West Nile Fever - An Emerging And Re-Emerging Infectious Viral Metazoonosis

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Abstract

In recent years, many emerging and re-emerging zoonoses which resulted in high morbidity and mortality in humans and animals have attracted the attention of international and national authorities. Among several zoonotic diseases, West Nile fever is an important viral metazoonosis from public health and economic point of view. The disease is caused by West Nile virus which was first isolated from human blood in 1937 from Uganda. The virus is reported in humans and in a wide variety of animals including equines from many countries of world including India, Europe, Africa and USA. The bite of infected mosquitoes belonging to the genus Culex is the principal mode of disease transmission both in humans as well animals. Disease in man is characterized by fever, cephalalgia, pain in eyes, muscles and joints, lymphadenopathy, meningoencephalitis and maculopapular eruption mainly on trunk. Diagnosis of West Nile fever can be established by virus isolation from clinical materials and detection of virus specific antibodies in the serum of patients. RT-PCR can also be tried to make a rapid diagnosis. Since it is a metazoonosis, measures to control the mosquitoes, wearing protective clothing, and use of repellent cream will certainly reduce the incidence of West Nile fever. We are of the opinion that active surveillance of disease in humans, birds, animals, and vector (mosquito) is imperative to forecast emergence and re-emergence of this important viral metazoonosis. In addition, involvement of public health veterinarian in the control of zoonoses programme is also emphasized.

Keywords: Horse, Metazoonosis, Mosquito, Public health, West Nile disease

Introduction

Emerging and reemerging zoonoses of multiple etiologies are a continuing threat to our human and animal population by causing extensive morbidity and death both in developed and developing countries (Pal,2013). Among several viral zoonoses, West Nile fever (West Nile encephalitis, West Nile meningitis) is an important emerging and re-emerging, viral metazoonosis which can cause serious and sometimes fatal illness in humans as well in animals (Hubalek and Halouzka,1999; Marfin and Gubler,2001; Pal, 2007). The disease is caused by West Nile virus (WNV), a member of the genus Flavivirus and the family Flaviviridae (Pal, 2007). The virus was first isolated in a blood sample of a human patient from the West Nile
province of Uganda in 1937 (Smithburn et al., 1940). This RNA virus was initially considered of minor public health importance (Gubler, 2007). It emerged from obscurity in 1999 when the first incursion of the virus into North America caused 62 cases of encephalitis and seven deaths in New York (Nash et al., 2001). Since that time, the virus has dramatically spread, and WNV activity has now been detected in all 48 continental states, the District of Columbia, and Puerto Rico (Petersen and Hayes, 2008). WNV causes both sporadic infection and outbreaks that may be associated with severe neurologic disease (Jupp, 2001).

West Nile virus (WNV) is found both in tropical and temperate regions. It mainly infects birds, but is known to infect humans, and other vertebrate mammals including horses (Pal, 2007; Leger et al., 2011). There are 30,000 human cases and 1172 deaths in USA since it was first reported in New York in 1999 (Carney et al., 2011). In USA, over 20,000 cases of WNV encephalomyelitis in equine are recorded (Ward, 2005). The virus can cause death rates up to 100% among avian species (Carney et al., 2011). The main route of human infection is through the bite of an infected mosquito (Pal, 2007). Approximately, 90% of WNV infections in humans are asymptomatic but, if it occurs, the clinical manifestation ranges from mild febrile and flu-like syndrome, termed West Nile fever to the neuroinvasive disease known as West Nile meningitis or West Nile encephalitis (CDC, 2011). WNV infection is recorded from many countries of the world including India and USA (Marfin and Gubler, 2001; Hayes and Gubler, 2006; Khan et al., 2011).

West Nile Virus infection can be diagnosed by different techniques but, the most efficient diagnostic method is detection of IgM antibody to WNV in serum or cerebral spinal fluid collected within 8 days of illness onset using the IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA). RT-PCR can also be used for rapid diagnosis (Pal, 2007; Leger et al., 2011). Prevention and control of WNV requires the education of the public, use of protective measures by individuals, control of breeding sites of mosquitoes at household level, the application of mosquito control measures and monitoring of WNV activity in birds, animals, mosquitoes, and humans (GuPTill et al., 2003; Pal, 2007). Therefore, the objective of this paper is to give an overview on West Nile fever as emerging and re-emerging metazoonosis.

