Mycobacterium simiae


Hamieh and colleagues reviewed the case records of 51 patients from whom *Mycobacterium simiae* was recovered in culture at the American University of Beirut Medical Center from 2004 to 2016. The mean age of the patients was 62.7 years old and 55% were male. Underlying lung disease was present in 38%. All but 3 of the 103 isolates were recovered from sputum or bronchoalveolar lavage specimens; there were single isolates from a lung biopsy, pleural fluid, and cerebrospinal fluid (the last from the only patient with extrapulmonary infection). Of note is that Hamieh et al indicate that *M. simiae* has been the most frequently isolated non-tuberculous mycobacteria (NTM) at their center in Beirut for the last 2 decades.

None of the 17 isolates tested were susceptible to rifampin, isoniazid, ethambutol, linezolid, streptomycin, or ciprofloxacin, while 30%, 19%, and 88% were susceptible to moxifloxacin, trimethoprim-sulfamethoxazole, and amikacin, respectively. In addition, 94% were susceptible to clarithromycin and 2 of 2 isolates tested were susceptible to clofazimine. Although approximately three-fourths of patients were symptomatic, only 24 (47%) met American Thoracic Society (ATS) criteria for NTM pulmonary disease [1]. Of the patients who met ATS criteria for disease, 10 received early (not defined) treatment, most often with clarithromycin together with either trimethoprim-sulfamethoxazole or moxifloxacin, with 2 patients receiving clarithromycin and clofazimine. Of the 10, 4 had an improvement or stabilization of disease; this was, however, also true of 4 of 14 patients not meeting ATS criteria who had not received treatment.

Coolen-Allou identified 97 patients from whom *M. simiae* had been isolated at 2 university hospitals in the French overseas department of Reunion Island from 2002 to 2017. These 97 represented 15.1% of all patients from whom an NTM had been recovered during that time. A single *M. simiae* isolate was recovered from a lymph node (in a human immunodeficiency virus–infected patient with a CD4 count of 9/mm³) while the rest were from sputum, bronchoalveolar lavage fluid, or gastric aspirates. Other additional NTM were also recovered from 22.7% of patients. Most *M. simiae* isolates were resistant to rifampin (85% resistant), ethambutol (89%), and isoniazid (92%), but only 4%, 8%, and 3% were resistant to amikacin, moxifloxacin, and ciprofloxacin, respectively; no isolates were resistant to clarithromycin.

The most frequently identified radiological findings were micronodular lesions, seen in one-half of patients, and a tree-in-bud pattern, seen in one-fourth. One-half of all the patients had non–cystic fibrosis bronchiectasis. ATS criteria for pulmonary NTM disease were met by 21 (21.6%) of the patients, and 71.4% had non–cystic fibrosis bronchiectasis. Only 8 of the 21 received treatment directed at *M. simiae* infection, while 4 received regimens with the intention of treating other mycobacterial infections. All 8, however, received clarithromycin or azithromycin in combination with 1 or more additional agents, often including ethambutol, moxifloxacin, or clofazimine. Of the 7 patients who completed the planned treatment course, 3 failed therapy or subsequently relapsed.

*M. simiae* is a slow-growing photochromogen and the only NTM that is niacin-positive. Like other NTM, it is an environmental organism and has been detected in tap water. First isolated from rhesus macaques in 1965, reports of detection of *M. simiae* have emerged from the Middle East, Cuba, the United States (Arizona and Hawaii), Asia and, with the report of Coolen-Allou and colleagues, Reunion, an island in the Indian Ocean. On that island, it accounts for 15.1% of the NTM identified, with an incidence 15 times higher than in metropolitan France.

The retrospective studies examined here provide evidence consistent with previous reports indicating that the isolation of *M. simiae* from respiratory secretions is associated with disease activity in only a minority of cases. In the small proportion for whom treatment is believed to be indicated, clarithromycin or azithromycin administration (presumably together with other agents) would be predicted to be effective, since none of the isolates tested in either study were resistant to clarithromycin. The results of such therapy reported by these groups, however, suggests that such therapy is frequently ineffective. If outcomes had been assessed using very recently developed criteria for response to treatment of NTM pulmonary disease [2].

References

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Neurotropic Herpesviruses and Alzheimer’s Disease


Alois Alzheimer, who died in in 1915 at 61 years of age, suggested the possibility that his eponymous disease was caused by infection. This hypothesis has continued to be explored, particularly with regard to neurotropic herpesviruses, and recent evidence has demonstrated a pathway by which this may occur.

Readhead and colleagues examined raw genomic data derived from 3 large human “brain banks” that contained material from large numbers of patients with Alzheimer’s disease (AD), sequencing >1400 samples. While evidence of multiple viral types was present, they found that human herpes virus (HHV) nucleic acid was prominent and that HHV-6A and HHV-7 were more abundant in the brains of patients with AD than in those with other neurodegenerative disorders. Furthermore, their abundance in AD brains correlated with the patients’ recorded dementia scores. These herpesviruses were more abundant in brain regions showing early changes in AD, including the superior temporal gyrus, the anterior prefrontal cortex, and the dorsolateral prefrontal cortex.

The investigators then developed network models to evaluate the interaction between virus and host genes. Among other things, they found that a micro-ribonucleic acid, miR-155, appeared to be suppressed by HHV-6a. Furthermore, knock-out of miR-155 in a murine model of AD resulted in larger amyloid plaques and higher concentrations of amyloid-β in the brain when compared to wild-type mouse brains. The overall findings suggest that virus-derived proteins may act as transcription factors capable of controlling the expression of genes associated with AD risk.

Amyloid-β deposition in plaques is a hallmark of AD. Of importance is that amyloid-β is not an inert substance, but actually is a component of the innate immune system, acting as a host defense peptide with both antimicrobial and immunomodulating activities. While oligomerization of amyloid-β is key to these activities, dysregulated oligomerization leads to the production of harmful, non-soluble fibrils and to plaque formation.

Eimer and colleagues demonstrated in cultured neural cells that amyloid-β binds to herpes surface glycoproteins, producing fibrils that protectively entrap herpesviruses (HHV-6a, HHV-7, HSV-1). Thus, while amyloid-β is protective against these neurotropic viruses, its oligimerization in response to their presence may potentially lead to the depositing of amyloid plaques that are seen in AD.

Infection with HHV-6 and/or HHV-7 is an almost universal feature of human existence and approximately two-thirds of the world population is infected with herpes simplex viruses. Most infections, especially of HHV-6 and HHV-7, occur in infancy, raising the question of how, if these infections are related to the development of AD, to account for the marked delay in the onset of dementia. Perhaps the best known example of a delay in the progression of a neurological disease after initial infection is the occurrence of subacute sclerosing panencephalitis, which occurs in approximately 1 in 10 000 individuals infected with the measles virus, generally only becoming clinically apparent 6–15 years later [1]. In the case of AD, infection with neurotropic herpesviruses persists throughout life and the data reviewed here suggest the possibility that brain damage results from the prolonged, perhaps intermittent, innate immune response in which amyloid-β controls the virus but simultaneously causes neurological damage.

Reference


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