CHAPTER

12

Swine Flu

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INTRODUCTION

Influenza (the "flu") is a seasonal respiratory illness caused by influenza viruses. Influenza is usually a mild and self-limited respiratory illness, but it has the potential to cause significant morbidity & mortality as it spreads widely in the community. In the last few years, we are experiencing a new strain of Influenza A virus called Swine origin of influenza virus (A/2009/H_1N_1). A highly contagious form of human influenza virus related to a virus formerly isolated from infected swine. The respiratory infection popularly known as swine flu is caused by this influenza virus first recognized in March 2009 and it speeded quickly across other countries within short span of time and resulted in recent big pandemic. This 2009 pandemic influenza A (H_1N_1) virus is continued to co-circulate following years along with seasonal influenza A and cased significant mortality among young people.

EPIDEMIOLOGY

The latest pandemic of swine flu was first noted in Mexico in March 2009, the outbreak rapidly spread worldwide affected nearly 195 countries and finally declared ended in August 2010. In India the swine flu outbreak killed 981 people in 2009 and 1763 in 2010. The mortality decreased in 2011 to 75. However during subsequent years the mortality gradually increased to 405 lives in 2012 and 699 lives in 2013. In 2015, the outbreak became widespread throughout India. The states of Gujarat and Rajasthan were the worst affected. H_1N_1 influenza A 2009 pandemic strain is now responsible for periodic seasonal outbreaks of influenza in India.

The average incubation period is 1-3 days (maximum of 7 days) and the main mode of transmission is through contact with large-particle respiratory droplets by sneezing and coughing. Other body fluids (eg, diarrheal stool) and fomites also play a role in transmission. Viral shedding begins the day prior to symptom onset and often to persist for five to seven days or even longer in children and in immunocompromised individuals.

RISK GROUPS

The risk factors for influenza complications are seen in

- Infants & children aged < 5 years and adults aged> 65 years
- Obese individuals
- Pregnant ladies
- Persons with asthma or COPD & other chronic pulmonary diseases,
- Persons with hemodynamically significant cardiac disease (both congenital & acquired)
- Persons who have immunosuppressive disorders or who are receiving immunosuppressive therapy & HIV-infected persons
- Persons with sickle cell anemia and other hemoglobinopathies
- Persons with diseases that requiring long-term aspirin therapy,
- Persons with chronic renal dysfunction
- Persons with cancer
- Persons with chronic metabolic disease, such as diabetes mellitus
- Persons with neuromuscular disorders, seizure disorders, or cognitive dysfunction that may compromise the handling of respiratory secretions
- Residents of any age of nursing homes or other long-term care institutions

ETIOLOGICAL AGENT

The influenza virus is a RNA virus belonging to the family Orthomyxoviridae with three main genera – Influenza A, B and C. Influenza A is further sub-typed into 16 distinct H types and 9 distinct N types based on the hemagglutinin and neuraminidase antigens on the surface of the virus as shown in the Figure 1.

Every year new strains of influenza virus emerge as its

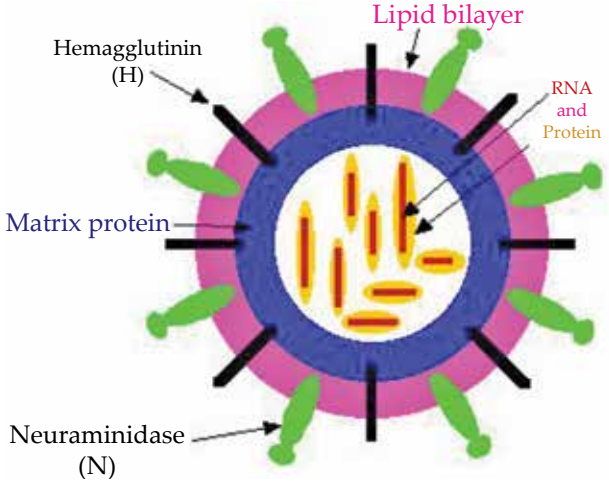

Fig. 1: Structure of Influenza virus

Table 1: Clinical features of Swine Influenza

Common clinical features	Extra pulmonary manifestations	Complications
Fever	CVS: Chest pain, Hypotension	Pulmonary: Progressive viral pneumonia, secondary bacterial pneumonia, ARDS
Sore throat	CNS: seizures, lethargy, altered mental status, weakness or paralysis	Extra- Pulmonary: CNS: Encephalitis, encephalopathy, GBS, ADEM
Rhinorrhea	Others: decreased urine output, cyanosis, dehydration	CVS: Myocarditis, pericarditis
Myalgia, arthralgia		Others: renal failure, rhabdomyolysis, ryes syndrome, hemophagocytosis, multi-organ failure syndrome
Headache		
Vomiting, diarrhea		