**Etiology**

The disease is caused by West Nile virus (WNV) is a single-stranded RNA virus of the family Flaviviridae, genus Flavivirus (Pal, 2007). Flaviviruses share a common size (40-60 nm) and symmetry (enveloped, icosahedral nucleocapsid), which encode seven non-structural proteins
and three structural proteins. The nucleic acid has a positive-sense, single-stranded RNA approximately 10,000-11,000 bases. The RNA strand is held within a nucleocapsid formed from 12 kDa protein blocks; the capsid is contained within a host-derived membrane altered by two viral glycoproteins (Nash et al., 2001)

**Host**

The virus has the potential to affect a wide range of vertebrates, including mammals, avians, reptiles and amphibians. The natural infection has been recorded in man and in many species of animals such as alligator, bat, chipmunk, crocodile, crow, dog, geese, gull, horse, jay, pelican, rabbit, robin, shunk, squirrel, vulture, whale (Jupp, 2001; McLean et al., 2002; Miller et al., 2003; Pal, 2007; Legert et al., 2011).

**Transmission**

The most important route of WNV transmission is through the bite of an infected mosquito (Pal, 2007). The main cycle of WNV is between mosquitoes and birds. Mosquitoes become infected with the virus when they feed on a bird infected with WNV. Approximately, 10 to 14 days after the mosquito bites the infected bird, the mosquito can transmit the virus to another bird or mammals, including humans. The mosquito injects the virus into the bird, animal, or man while taking a blood meal. Other modes of WNV transmission are through blood transfusion, organ transplantation, breast feeding and percutaneous inoculation (Campell et al., 2002; Ravindra et al., 2004, WHO, 2011).

There is no published evidence of person-to-person transmission of WNV, however, transmission through shared, contaminated needles is possible. Touching or sharing utensils with a person infected with WNV does not pose a risk of infection (CDC, 2011, WHO, 2011). The human and horse are considered as dead end hosts and do not play a role in transmission cycle of virus (Murray et al., 2010).

**Clinical Spectrum**

**Humans**

The incubation period of disease is usually 3 to 14 days (CDC, 2011). Infection with WNV is either asymptomatic in around 80% of infected people, or can lead to West Nile fever or severe West Nile disease. About 20% of people who become infected with WNV develop West Nile fever exhibiting symptoms such as fever, headache, tiredness, and body aches, nausea, vomiting, occasionally with a skin rash on the trunk of the body and swollen lymph glands (Peterson and
Marfin, 2002; Pal, 2007; Paz and Semenza, 2013). The symptoms of severe neuroinvasive disease include headache, high fever, neck stiffness, stupor, confusion, seizure, chorioretinitis, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis (Peterson and Marfin, 2002; CDC, 2011). People over the age of 50 and some immunocompromised persons such as transplant patients are at the highest risk for getting severely ill (CDC, 2011).

**Animals**

Most infections in animals are subclinical. WNV infection in horses typically cause listlessness, depression, somnolence, listlessness, apprehension, hyperexcitability and meningoencephalitis (Martin et al., 1995). Approximately 90% of symptomatic cases in horses result in neurological disease with case fatality rates of 30-40% (Venter et al., 2011). The abortion is also recorded in mare WNV (Venter et al., 2011). The virus has been detected in over 250 species of birds. Some species of birds are highly susceptible to fatal outcome (Steele et al., 2000; McLean et al., 2002). General signs of infection in birds include lethargy, recumbency, and in some cases, hemorrhage. Little is known of the clinical manifestation of WNV in other vertebrates, such as reptiles and amphibians and other mammals. In North America, captive alligators have died from WNV infection (Miller et al., 2003), and fatal infections have been informally reported in approximately 20 species of mammals besides horses and humans. In sheep, WNV may cause abortion, stillbirth and neonatal death (Barnard and Gubler, 1986)

**Epidemiology**

West Nile Virus is one of the most widely distributed of all Arboviruses with an extensive distribution in Africa, Middle East, parts of Europe, former Soviet Union, South Asia, and Australia. The disease occurs in summer and is both endemic and epidemic. It was identified in birds in Nile delta region in 1953. Before 1997, WNV was not considered pathogenic for birds, but at that time in Israel a more virulent strain caused the death of different bird species presenting signs of encephalitis and paralysis. Human infections attributable to WNV have been reported in many countries of the world (Gubler, 2007; CDC, 2011, Paz and Semenza, 2013). In 1999, a WNV circulating in Israel and Tunisia was imported in New York producing a large and dramatic outbreak that spread throughout the continental USA in the following years. WNV outbreaks in USA highlighted that importation and establishment of vector-borne pathogens outside their current habitat represent a serious danger to the world (Hayes et al., 2005). The
largest outbreaks occurred in Greece, Israel, Romania, Russia and USA. The main outbreak sites of WNV infections are on major birds migratory routes (CDC, 2011). The virus is transmitted through mosquito vectors, which bite and infect birds. The birds are amplifying hosts, developing sufficient viral levels to transmit the infection to other biting mosquitoes which go on to infect other birds and also humans. The infected mosquito species vary according to geographical area (Hayes et al., 2005).

