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SWINE FLU - PAST AND A CONCERN FOR FUTURE

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INTRODUCTION

Influenza viruses are viruses which cause mild to severe respiratory infections. They belong to the family *Orthomyxoviridae* and are classified into three types, A, B, and C, based on the variation in the structure of their surface proteins. Influenza A infects many mammals and aquatic birds and is the most common and the most severe pathogen among the three types. Influenza B is almost exclusively a human pathogen, whereas Influenza C causes milder disease and is less common than the other types. Influenza A viruses are further classified into subtypes based on the surface glycoproteins hemagglutinin (1-16 subtypes of HA) and neuraminidase (1-9 subtypes of NA). At a given time, the most common subtypes circulating in' human populations are H1N1 and H3N2. The last century witnessed three Influenza pandemics - the Spanish Flu caused by H1N1 (1918-1920), the Asian Flu caused by H2N2 (1957-1958), and the Hong Kong Flu caused by H3N2 (1968-1969). The first pandemic of the present century was caused by the 2009 H1N1 Influenza A virus, also known as HINlpdm of the H1N1 subtype. This virus was formerly also known as swine flu as it contains a unique combination of gene segments from human, avian, and segments from the so-called triple reassortant swine viruses that emerged in North American pig populations in the late 1990s. No major Influenza virus activity was reported in pigs when the outbreak was recognized in humans, however, pigs can be experimentally and naturally infected with 2009 H1N1 viruses, resulting in mild respiratory infection.

Spread of Pandemic

The 2009 H1N1 Influenza virus first appeared in Mexico in March, 2009, and in California in the United States in April, 2009, and swept the globe with unprecedented speed. The World Health Organization (WHO) declared a "public health emergency of international concern" in April, 2009, and within two months, announced the highest alert level (phase 6, pandemic) in June, 2009, which indicates widespread community transmission in at least two continents. Globally, 214 countries reported H1N1 cases, with more than 18 thousand deaths reported in the pandemic phase. In India, the first case of the H1N1 flu was confirmed in Hyderabad in May, 2009; thereafter cases were detected in other parts of the country. Overall, more than 2 lakh persons were tested for pandemic Influenza A H1N1, and there were more than 50 thousand positive cases and approximately 3 thousand deaths in India, In August, 2010, WHO declared the Post Pandemic Phase and that Influenza A H1N1 ceased to be a public health emergency of International concern. The cases have further decreased in 2011 Again the cases have increased in 2015 in India and presently only sporadic cases of H1N1 are reported from various parts of the world.

Clinical Features

The clinical manifestations vary from asymptomatic infection to serious fatal illness. Influenza-like illness (ILI) is defined as a fever of > 37.8°C *(*> 100°F) plus cough and/or sore throat in the absence of any cause other than Influenza. Most cases of 2009 and 2015 H1N1 infection presented as mild upper respiratory tract illness, however, in some instances, the disease progresses in severity resulting in multi-organ failure, respiratory failure, acute respiratory distress symptoms (ARDS), and sometimes death. Pathological findings include diffuse alveolar damage, hemorrhagic interstitial pneumonitis, and peribronchiolar and perivascular lymphocytic infiltrates. The risk of severe disease increases with underlying chronic conditions such as asthma, autoimmune diseases, cardiovascular diseases, diabetes, and obesity.

Diagnosis

For diagnosis of Influenza, specimens like nasopharyngeal swab with synthetic tip (polyester or dacron), nasal wash, bronchoalveolar lavage (BAL) or endotracheal aspirate can be collected. All diagnostic laboratory work on samples from suspected patients should be done in a biosafety level 2 (BSL-2) laboratory. The gold standard for laboratory diagnosis of the 2009 H1N1 Influenza is the real-time reverse transcriptase polymerase chain reaction (rRT-PCR) test, which is tailored to the specific detection of this virus. A single step rRT-PCR approach targeting the matrix gene of the Influenza A/HlNlpdm was designed by CDC and is used

worldwide. A number of other diagnostic tests are also available, but they differ in their sensitivity and specificity. Rapid diagnostic tests have high specificity but variable sensitivity. Isolation of the virus in cell culture or embryonated eggs is diagnostic, but it may not yield timely results.

Other nucleic acid amplification techniques have also been evaluated, amongst which, Loop-mediated isothermal amplification (LAMP) is a specific, efficient and rapid technique that is similar to PCR amplification but the DNA amplification is performed under isothermal conditions. A one-step, single-tube LAMP assay for clinical diagnosis of H1N1 Influenza virus was found to be tenfold more sensitive than the WHO approved rRT-PCR with the advantage of naked- eye visualization of gene amplification by means of SYBR Green I dye within 30 minutes compared to 2 to 3 hours for a rRT-PCR. Other newer techniques which have been used include Nucleic acid sequencing-based amplification (NASBA) which is a suitable and robust alternative technique for field Influenza A virus surveillance, and Pyrosequencing, which can be used for genotyping and sequencing disease genes. Pyrosequencing, combined with RT-PCR techniques, has provided rapid, high-throughput and cost-effective screening of NA inhibitor-resistant Influenza A viruses.

Management

A majority of patients infected with the H1N1 pdm Influenza A virus can be treated with simple supportive care at home using antipyretics (e.g. acetaminophen or ibuprofen). Antiviral therapy should be started empirically as soon as possible for persons with suspected probable or confirmed Influenza and illness requiring hospitalization; progressive, severe or complicated illness regardless of previous health status; and/or high risk for severe disease. The virus can be treated with neuraminidase inhibitors like oseltamivir and zanamivir, but is resistant to ion channel inhibitors like amantadine and rimantadine. Oseltamivir resistance has now been reported, both in oseltamivir-treated and -untreated individuals. Also, in contrast to 2009 H1N1 viruses a majority of seasonal H1N1 viruses are now resistant to oseltamivir. A concern therefore exists that in future these pandemic viruses may acquire this resistance trait through mutation.

Vaccines

The CDC recommends annual flu vaccination for all but infants less than 6 months of age, with an even stronger recommendation for high-risk groups, i.e., children, pregnant women, patients with comorbidities, morbid obesity, and the elderly. Several candidate vaccines were developed in which the HA and NA genes of A/California/07/ 2009 virus were combined with the remaining genes of A/Puerto Rico/8/34 (HlNl) virus, the virus commonly used for human Influenza vaccine production, and the first vaccines against 2009 HlNl viruses were approved in September of 2009. Vaccine safety has been monitored closely and the percentage of serious adverse reactions was similar to that observed with seasonal Influenza vaccines. A particular focus has been on cases of Guillian-Barre syndrome (GBS), a neurologic disease that occurred at a higher incidence with earlier HlNl vaccines, and currently there is no indication that there were increased number of cases of GBS with 2009 HlNl vaccine as compared to the seasonal Influenza vaccines.

CONCLUSION

The recent pandemic of the swine-origin HlNl Influenza A virus and the continuing circulation of highly pathogenic avian H5N1 Influenza A virus stress the need for rapid and accurate identification of Influenza viruses for surveillance, outbreak management, diagnosis and treatment. Much has been learnt about the evolution of this virus; however, it is still not possible to predict when the next pandemic will occur and which virus will be responsible. Hence, an improved surveillance at both national and international levels in humans as well as swine and avian hosts appears to be crucial for early detection and prevention of future Influenza pandemics.

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