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Extra Credit Assignment

The Nipah Virus

September 1998 there was an increasing number of people were presenting with encephalitis and respiratory disease in northern Malaysia. The problem that lead to the continual spread of this disease around Malaysia and to Singapore is that initially people believed that the infectious agent was Japanese Encephalitis, which was not the correct infectious agent. It is thanks to Dr. Kaw Bing Chua, and his fight for people to realize that it was not Japanese Encephalitis, that they were able to identify the correct infectious agent, the Nipah Virus.

Outbreak and Discovery

The first incidence of outbreak was recorded in September 1998 in the northern part of Malaysia. There were, however, infectious signs in the swine population in early 1997, but at the time the Veterinary Research Institute assumed the pigs' deaths were due to classical swine fever. The lack of connection between these incidences lead to the country's senior consultant virologists declaring that it was a Japanese Encephalitis epidemic, and resulted in intensive fogging for mosquitos, and rushed spread of vaccines. When this didn't stop the spread, Dr. Chua began to theorize that there was some other infectious agent. At that time, however, the only concern for Dr. Chua's University was just to confirm Japanese encephalitis. Thus, only measurement of Japanese encephalitis-specific IgM was carried out in the laboratory and subsequently a post-doctorate scientist (Dr. Brindha RN) was recruited to perform the Japanese encephalitis RT-PCR test on the same clinical samples. A high rate of positive Japanese encephalitis-IgM serology was reported, although quite a proportion of patients' sera that were tested positive in the department were subsequently found to be of false positive by Division of Arbovirus Diseases and CDC. Still, officials reported to the Ministry of Health that 40% of the cases were confirmed Japanese encephalitis, and that 100% confirmation was not required.

It wasn't until late February of 1999 that Dr. Chua became officially involved in the investigation when a patient came into the University Malaya Medical Centre. When testing the patient's serum, the doctor did find that is was positive for Japanese encephalitis -IgM, but still, Dr. Chua felt there was some novel or unusual agent causing the infection, and wanted to run viral cultures. The problem came in convincing the head of the department to let him run the cultures, even though the head of the department completely believed the outbreak was due to Japanese encephalitis virus. It took working behind the back of the head of the department, and eventually traveling to the United States to use better equipment, such as electron microscopy, to find out that the infectious agent wasn't Japanese encephalitis virus, but a paramyxovirus. Dr. Chau's one thing to say on his long fight to prove that it was a new virus is that "epidemiology and clinical knowledge opened the mind to the possibility of other virus than Japanese encephalitis during the 1998/99 Malaysian viral encephalitis outbreak. Viral culture led to discovery of the novel infective agent which was not possible with serology and RT-PCR."

Control and Prevention

Once the Malaysian government knew it was a paramyxovirus, they had to figure out where it was coming from, seeing as paramyxoviruses often are spread from livestock. One big clue that allowed them to figure out that it was spread from pigs was that no Muslims were being infected because Muslims don't handle pigs. Once they knew it was pigs the began one of the countries larges livestock culling, which effectively stopped the spread of the virus. The next question what where did the pigs get it from? After testing the pigs, it was found that the swine were not the natural reservoir, but were infected from contagious bat feces and urine, and that the fruit bat was the natural reservoir. It was also revealed that there had been previous outbreaks in swine, but due to the fact that pig farmers use to have small herds of pigs that were very isolated, the virus didn't

spread. It was the economic boom in Malaysia that began the epidemic, where pig farmers had more demand, leading to larger herds, that were in closer contact with other herds. This allowed the rapid spread or the virus through the pigs, and then onto humans. There is also the question of the sudden increase of infection in pigs, which is often attributed to the loss of natural habitat for the bats, pushing them to live closer and closer to humans, causing more spread of disease.

Transmission, Clinical Presentation, Diagnosis, and Treatment

Being transmitted from pigs isn't the only way that Nipah virus has spread to humans. Later outbreaks in Bangladesh and India, it was found that consumption of raw date palm sap and contact with bats lead to infection. As a side note, the prevention of spread by this method is to not eat raw date palm sap. The virus can also be spread person-to-person, and is most common in family and caregivers of Nipah virus infected patients.

The clinical symptoms of Nipah virus infection varies depending on the species infected. In pigs the main symptoms were respiratory, and some neurological symptoms. In humans, the symptoms are similar to that of influenza, with fever and muscle pain, but some cases also result in inflammation of the brain that leads to disorientation and/or coma. The incubation period of the virus is 4 to 18 days. The virus can also lead to latent infection, which is harder to diagnose because infection may have happened a while ago. Further, those who may have recovered from an acute episode may also have a relapse. Nevertheless, magnetic resonance of the brain is helpful in differentiating Nipah encephalitis from other encephalitis as well as in defining between acute and late onset or a relapsed form of the disease. There is also a wide range of fatality rate, anywhere from 9 to 75% depending on strain.

When a patient presents with these symptoms they must be tested to diagnose them with Nipah Virus. To do this the patients need a serology, histopathology, PCR and virus isolation. The problem is that most countries in South-East Asia do not have adequate facilities for diagnosing the virus. This makes it hard to accurately track outbreaks in the area. If a patient is diagnosed with NiV the next step is treatment. There is no effective treatment for Nipah virus disease, and it is limited to supportive care, such as ribavirin, which may alleviate the symptoms of nausea, vomiting, and convulsions, or decreasing fever, and controlling neurological symptoms. If patients present respiratory symptoms, they may require a ventilator.

There is currently a vaccine being developed, looking at a recombinant sub-unit vaccine that is so far effective in cats. Establishing appropriate surveillance systems will be necessary so that NiV outbreaks can be detected quickly and appropriate control measures initiated.

Classification

The Nipah virus is one of two highly pathogenic paramyxoviruses that have emerged in recent years that have unique genetic constitution, high virulence, and wide host range. This makes them unique from other paramyxoviruses and lead to classify them into a new genus, Henipavirus, with in the *Paramyxoviridae* family. The center for Disease Control and Prevention classify the Nipah virus as a category C agent, and is one of several viruses identified by WHO as a likely cause of a future epidemic in a new plan developed after the Ebola epidemic for urgent research and development before and during an epidemic toward new diagnostic tests, vaccines and medicines. It should also be noted that the origin of the Nipah virus is most likely to have occurred before the 1999 outbreak, and it is believed to have originate in 1947. Also, there are two clades of this virus, one believed to have originate in 1995, and another in 1985. It is also estimated that the mutation rate of Nipah virus is 6.5×10^{-4} substitution/site/year, which is similar to other RNA viruses, and the likely cause of new outbreaks.

Conclusion

It is cases like the outbreak and discovery of Nipah virus that teach us that we need to be wary of new outbreaks, and to think about every possible infectious agent before jumping to conclusions. It should also be noted that as a species we should become more and more wary of emerging zoonotic viruses as there is more loss of natural habitats, and more overlap between wild species and human race

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