Case Report

Potential therapeutic effect of ninjinyoeito for the treatment of pulmonary nontuberculous mycobacterial infections: A case report

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Abstract

A 40-year-old man presented with refractory pulmonary *Mycobacterium avium* complex infection, despite administration of antituberculous drugs for 2 years. We administered ninjinyoeito (NYT) to the patient, who experienced weight gain and demonstrated marked reduction in the lung cavity lesions. Thus, the traditional Japanese medicine, NYT could serve as an adjunct to the conventional pharmacotherapy for pulmonary *Mycobacterium avium* complex infection.

Keywords: *Mycobacterium avium* complex infection, ninjinyoeito, nontuberculous mycobacterial disease, traditional Japanese medicine

Introduction

Nontuberculous mycobacterial disease is caused by infection with weakly pathogenic acid-fast bacilli, other than *Mycobacterium tuberculosis*, which can be contracted from the natural environment, including soil, water, dust, etc. Therefore, the decrease in local and systemic resistance of the host is an important cause for the onset of infection.[1] We encountered a case which could potentially benefit from the therapeutic effects of ninjinyoeito (NYT) (Ren Shem Yang Rong Tang) for the treatment of nontuberculous mycobacterial pulmonary infection.

Case

Chest computed tomography revealed a cavity in the upper right lung in a 40-year-old man. A diagnosis of pulmonary *Mycobacterium avium* complex infection was made with the help of bronchoalveolar lavage culture. The patient was prescribed ethambutol, rifampicin, and isoniazid for 1 year, and a combination of four antituberculous drugs: rifampicin, ethambutol, clarithromycin, and levofloxacin, for the subsequent year, which eventually proved to be ineffective. The patient's height was 180 cm, weight was 60 kg, and body mass index was 18.5 kg/m^2. The patient complained of general malaise and anorexia. Subsequently, 7.5 g/day NYT extract (Kracie Co., Ltd, Tokyo, Japan), which is a Kampo preparation used for the treatment of general fatigue and loss of appetite, was administered.[2] Reports indicate that this medication is effective for treating infections caused by *Mycobacterium fortuitum*,[2,3] when administered in combination with antituberculous drugs. Six months after treatment with NYT, the patient's body mass index increased to 22 kg/m^2, and a subsequent chest computed tomography scan revealed significant reduction in the size of the lung cavity. The patient discontinued the use of the antituberculosis drugs and the disease did not recur [Figure 1a, b].

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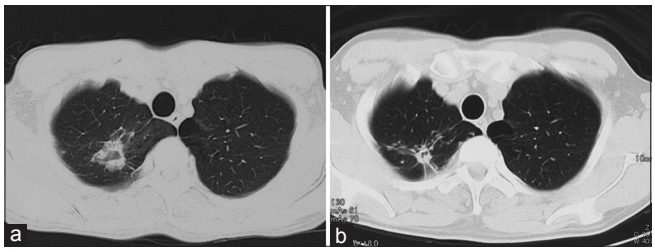

Figure 1: Chest computed tomography images: (a) before Ninjinyoeito administration, and (b) 6 months after administration of Ninjinyoeito

The patient continued taking NYT for one and a half years without adverse effects and discontinued it subsequently. No lung cavities have been observed in the patient since treatment with a combination of NYT and antituberculosis drugs.

Discussion

NYT has been used for treating respiratory tract infections for 900 years in traditional Japanese medicine. Moreover, clinical and laboratory studies have reported its efficacy in treating mycobacterial infections.[4] The efficacy of NYT for treating infections was demonstrated by *P. aeruginosa* and *Listeria* infection models.[5,6] It is speculated that NYT has a wide range of actions against the biological defenses of pathogenic microbes. It is thought that the destruction of mycobacteria by the activation of the alveolar macrophages is essential for the healing of mycobacterial infections.[7] However, elevation in interleukins 1 and 6 and granulocyte-macrophage colony-stimulating factor and an increased action of macrophages in the peripheral blood have been reported in the Listeria infection model after exposure to NYT. Moreover, it is possible that NYT promotes the activation of alveolar macrophages in acid-fast bacterial infections, which was probably the mechanism of action of NYT in this case. Immunological assessments were not performed for this patient, and the impact of NYT on the patient's general condition was not assessed, except for the resultant significant weight gain. Weight gain is an important indicator of improvement in the general health status. NYT has also been reported to reduce fatigue and improve the quality of life in patients undergoing dialysis and cancer survivors.[8,9] NYT may have a wide range of effects to improve patient conditions. Therefore, it can be used as an adjunct in the treatment of nontuberculous mycobacterial infection.

