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Kyasanur Forest Disease (KFD): Rare Disease of Zoonotic Origin

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ABSTRACT

Kyasanur forest disease (KFD) is a rare tick borne zoonotic disease that causes acute febrile hemorrhagic illness in humans and monkeys especially in southern part of India. The disease is caused by highly pathogenic KFD virus (KFDV) which belongs to member of the genus Flavivirus and family Flaviviridae. The disease is transmitted to monkeys and humans by infective tick Haemaphysalisspinigera. Seasonal outbreaks are expected to occur during the months of January to June. The aim of this paper is to briefly summarize the epidemiology, mode of transmission of KFD virus, clinical findings, diagnosis, treatment, control and prevention of the disease..

Keywords: Flavivirus; India; kyasanur forest disease; monkey fever; ticks.

INTRODUCTION

Kyasanur forest disease (KFD) is a viral ailment seen in both wild primates and humans living near forested areas. The disease causes high incidence of acute febrile illness progressing to haemorrhages with mortality in 2-10% of the cases.[1] The disease was named after the forest area where it was first discovered as Kyasanur forest disease (KFD) and the virus was named as KFD virus (KFDV). It is also termed locally as Monkey Disease or Monkey Fever because of the fact that the disease was first isolated from monkeys in Kyasanur forest in Shimoga district killing several of them in the year 1957.

The virus KFD belongs to Russian Spring Summer Encephalitis group, an RNA genome virus of family Flaviviridae.[2] KFDV has a genomic organization consisting of a single-stranded RNA molecule of nearly11 kb encoding a polyprotein which is cleaved into three structural and seven non-structural proteins.[3]

ORIGIN AND EPIDEMIOLOGY

The disease which is reported to be public health issue is detected endemic in Sagar taluk, Shimoga district in January 1957, caused by two species of monkeys viz. the black faced langur (Semnopithecus entellus) and the red faced bonnet monkey (Macacaradiata).[2] KFDV or associated viruses are also present in other areas of India, including parts of Kutch district, the Saurashtra region in Gujarat state, and in parts of West Bengal state, in forested regions west of Kolkata.[4]

In subsequent years the disease is reported to have been documented from Uttar Kannada, Udupi, Mangalore and Chikmagalore districts of Karnataka state. The transmission usually happens during the winter and summer months.[5] The disease is showing wider distribution and diffusion in areas like Chamrajnagara and Tirthalli in Karnataka,[6] Tamil Nadu,[7] and Wayanad district in Kerala state [8] during the past few years. The first human sporadic case of KFD was reported in the Wayanad district last year.[9] In Kerala, KFD has been documented in humans from Noolpuzha of Wayanad district in May 2013 and three cases from Nilambur of Malappuram district in June 2014. KFDV infection inmonkeys are reported from Mannar, Alappuzha District in April 2014. Though in 2013 and 2014 only one confirmed case each were reported but in the year 2015 KFD has manifested as an outbreak in two districts in Kerala, affecting nearly 50 persons and killing more than 10 people.[10]

Two positive cases of KFD have been reported in various parts of Wayanad district recently- seven cases from the Cheeyambam tribal hamlet in Pulpallygrama

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Panchayat and one each from Padinharethara, Periya and Poothadigramapanchayaths.

The exact nature of spread of KFDV and its origin are not clear. There is a school of thought that says that the virus might have been introduced to India in 1957 via migrant birds; but the confusion that needs to be cleared is that why KFDV stopped being introduced into India by migrant birds or was not carried to other parts of India.

The virus may have got adapted to the regional, environmental/ecological conditions and did not spread to other parts of the country. Available evidence indicates that migratory birds are unlikely to be responsible for the apparent introduction of KFD virus to the unique location in India. [1]

Another possibility is that KFDV might have been introduced to India a long time ago through the slave trade and silently propagated in the subcontinent, stemming in an epidemic only in the year 1957, when it was first identified and reported. There is a high possibility that KFD was present before 1957 without being reported. [11]

Commercial farming operations after clearings of forestland and intermingling of humans and livestock with native animal populations resulted an increase in vector borne disease. There has been drastic change in the ecosystem from relentless deforestation would have caused the monkeys to spend an increasing time on the forest floor and therefore to be exposed to the ticks. This would lead to amplification of the virus and bring man into contact with the virus for the first time.

