

A Rare and Challenging Case of Pulmonary *Mycobacterium genavense* in an Immunocompetent Adult

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ABSTRACT

Mycobacterium genavense, a non-tuberculous mycobacterium (NTM), usually affects patients severely immunodeficient from human immunodeficiency virus (HIV) infection or any other immunocompromised states. We reported a case in a 70-year-old female with well-controlled diabetes and history of proximal cystic bronchiectasis. She presented with 2 months history of cough, haemoptysis, and night sweats of which serial sputa were positive for acid-fast bacilli and the culture repeatedly grew *M. genavense*. Treatment with rifampicin, ofloxacin, and clarithromycin was complicated with drug-induced liver injury and intractable gastrointestinal side effects. We also presented a brief review of relevant literature.

KEYWORDS: Non-tuberculous mycobacterium, *Mycobacterium genavense*, pulmonary, immunocompetent

INTRODUCTION

Mycobacterium genavense was identified as one of the non-tuberculous mycobacteria in 1992 [1]. Since then, it had been reported to cause life threatening infection in severely immunodeficient patients with human immunodeficiency virus (HIV) infection [1]. In HIV-negative patients, disseminated *M. genavense* infection had also been reported, however, these patients were usually in immunocompromised state, such as those with long-standing chronic lymphocytic leukaemia [2], those undergoing immunosuppressive therapy [3] and solid organ transplant recipients [4]. To the best of our knowledge, there had only been 2 cases of *M. genavense* infection reported in healthy individuals [5, 6].

CASE PRESENTATION

A 70-year-old lady with type 2 diabetes mellitus (HbA1c of 6.7%), ischaemic heart disease, bronchial asthma (controlled with fluticasone/salmeterol inhaler combination and theophylline), and history of right total mastectomy with chemotherapy for right breast

cancer 20 years ago, was referred to respiratory team in December 2013 with an incidental finding of a cavitating left lung mass found during cardiac MRI. Subsequent CT thorax showed a lung lesion with multiple cavities (see picture). Bronchial washing and bronchoalveolar lavage were negative for acid fast bacilli, culture did not grow any organism, and cytology were negative for malignancy. Two sequential CT thorax 6-month apart showed a relatively similar lesion in size and characteristic.

A year later, she presented again with 2 months worsening cough, associated with occasional haemoptysis, night sweats, and significant weight loss. Physical examination of the lungs showed no abnormality and no cervical or axillary lymphadenopathies. Cardiovascular and abdominal examinations were unremarkable. Full blood count, liver function test and renal profile were within the normal range. Erythrocyte sedimentation rate were only slightly elevated. Screening for HIV, Hepatitis B and C were all negative. Sputum acid fast bacilli were positive 1+ on two occasions. In view of the symptoms and positive sputum smear for AFB, she was

commenced on a fixed dose combination of rifampicin, isoniazid, ethambutol, and pyrazinamide (Akurit-4). After 21 days of treatment she improved in that her weight increased and the cough frequency reduced. Sputum culture at the start of treatment confirmed *M. genavense*. Unfortunately, she developed drug induced hepatitis with intractable vomiting after 1 month of treatment with ALT 505 U/L, AST 677 U/L, total bilirubin 71 mg/dL, and GGT 196 U/L which resolved after withholding Akurit-4. She denied concurrent consumption of traditional medications or other hepatotoxic drugs.

After two months of treatment, the sputum for acid-fast bacilli was still positive. On this occasion the sputum culture again grew *M. genavense*. In view of these, we decided to re-challenge her with clarithromycin, rifampicin, and ofloxacin. Full dose of each drug (rifampicin 450mg once daily, ofloxacin 400mg twice daily and clarithromycin 500mg twice daily) was achieved within 2 months. At 3 months, sputum acid fast bacilli were still heavily positive. Molecular Line Probe Assay of her sputum sample did not detect the presence of mycobacterium gene and the Gene Xpert MTB/RIF showed no resistant organism. She developed vomiting with the medications. However, in view of the heavily positive AFB smear which grew *M. genavense* twice, and persistence of initial symptoms, we decided to continue the treatment regime under strict supervision.

In September 2015, after 9 months of uninterrupted treatment, she continued to have vomiting and dizziness, in which neither anti emetics nor adjusting the dose of the medications help to relieve her symptoms. She lost about 8 kilograms in weight due to vomiting and her quality of life was much reduced. At this point, the repeat sputum acid fast bacilli became negative and therefore a decision was made to stop the treatment. One month after stopping treatment, she felt better, the side effects subsided, her appetite improved and she gained weight by 2 kilograms. At the last clinic review about 2 years after treatment discontinuation, she remained well, and was only occasionally troubled by her asthma.

DISCUSSION

In 1992, fastidious organism of *Mycobacterium genavense* has been described to cause disseminated infections in patients infected by Human Immunodeficiency Virus (HIV) [7].

