P1434
Poster Session V
Molecular epidemiology of viruses

GENETIC ANALYSIS OF POST-PANDEMIC INFLUENZA A(H1N1)PDM09 HAEMAGGLUTININ VIRUS VARIANTS THAT CAUSED MILD, SEVERE AND FATAL INFECTIONS IN N. GREECE

A. Melidou[1], M. Exindari[1], G. Gioula[1], N. Malisiovas[1]

[1]Microbiology Dept. Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

Objectives

Since its first appearance, the pandemic influenza A(H1N1)pdm09 virus has caused increased number of infections, with considerable morbidity and mortality in northern Greece and worldwide. Genetic analysis of post-pandemic influenza A(H1N1)pdm09 strains that circulated in northern Greece, included mild, severe and fatal infections in order to investigate the correlation with disease severity, as the virus evolved.

Methods

One thousand eight hundred and seventy pharyngeal swabs were examined, out of which 848 were positive for A(H1N1)pdm09. A total of ninety infections caused severe pneumonia and 49 were fatal. Genetic analysis of the HA sequences was done to 102 northern Greek strains, isolated from 33 fatal and 69 non-fatal cases. Antigenic analysis was performed to a representative number of viruses (10%).

Results

Most viruses clustered with group 6 viruses, whereas a number of viruses clustered with groups 3,4,5 and 7. No viruses clustered with groups 1,2 or 8. The coexistence of different clusters indicated co-circulation of lineages in northern Greece. Genetic analysis showed that the HA amino acid sequences were largely similar to the vaccine strain, with sequence similarity of 96-99%. The most divergent strain was A/Thessaloniki/385/2011, isolated from a fatal case, which had 12 amino acid variations compared to the vaccine strain. Antigenic analysis of representative viruses showed that the vast majority were antigenically similar to the vaccine virus, A/California/7/2009. Two viruses belonged to the 3rd phylogenetic clade that showed reduced HI titres, however none of the analyzed HA sequences carried amino acid substitutions at positions 153-155 of the HA, which are also associated with reduced HI titres. Several viruses accumulate variations at antigenic sites of the HA. It has been observed that certain signature amino acid changes, such as P83S, D97N, S185T, S203T and I321V, persisted from the pandemic period, indicating that they offer some selective advantages to the virus. Notably, the D222G variation was detected at 6 fatal or severe cases only, supporting the association of this mutation with increased pathogenesis of the virus. The twice observed variation N287S resulted to a loss of an N-linked glycosylation site of the virus. Other variations, such as Q293H, which were observed during the pandemic, were negatively selected, as they probably did not contribute to the virus fitness. Interestingly, some persistent variations were observed at amino acid residues near antigenic sites, such as I116V, S143G, V152I, K171R, S185T, S203T, D223R.

Conclusions

There is an obvious trend of the new virus strains to accumulate amino acid changes at antigenic and receptor binding sites and to form new phylogenetic groups. Constant virological and molecular surveillance is important to monitor the efficacy of the vaccine and assess the severity of each influenza season in relation to the pathogenicity and transmissibility of circulating genetic variants.