were performed for diagnosis.**
Results: **Bronchoalveolar lavage culture combined metagenomic next-generation sequencing showed Nocardia Gelsenkirchen.**
Conclusions: **Positive G test and sputum culture were not specific, while bronchoalveolar lavage culture and NGS gave more information for a differential diagnosis between nocardia and aspergillus fumigatus.**
(Clin. Lab. 2019;65:xx-xx. DOI: 10.7754/Clin.Lab.2018.181105)

Correspondence:
Yan L. Ge
Department of Respiratory Medicine
North China University of Science and
Technology Affiliated Hospital
Jianshe Road 73
063000, Tangshan, Hebei
China
Email: geyanlei1983@qq.com

Ai S. Fu
Department of Respiratory Medicine
North China University of Science and
Technology Affiliated Hospital
Jianshe Road 73
063000, Tangshan, Hebei
China
Email: maxfas@163.com

KEY WORDS

invasive pulmonary aspergillosis, nocardia, NGS, alveolar lavage culture

Case Report accepted December 1, 2018

CASE PRESENTATION

Nocardia species belonging to filamentous bacteria are commonly confusing and difficult to diagnose in routine sputum practice because they share many overlapping cytomorphological features (thin, beaded, branching, Gram-positive [1]) with other genera, for example, actinomyces [2-4]. Although sputum culture could distinguish between nocardia and aspergillus fumigatus, however for the ultimate diagnosis, sputum culture provided limited help. On the one hand, nocardia grows very slowly, sometimes, routine sputum practice could get a false negative result and, on the other hand, sputum culture is not the golden criteria for invasive pulmonary aspergillosis [5-7]. Meanwhile, invasive pulmonary aspergillosis and nocardia overlap in clinical and radiological presentations, so differentiating between nocardia and invasive pulmonary aspergillosis is confusing [8,9]. Invasive pulmonary aspergillosis is an important cause of life-threatening infection in patients, especially those in immunocompromised status, so when patients show evidence of susceptible invasive pulmonary aspergillosis, physicians usually are prone to give powerful anti-fungal therapy [10,11]. We report a case of susceptible invasive pulmonary aspergillosis in a diabetes patient who received anti-fungal therapy for two months with progressive radiological presentations ultimately diagnosed as nocardia through bronchoalveolar lavage culture combined with metagenomic NGS.

A 53-year-old female non-smoker diabetes patient was admitted in our respiratory department complaining of shortness of breath and fever for 2 weeks on 15 January 2017. The maximum body temperature was 39.0°C and did not drop to normal until the use oral non-steroidal drugs. She had associated symptoms including cough and yellow sputum, but without chest pain or hemoptysis. The laboratory tests showed serum beta-D-glucan by G test and aspergillus fumigatus sputum culture were positive, the chest computed tomography (CT) scan demonstrated multiple consolidations, ground-glass shadow, tracheobronchial wall thickening in bilateral lung (upper lobe and middle lobe of right lung, upper lobe and ligule of left lung) (Figure1A - D). So, the patient was diagnosed with invasive pulmonary aspergillosis and was treated with anti-fungal medication for two months. Following two months of anti-fungal treatment, she still had intermittent fever, the maximum body temperature was 38.0°C and did not drop to normal without treatment. She had not received a chest CT scan in those two months until she felt gradual aggravation of dyspnea. She was admitted due to dyspnea and the chest CT scan showed aggravation of the original lesion, especially in the middle lobe of the right lung. A new cavity appeared in the ligule of the left lung (Figure 1E - H). She had undergone bronchoalveolar lavage on the day she was admitted. No obvious abnormality was found under bronchoscope. Bronchoalveolar lavage culture combined with metagenomic NGS was performed. Bronchoalveolar lavage culture and metagenomic NGS culture manifested Nocardia Gelsenkirchen. She was then started on sulfamethoxazole and the symptoms of dyspnea and fever obviously improved after one month of treatment. The chest CT scan showed lung lesions improved significantly (Figure 1E - H).