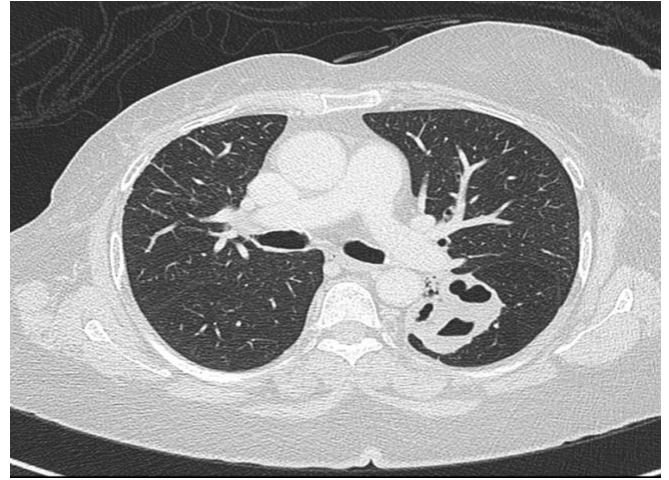


Figure 1 CT thorax showed a lung lesion with multiple cavities; some of which show air-fluid level seen, at the upper segment of the left lower lobe. This lesion measures 4.6 (AP) x 4.7 (W) x 5.9 (CC) cm.

After the introduction of anti-retroviral agents, the epidemiology of the pathogen had changed. Disseminated infections of *M. genavense* were reported in non-HIV patients who were severely immunocompromised [2-4]. Most of the patients with disseminated *M. genavense* infection have similar clinical symptoms as those of *Mycobacterium avium complex*, characterised by fever, diarrhoea, weight loss, anaemia and lymphadenopathy [8].

Mycobacterium genavense has rarely been isolated from the gastrointestinal tract of healthy individuals [9]. Hence it is important to distinguish between colonization and true infection. Two cases of *M. genavense* in healthy immunocompetent patients have been reported. The first case was reported in 1995, a 41 year old woman with severe lymphadenitis caused by a fastidious mycobacterium closely related to *M. genavense*, whose brother had died from an unidentified mycobacterial infection 20 years back [5]. The second case was reported in 2010, a case of disseminated *M. genavense* in a healthy 15 year old Japanese boy, who developed tumorous lesions in the gastrointestinal tract resulting in stenosis of ileocecal valve [6].

Our patient had symptoms suggestive of pulmonary tuberculosis. Her sputum was positive for acid fast bacilli and sputum culture grew *M. genavense* twice. She was not in an immunocompromised state. Her diabetic control was good with HbA1c of 6.7%, she required oral prednisolone only during her asthma exacerbation that occurred once or twice a year, and the chemotherapy for her breast cancer was 20 years ago. We commenced anti-tuberculous treatment and her symptoms improved. However, she could not tolerate the side effects of the treatment, hence the dilemma of her management started.

As we know, there is no standard treatment for *M. genavense* infection. In the first case by Bosquee et al, the patient responded to combination of rifabutin (150mg b.i.d.), clofazimine (100mg b.i.d.), clarithromycin (1g b.i.d.), and ethambutol (1200 mg daily) that were prescribed for 10 months [5]. In the second case, the patient responded to combination of clarithromycin, ethambutol and rifampicin (the dosage and duration were not stated in the case report) [6]. In another study on non-tuberculous mycobacterium (NTM), susceptibility testing showed that *M. genavense* is sensitive to rifampicin, fluoroquinolones, and macrolides [10]. For our patient we have decided to treat the patient with rifampicin, ofloxacin and clarithromycin.

This case illustrates the importance of identifying a rare and unique NTM infection, especially in our population with high index of tuberculosis prevalence. NTM may provide confusion in deciding our initial treatment plan for smear positive patients. Given the higher prevalence of mycobacterium tuberculosis in our population, in clinical practise, smear positive acid-fast bacilli specimens will be treated presumptively with standard anti-tuberculosis treatment for 2 months, until the culture results revealed the true nature of the Mycobacterium species.

CONCLUSION

This is the first case of pulmonary *M. genavense* infection reported in Malaysia, and it occurred in an immunocompetent patient. The treatment guidelines for *M. genavense* are not well-established, unlike other NTM such as *M. abscessus* and *M. avium complex*. The decision on the treatment option and duration has to be

tailored on case by case basis. It is important to find balance between treating the disease and managing the side effects of the treatment. Cure is not always the objective if it meant compromising the patient's wellbeing and therefore no treatment is sometimes the best option. If the disease did not compromise the patient's well-being and that the treatment caused severe side effects, one might have to consider withholding treatment and opt for watchful waiting. More data and experiences are needed to help manage infections by NTM which remains unexplored, especially in Malaysian population.

Conflict of Interest

Authors declare none.

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