MODE OF TRANSMISSION OF KFD VIRUS

KFD developed with surge in human and domestic animal population which altered the ecosystem in places where the virus had previously circulated between wild animals and its vectors. The disease is transmitted to monkeys and humans by bite of infected Haemaphysalis ticks especially at its nymphal stage.[9] KFDV then is transmitted to other ticks feeding on the infected animals.

KFD virus has been isolated from 16 species of ticks. However, Haemaphysalisspinigera is considered as the main vector. In enzootic state, KFD virus circulates through small mammals such as rodents, shrews, ground birds and tick species. Out of this mainly rodents, have long been considered reservoirs for the tick-borne flaviviruses. They can become infected by a virus and develop a low-level viremia which will be sufficient for transmission to a blood-feeding arthropod, without becoming ill. Rodents are ideal maintenance hosts, because their generation time is short, so that there is nearly always a large population of naive animals. The short life span of mosquitoes limit the vertical transmission of viruses and maintain the viruses within the in mosquito populations. In contrast, ticks may live for several years. [12]

When monkeys come in contact with the infected ticks, they get amplified and disseminate infection creating hot spots of infection. The people who pass through the forest either for cattle rearing or collecting firewood can get infected.

Large animals like goats, cows and sheep may become infected with KFD but play a limited role in the transmission of the disease due to insignificant viremia in them. These animals provide the blood for ticks and it is possible for infected animals with viremia to infect other ticks, but transmission of KFDV to humans from these larger animals is rare.[13-14] Human is dead-end in natural cycle of the virus.

Ticks have a definite stage-wise seasonal activity. The adults become active after a few monsoon rains in June. The adult population reaches its peak during July and August and gradually declines in September. Each fed female lays large number of eggs. Larvae preferably feed on small animals like rodents, shrews etc. Larval population builds up in the monsoon months but remains dormant under the forest litter and becomes suddenly active when the litter dries up during the post monsoon months-October to December. Nymphal activity is high from January to May. Neutralizing antibodies have been found in cattle, buffaloes, goats, wild boars, porcupines, squirrels, flying squirrels, rats, mice, shrews and a number of bird species.

Black-naped hare, porcupines, flying squirrels, Malabar giant squirrels, three stripped squirrels, gerbils, mice, long tailed tree mice and shrews have been shown to circulate high titer of virus. KFD virus may be persisting in latent form in the organs, mainly in the brain tissues of experimentally diseased rodents.

CLINICAL FEATURES

In monkeys, KFDV causes acute febrile illness, haemorrhagic enteritis.[15] When infected monkeys die, ticks drop from the body, thereby generating hotspots of infectious ticks that further spread the virus.

Humans have an incubation period of 3-8 days followed

by chills, headache and high fever about 40^{0}C for 3-4 days. After the onset of initial symptoms there could be severe myalgia, cough, diarrhoea, vomiting, photophobia and bleeding problems. Papulo-vesicular eruption of the soft palate is an important diagnostic sign in some patients. Bleeding signs from gums, nose, in sputum, bleeding from gastrointestinal tract resulting in dark faeces (malena) and fresh blood in the faeces are commonly seen. Cervical and axillary lymph nodes are usually palpable. After 1-2 weeks of symptoms, some patients recover without complication. The convalescent phase after the onset of disease is generally prolonged almost up to 4 weeks. Relapse of the symptoms, often observed after 1 to 2 weeks of the first febrile period, lasts for 2 to 12 days. During infection by KFDV, the virus titre remains high for 10 days after onset of symptoms.[16]

Abnormal low blood pressure, low red blood cell count, leucopenia and accompanying thrombocytopenia are constant haematological features in KFD. Intra-alveolar haemorrhage, resulting into secondary infection and extensive gastrointestinal haemorrhages are terminal complications that could lead to casualty.[17]