The primary initial symptoms of nontuberculous mycobacteriosis, which include coughing and expectoration are nonspecific and are often encountered by primary care physicians. It has been reported that the onus of treating nontuberculous mycobacteria is shifting from primary care physicians to respiratory specialists in recent years, owing to the complexity of treatment for nontuberculous mycobacteriosis.[10] However, primary care physicians still play an important role and will continue to do so. NYT can be used safely in patients with nontuberculous mycobacterial infections, and can halt or improve the progression of the disease, with fewer side effects. Therefore, we think NYT is a useful drug for primary care physicians. We think that using NYT as an adjunct to antituberculous drugs may enhance their therapeutic effect.

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Declaration of patient consent

The author certifies that all appropriate patient consent forms were obtained. The patient has provided consent for the publication of the radiographic images and other clinical information in the journal. The patient understands that his name and initials will not be published, and that efforts will be made to conceal his identity, but that anonymity cannot be guaranteed.

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Conflicts of interest

T. Nogami received lecture fees from Tsumura and Co, and T. Nogami's affiliation gained a research grant from Tsumura and Co., although unrelated to this case report.

References

1. Daley CL. Mycobacterium avium complex disease. Microbiol Spectr 2017;5:2-3.
2. Miyano K, Nonaka M, Uzu M, Ohshima K, Uezono Y. Multifunctional actions of ninjinyoeito, a Japanese kampo medicine: Accumulated scientific evidence based on experiments with cells and animal models, and clinical studies. Frontr Nutr 2018;5:93.
3. Nogami T, Sekiya N, Mitsuma T, Yamaguchi T. [A case of pulmonary Mycobacterium fortuitum infection successfully treated with kampo treatments]. Kekkaku 2006;81:525-9. [Article in Japanese]
4. Tomioka H, Tatano Y, Shimizu T, Sano C. Clinical and basic studies on therapeutic efficacy of herbal medicines against Mycobacterial infections. Medicines (Basel) 2019;6. pii: E67. doi: 10.3390/medicines6020067.
5. Miura S, Takimoto H, Yoshikai Y, Kumazawa Y, Yamada A, Nomoto K. Protective effect of Ren-shen-yang-rong-tang (Ninjin-youei-to) in mice with drug-induced leukopenia against *pseudomonas aeruginosa* infection. Int J Immunopharmac 1992;14:1249-57.
6. Yonekura K, Kawakita T, Saito Y, Suzyki A, Nomoto K. Augmentation of host resistance to *Listeria monocytogenes* infection by a traditional Chinese medicine. Ren-shen-yang-rong-tang (Japanese name: Ninjin-youei-to). Immunopharmacol Immunotoxicol 1992;14:165-90.
7. Suzuki K, Lee WJ, Hashimoto T, Tanaka E, Murayama T, Amitani R, *et al.* Recombinant granulocyte-macrophage-colony-stimulating factor (GM-CSF) or tumor necrosis factor-alpha (TNF-α) activate human alveolar macrophages to inhibit growth of *Mycobacterium avium* complex. Clin Exp Immunol 1994;98:169-73.
8. Hsiao PJ, Lin KS, Chiu CC, Chen HW, Huang JS, Kao SY,

et al. Use of traditional Chinese medicine (Ren Shen Yang Rong Tang) against microinflammation in hemodialysis patients: An open-label trial. Complement Ther Med 2015;23:363-71.

9. Xu Y, Chen Y, Li P, Wang XS. Ren Shen Yangrong Tang for fatigue in cancer survivors: A phase I/II open-label study. J Altern Complement Med 2015;21:281-7.
10. Axson EL, Bloom CI, Quint JK. Nontuberculous mycobacterial disease managed within UK primary care, 2006-2016. Eur J Clin Microbiol Infect Dis 2018;37:1795-803.