Table 2: Diagnostic tests for Swine Flu

Nonspecific findings:	Specific findings
CBC: Leucopenia, thrombocytopenia, Anemia	RT- PCR: Highly sensitive * very high specific, usually recommended test for clinical diagnosis faster turnaround time (nasopharyngeal or throat swab in sick patient lower respiratory samples)
LFT: Raised liver enzymes, & elevated bilirubin	Viral culture: Moderately sensitive, highest specificity, usually recommended for public health surveillance , not useful in clinical situations due to long turnaround time
Others: Increased CPK & LDH	Rapid antigen test: The sensitivity widely varies and negative test will not rule out influenza. Not recommended nowadays.
X-ray: Bilateral infiltrates (lower lobe predominance) & features of ARDS	
CT chest: Patchy consolidation or ground glass opacities	

Table 3: Antiviral agents against Influenza

	Oseltamivir (NA inhibitor)	Zanamavir (Na inhibitor)	Amantadine & Rimantadine (M2 inhibitor)
Swine Influenza	Susceptible	Susceptible	Resistant
Seasonal H1N1	Mostly susceptible	Mostly susceptible	Mostly resistant
Seasonal H3N2	Susceptible	Susceptible	Resistant
Influenza B	Susceptible	Susceptible	Resistant

genes undergo point mutations leading to an 'antigenic drift'. This process helps the virus to evade host defense mechanism. The influenza A virus is different when compared to other two influenza viruses by having a segmented genome with eight single stranded RNA segments. When the host cell is infected with more than one influenza virus, these genes have the opportunity to get reassorted and produce a very different strain altogether. This process is called 'antigenic shift' is mainly responsible for pandemics strains of influenza viruses. The current swine origin influenza A virus 2009 train has undergone triple reassortment and contains genes from the avian, swine and human viruses.

PATHOGENESIS

Virus-containing droplet particles may settle on nasopharyngeal, tracheobronchial,conjunctival, or other respiratory mucosal epithelial cells. In contrast to the other seasonal influenza virus, the A/2009/H_1N_1 virus also binds to the 2, 3-linked sialic acid receptors that are present in the lower respiratory tract and cause diffuse alveolar damage. This finding may partially explain the predilection of this new virus to cause pneumonia in healthy individuals. After the initial illness, the host usually mounts a protective mmune response which involves a rise in antibody titers as well as T cell activation. The production of interferon in the respiratory mucosa is associated with a fall in virus shedding. Specific histopathologic findings in the lungs included edema, hyaline membranes , fibrin , hemorrhage , inflammation , type II pneumocyte hyperplasia and organizing fibrosis..

CLINICAL MANIFESTATIONS

CASE DEFINITIONS

Probable case of Influenza: (Influenza-like illness (ILI)) is defined as fever (temperature of 100ºF [37.8ºC] or greater)

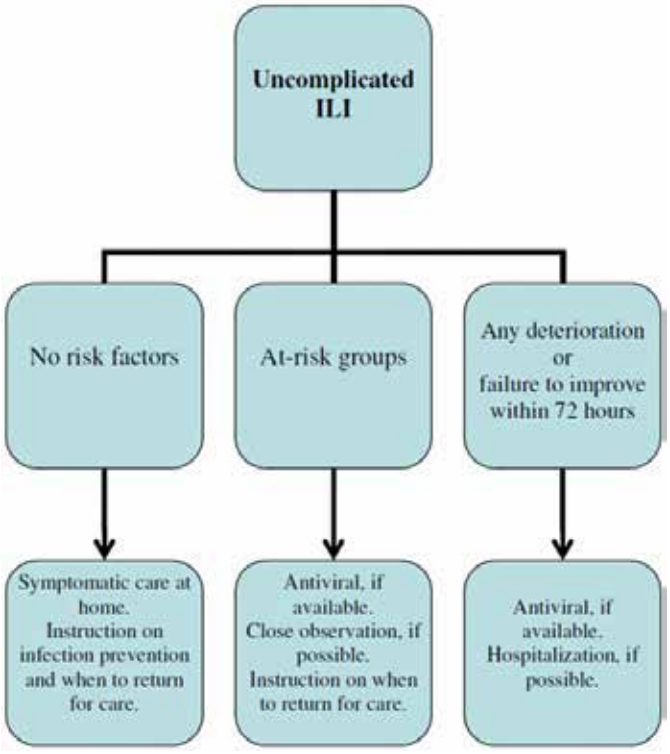

Fig. 2 Clinical algorithm for the management of suspected Swine flu

with cough or sore throat in the absence of a known cause other than influenza (Table 1).