Since the first discovery of WNV, infrequent human outbreaks were mostly reported in groups of soldiers, children, and healthy adults in Israel and Africa. These outbreaks were associated with only minor illness in the majority of patients; some case fatalities were associated with increasing age. In one of the largest outbreaks reported, thousands of self-limited and relatively mild clinical cases, consisting of fever, rash, and polyarthralgias occurred in South Africa, resulting in an epidemic attack rate of 55% (Jupp, 2001; Petersen, and Roehrig, 2001; Zeller and Schuffenecker, 2004). Outbreaks of WNV infection associated with severe neurologic disease have been reported from many countries of the world. The mortality occurred more often in elderly patients (Zeller and Schuffenecker, 2004; Hayes and Gubler, 2006; Peterson and Hayes, 2006; CDC, 2011; Paz and Semenza, 2013, WHO, 2013).

**Diagnosis**

Various tests are employed to diagnose WNF infection. The most efficient technique is detection of IgM antibody to WNV in serum or cerebral spinal fluid (CSF) collected within 8 days of illness onset using the IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA). Since IgM antibody does not cross the blood-brain barrier, IgM antibody in CSF strongly suggests central nervous system infection. IgM can be detected in nearly all cerebrospinal fluid (CSF) and serum specimens received from WNV infected patients at the time of their clinical presentation. Serum IgM antibody may persist for more than a year. Patients who have been recently vaccinated against or recently infected with related flaviviruses such as yellow fever, Japanese encephalitis, dengue may have positive WNV MAC-ELISA results. IgG antibody sero-conversion (or significant increase in antibody titers) in two serial specimen collected at a one week interval by ELISA, neutralization assay, TaqMan reverse transcriptase PCR method, RT-PCR technique, and virus isolation by cell culture are other methods to confirm WNV infection (Lanciotti et al., 2000; CDC, 2011).

**Treatment**
Currently, there are no effective medicines available for the management of WNV infection. Treatment in patients with severe disease may require supportive therapy such as hospitalization, mechanical ventilation, intravenous fluids and prevention of secondary infections (Campbell et al., 2002). Hitherto, no vaccine is available to protect the humans. Although several potential treatments have been suggested for WNV encephalitis, no evidence is available yet to document the efficacy of these chemotherapies. Agarwal and Peterson (2003) have recommended the use of human immunoglobulin in the treatment of WNV infection.

**Prevention and Control**

In the absence of a human vaccine, certain measures such as application of repellent cream on exposed skin, wearing of protective clothing, avoidance of outdoor activities during peak mosquito biting time, drainage of standing water from pit, disposal of all plastic containers, rubber tires, tin cans, and any other water holding containers, proper cleaning of gutters, spraying of insecticides in buildings, regular testing of blood and organ donors, use of gloves when handling sick animal or their tissues and during slaughtering, careful collection and handling of clinical samples, and health education will certainly reduce the risk of infection to people (Devine, 2003; Pal, 2007).

Vaccines have been developed for horses. Commercial vaccine can protect the animal up to one year. Hence, it is imperative that initial shot should be followed by booster after 3 to 6 months and than regular annual shots to maintain immunity round the year (Ward, 2005).

Carney and others (2011) have suggested the establishment of the dynamic continuous area space time (DYCAST) system. This is a biologically based spatiotemporal method that uses public reports of dead birds to identify areas at high risk for WNV transmission to human beings. It is important to start biosurveillance programme for global health security against many infectious diseases including WNV infection.

**Conclusion**

West Nile fever, a highly infectious emerging and re-emerging viral metazoonosis of global significance, is caused by West Nile virus. Birds are the natural reservoir and amplifying host. A spectrum of clinical condition from asymptomatic infection to death are observed in man and animals. Predisposing factors include immunosuppression, organ transplantation, very young and old age, and pregnancy. Detection of IgM antibody to WNV in serum or CSF by ELISA is the most efficient diagnostic tool. Presently, no drug to treat or vaccine to prevent human infection is
available, and hence mosquito control and personal protection from mosquito bite can reduce the rates of WNV infection. The early season death of birds from West Nile virus may be considered as warning of human infection. The development of potent, safe and less expensive vaccine to protect susceptible persons is emphasized. In addition, additional research on the pathogenesis and chemotherapy of WNV infection is warranted.

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