DISCUSSION

Nocardia species are aerobic Gram-positive filamentous bacteria, which are recognized as one of the ubiquitous environmental bacteria, which can cause suppurative lung, central nervous system, and skin infections when humans, especially immunocompromised individuals, are exposed to these Actinobacteria stems from direct contact with contaminated environmental matrices [12]. Nocardia could cause multiple organ lesion. Pulmonary nocardiosis are common lesion, the clinical presentation include cough, dyspnea, symptoms similar to tuberculosis poisoning, such as fever, night sweats, weight loss, and fatigue and so on [13]. The chest radiograph usually shows nodular and/or consolidation infiltrate, sometimes co-existing cavitary lesions and pleural effusions. Consolidation infiltrate combined cavitary lesions are also common lesions in invasive pulmonary aspergillosis. Risk factors for invasive pulmonary aspergillosis and pulmonary nocardiosis are acquisition of infection include depressed cell immunity [14]. Though positive G test and sputum culture could provide evidence for invasive pulmonary aspergillosis, especially in immunocompromised individuals, while both of them were not a specific index. At the same time, invasive pulmonary aspergillosis and nocardia overlap in clinical and radiological presentations, so differentiating between nocardia and aspergillosis is confusing [15]. In this patient, invasive pulmonary aspergillosis mimicked pulmonary nocardia and led to a delay in correct diagnosis causing the patient tremendous economic burden due to the expensive antifungal drug. Bronchoalveolar lavage culture and NGS can provide more information for the differential diagnosis between nocardia and aspergillus fumigatus. After the bronchoalveolar lavage culture and NGS showed consistent results, the patient received precise treatment, and the patient's symptoms and chest CT scan improved significantly.

For this patient, our lesson is that we considered positive G test and sputum culture as diagnostic criteria for invasive pulmonary aspergillosis. For this patient, both were not a specific index, while according the results, we started administration of expensive anti-fungal drugs for two months, but did not arrange the chest CT timely to assess the effect of anti-fungal therapy.

CONCLUSION

Though positive G test and sputum culture could provide evidence for invasive pulmonary aspergillosis, especially in immunocompromised individuals, they did

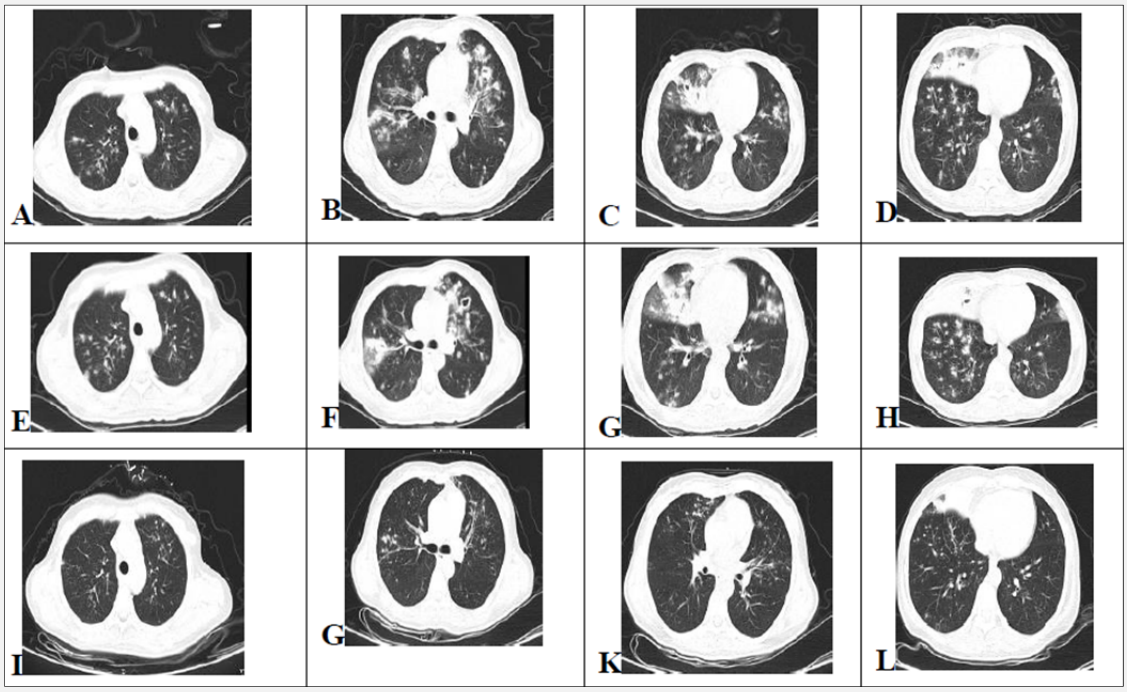

Figure 1. Patient imaging results.

The chest CT scan demonstrated multiple consolidation, ground-glass shadow, tracheobronchial wall thickening in bilateral lung (upper lobe and middle lobe of right lung, upper lobe and ligule of left lung) (Figure1A - D). The chest CT scan showed aggravation of original lesion, especially in the middle lobe of right lung, a new cavity appeared in the ligule of the left lung after two months of anti-fungal treatment. (Figure 1E - H). The chest CT scan showed lung lesions improved significantly after one month of administration of sulfamethoxazole (Figure 1E - H).

not provide a specific index. Bronchoalveolar lavage culture and NGS can give more information for a differential diagnosis between nocardia and aspergillus fumigatus.