A confirmed case of pandemic H_1N_1 influenza A is defined as an individual with an ILI with laboratory-confirmed H_1N_1 influenza A virus detection by real-time reverse transcriptase polymerase chain reaction (rRT-PCR) or culture (Table 2).

DIAGNOSIS

MANAGEMENT

Common anti-viral agents used to treat influenza viruses are neuraminidase inhibitors and M protein inhibitors, their activity against common influenza viruses are shown in Table-3

INDICATIONS FOR TREATMENT

- Illness requiring hospitalization
- Progressive, severe, or complicated illness, regardless of previous health status
- Extremes of age
- Pregnant women and women up to two weeks postpartum
- Individuals with high risk medical conditions .and those who were obese

PRIMARY REGIMENS FOR ADULTS

- Oseltamivir 75 mg po bid x 5 days OR Zanamivir 2 inhalations (5 mg each) bid x 5 days
- Oseltamavir can cause diarrhoea, nausea, vomiting and abnormal behaviour. Zanamavir can cause bronchospasm.

ALTERNATIVE & NEWER REGIMENS

Peramivir 600 mg (FDA approved for single dose intravenous). It has got longer duration and may be considered for severe disease). Commonest adverse effect of peramivir is rash.

Zanamivir 600 mg IV q12h for at least 5 days (Investigational) can be considered for patients with inability to take oseltamivir orally and contraindications to inhaled zanamivir or who have progressive disease despite at least 5 days of therapy, or suspected or confirmed oseltamivir resistance.

OTHER SUPPORTIVE CARE

Supportive management including IV fluids, antipyretics, and oxygen support for hypoxic patients and Low tidal volume ventilation for mechanically ventilated patients may be necessary. It is recommended that patients with pandemic H1N1 influenza A, who developed pneumonia be treated empirically for community-acquired pneumonia (CAP) given the risk of secondary bacterial pneumonia. Adjunctive approaches have been evaluated including extracorporeal membrane oxygenation, N-acetyl cysteine, and glucocorticoids, but further studies are required to clearly know their role.

Clinical algorithm to manage swine flu is shown in Figure 2 below.

PREVENTION

Measures to prevent swine flu spread include use of face mask (triple layer surgical mask), frequent hand wash and adherence to cough etiquettes by the patient. Contact surfaces should be disinfected with sodium hypochlorite or household bleach 5%. Adult patients need to be isolated till their symptoms had subsided. In children the isolation period is little longer due to prolonged excretion of viruses.

ANTIVIRAL PROPHYLAXIS

The post exposure antiviral prophylaxis could be considered for adults and children who had close contact with a confirmed or suspected case and also fell into one of the following categories:

- Adults who are at high risk for complications of influenza
- Pregnant women and women who are up to two weeks postpartum
- Children who are <5 years of age or who are at high risk of complications of influenza
- Healthcare workers and emergency medical personnel

DOSE & REGIMENS

Oseltamivir 75 mg po once daily for 10 days..

Zanamivir inhaled powder, 10 mg, once daily.

VACCINATION

The CDC\) recommended that H_1N_1 influenza vaccine be given to all patients from six months of age and older.

Priority is given to health care personnel and the above mentioned high risk groups.

Inactivated influenza vaccine (IIV), recombinant influenza vaccine (RIV) and live attenuated influenza vaccine (LAIV) are all what are available. IIV is the most common used. The selection of vaccine subunits is based on the strain prevalence during the previous year influenza activity. Efficacy is 70 to 80 %. It takes 2 to 3 weeks for the immunity to develop. Immunogenicity is retained if pandemic and seasonal influenza vaccines are coadministered..

The small excess risk of Guillain-Barré syndrome and narcolepsy is observed with the use of vaccine. Other neurologic syndromes, such as transverse myelitis and opsoclonus myoclonus syndrome has also been reported. It is generally well tolerated and there is no safety concern for the pregnant woman.

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