Human West Nile Virus Disease Outbreak in Pakistan, 2015–2016

Like most of the world, Pakistan has seen an increase in mosquito-transmitted diseases in recent years. The magnitude and distribution of these diseases are poorly understood as Pakistan does not have a nation-wide system for reporting disease. A cross-sectional study to determine which flaviviruses were causing of arboviral disease in Pakistan was instituted. West Nile virus (WNV) is a cause of seasonal fever with neurotropic findings in countries that share borders with Pakistan. Here, we describe the active and persistent circulation of WNV in humans in the southern region of Pakistan. This is the first report of WNV causing neurological disease in human patients in this country

Patient Enrollment

A cross-sectional, observational study was performed to identify which arboviruses [DENV, WNV, and Japanese encephalitis virus (JEV)] were the cause of acute undifferentiated febrile illness in selected basic health and and/or district hospitals of the Sindh region of Lakis an. Patients were enrolled under information sent procedures which were reviewed and approved by the Ethics Pevev Committee at Aga and a provestity and the Informational

Figure 2. Locations of the patient enrollment sites in the Sindh region of Pakistan



Review Board at the University of Florida . All enrolled subjects gave written informed consent in accordance with the Declaration of Helsinki. Patients presenting with the CDC clinical description of arboviral disease including findings of rash, headache, arthralgia, myalgia, gastrointestinal distress, acute hemorrhagic fever, acute flaccid paralysis, encephalitis, meningitis, and/or unexplained fever were recruited .Patients younger than 10 years and older than 90 years were excluded. Briefly, all patients were tested for DENV NS1 antigen unless affected primarily by neurologic abnormalities. All NS1-negative sera were evaluated for exposure to WNV or JEV via IgM capture ELISA for JEV and WNV. Five study sites were established, and personnel were trained throughout the Sindh province in Pakistan (Figure 2). These sites included medical colleges, teaching hospitals, and civil hospitals.(Khan, Barr et al. 2018)

Virology and Pathogenesis

West Nile virus is one of nore than 70 viruses of the family Flaviviridae and e genus Flavivirus. West Nile virus is a new energy spanese encephalitis virus and anendemic North American flavivirus. The west Nile Virus is Divided Into Five of 1) geneti Lineage .In outbreak Of human Body to 1st and 2nd Lineage Is associated .The lineage one can be further divided into three sub lineage , La,Lband Lc.[FJ,D avis CT, TeshRB, Barrett AD2012]

Lineage La is Africa, the Middle East, and Europe constitute. The lineage lb is present in kunjin virus from Australasia. The virus which are present in india have a one virus linage of lc. Basically lc virus is present in india. The initial North American isolates (East Coast genotype) identified in 1999 in New York City have been most closely related to a lineage 1a West Nile virus isolated from Israel in 1998. The viral transmission in North America Mosquito virus vector effective in their efficacy by replacement of genotype .Mosquito salivary components introduce the infection in vertebrates .These infections are occur in dendritic cell e.g skin resident and occur in target cell which are called keratinocyte. These infection are introduced by different mechanisms like focalized suppression of immune effectors cell trafficking to the site of inoculation. Infection is transfer from dendritic cell to nervous system by different step. Firstly infection is transfer into lymph node and then potentially transfer into ovisceral organs and then transfer into nervous system. Lim PY ,Behr M J ,Chadwick CM,ShiPY,Bernard 2011]

Figure 3 :Schematic of Pathogenesis of West Nile Virus Infection



Following the bite of an infected mosquito, infection begins in keratinocytes and immune cells in the epidermis and spreads to draining lymph nodes. Viremia originating in the lymph nodes disseminates infection to peripheral organs.

West Nile Virus In Central Nervous system

West Nile virus have the capacity to replicating and eliciting pathology in brain.when the West Nile virus is present in excess amount in central nervous system then it caused the disease which is called the neuroinvasiv disease in human body. The neuroinvasiv disease have the mechanism .And this mechanism is described into four steps:

(1)Direct infection of the vascular endothelium and subsequent entry to the central nervous system.

Figure 4 West Nile Virus Neuroinvasive



Potential mechanisms for neuroinvasion of West Nile virus include (1) direct infection of the vascular endothelium and subsequent entry to the central nervous system, (2) viral passage through the vascular endothelium due to disruption of the blood-brain barrier integrity by vasoactive cytokines, (3) a Trojan horse mechanism through which infected monocytes are trafficked into the central nervous system, or (4) retrograde axonal transport to the central nervous system following infection of peripheral neurons.