Acknowledgment:
We thank the other members of the Department of Respiratory Medicine of North China University of Science and Technology Affiliated Hospital for their critical comments.

Declaration of Interest:
No conflicts of interest.

References:

1. Fatahi-Bafghi M, Heidarieh P, Rasouli-Nasab M, Habibnia S, Hashemi-Shahraki A, Eshraghi SS. Comparison of restriction enzyme pattern analysis and full gene sequencing of 16S rRNA gene for Nocardia species identification, the first report of Nocardia transvalensis isolated of sputum from Iran, and review of the literature. Antonie Van Leeuwenhoek. 2016;109:1285-98 (PMID: 27613736).

2. Tamakoshi J, Kimura R, Takahashi K, Saito H. Pulmonary Reinfection by Nocardia in an Immunocompetent Patient with Bronchiectasis. Intern Med. 2018;57:2581-4 (PMID: 29607954).

3. Yasuike M, Nishiki I, Iwasaki Y, et al. Analysis of the complete genome sequence of Nocardia seriolae UTF1, the causative agent of fish nocardiosis: The first reference genome sequence of the fish pathogenic Nocardia species. PLoS One. 2017;12:e0173198 (PMID: 28257489).

4. Wei M, Wang P, Qu J, et al. Identification and antimicrobial susceptibility of clinical Nocardia species in a tertiary hospital in China. J Glob Antimicrob Resist. 2017;11:183-7 (PMID: 28870771).

5. Hamadani M, Benson DM, Blum W, Garzon R, Devine SM. Pulmonary Nocardia and Aspergillus co-infection in a patient with chronic graft-versus-host disease. Transpl Infect Dis. 2008;10:24-6 (PMID: 17651365).

6. Li L, Jiang Z, Shao C. Pulmonary Aspergillus Overlap Syndromes. Mycopathologia. 2018;183:431-8 (PMID: 29067630).

7. Sehgal IS, Choudhary H, Dhooria S, et al. Diagnostic cut-off of Aspergillus fumigatus-specific IgG in the diagnosis of chronic pulmonary aspergillosis. Mycoses. 2018;61:770-6 (PMID: 29920796).

8. Joung MK, Kong DS, Song JH, Peck KR. Concurrent nocardia related brain abscess and semi-invasive pulmonary aspergillosis in an immunocompetent patient. J Korean Neurosurg Soc. 2011; 49:305-7 (PMID: 21716631).

9. McCallum BJ, Amrol D, Horvath J, Inayat N, Talwani R. A case of allergic bronchopulmonary aspergillosis leading to pneumonia with unusual organisms. South Med J. 2005;98:1135-8 (PMID: 16351036).

10. Wang T, Zhang T, Meng T, et al. A strategy for designing voriconazole dosage regimens to prevent invasive pulmonary aspergillosis based on a cellular pharmacokinetics/pharmacodynamics model. J Transl Med. 2018;16:157 (PMID: 29880050).

11. Blanchard E, Gabriel F, Jeanne-Leroyer C, Servant V, Dumas PY. [Invasive pulmonary aspergillosis]. Rev Mal Respir. 2018; 35:171-87 (PMID: 29478757).

12. Eschapasse E, Hussenet C, Bergeron A, Lebeaux D. [Respiratory infections caused by slow-growing bacteria: Nocardia, Actinomyces, Rhodococcus]. Rev Mal Respir. 2017;34:661-71 (PMID: 28688759).

13. Le Coustumier EM, Denes E, Martin C, Weinbreck P. [Nocardiosis: A retrospective case series of 19 patients]. Rev Med Interne. 2017;38:81-9 (PMID: 27659745).

14. Khadka P, Basnet RB, Rijal BP, Sherchand JB. Correction to: Pulmonary nocardiosis masquerading renascence of tuberculosis in an immunocompetent host: a case report from Nepal. BMC Res Notes. 2018;11:505 (PMID: 30045768).

15. SAl-Anazi KA, Aljurf MD, Al-Mohareb FI, Al-Dabal L, Zaitoni M, Halim M. Successful management of invasive pulmonary nocardiosis and aspergillosis in a patient with T-cell lymphoma: a case report. Clin Med Case Rep. 2008;165-71 (PMID: 24179349).