Clinically, KFD resembles Omsk hemorrhagic fever (OHF), which occurs in the Omsk Oblast in Siberia. The other tick- borne viral disease antigenically related to KFD and OHF is tick-borne encephalitis.[1]

In monkeys blood clots were observed in post-mortem findings in the anus, haemorrhage in lungs, moderate swelling and pallor of the renal cortex, brain, and adrenals. Nonpurulent encephalitis with focal microgliosdis, perivascular cuffing are the common lesions in brain. Anal haemorrhage, pallor of adrenal cortex, focal liver necrosis with cytoplasmic inclusion bodies, necrosis in small and large intestines are common.[17]

Histologically liver shows focal hepatocellular degeneration, fatty changes, necrosis, degenerative changes in central and midzonal cells, including vacuoles and pigments with the presence of eosinophil cytoplasmic inclusions. In the kidneys there were marked degenerative changes in the tubules. In humans gross findings are pallor of the liver, kidneys, adrenals and brain. Degenerative changes are also seen in liver, kidney with mild myocarditis and encephalitis.[18]

DIAGNOSIS

Diagnosis is basically through virus isolation from blood and through serological findings. Human sera can be tested for KFDV RNA by real-time RT-PCR, RT-n PCR assay, and anti-KFDV IgM and IgG by ELISA. Laboratory tests include Hemagglutination inhibition, immunofluorescence and virus neutralization tests. [19]

TREATMENT, PREVENTION AND CONTROL

The prime importance should be given to control and prevent the disease. An apt and appropriate supportive therapy that reduces mortality in humans which includes analgesics and antipyretics, intravenous fluids for those with hypotension, blood transfusion or fresh frozen plasma and platelets for those with hemorrhagic symptoms, antibiotics for bronchopneumonia, and corticosteroids and anticonvulsants for neurological symptoms.

For management of KFD cases, efforts should be done to ensure ample staff and infrastructure at primary andsecondary health-care facilities. State government should take initiative to educate the villagers and tourists who visit the forest in Karnataka state about using repellent and gum boots and having prior vaccination. Whenever monkey deaths are reported, rapid action is taken to convey information to health officers and veterinary staff for necropsy of monkeys, collection of specimens for diagnosis of monkey samples, and proper disposal of dead monkeys. Education has to be provided in local languages every year. As soon as suspected cases are notified they are referred to National Institute of Virology (NIV), Pune for investigation and confirmation.

Vaccination of villagers and forest workers proved to be very effective in preventing the disease. For prevention and control of KFD vaccination with formalin-inactivated tissue-culture vaccine has been the primary approach. [20] The Vaccines based on inactivated viruses as antigens have shown a certain level of adverse reactions, especially in children, and this has to be carefully balanced with their efficacy and durability. [20]

The current vaccine strategy used in India includes a two-dose vaccine at an interval of one month. The initial series is followed by a booster at 6-9 months and subsequent boosters every 5 years. [21] The strategy also involves mass vaccination in areas reporting laboratory evidence of KFD activity and in villages within a 5-km radius of such areas.[22]

Improper storage of the vaccine could be one of the reasons for surfacing of KFD inspite of routine vaccinations. Vaccination of the tribal population is the need of the hour along with improved surveillance, health education, and prevention efforts targeted at ticks or prevention of tick bites.

Treating the forest floor with an efficient insecticide is suitable for killing ticks. This is particularly useful to clear infection following detection of monkey deaths. The use of spray insecticides has been recommended in a 50-m radius around a dead monkey. Tick repellents such as DEET, DMP, DBP provide 90-100% protection against tick bite. Tick bites are best prevented by preventing people from visiting tick-infested areas or by wearing long trousers that are tucked into boots.

Dipping is the primary method of tick control for livestock and has been found to be highly effective for controlling several tick-borne diseases. Spraying is another method used to apply the chemical acaricides that kill ticks. [23-25]

BIOSAFETY CONCERNS

Internationally, KFD virus is ranked as one of the highest risk categories of pathogens belonging to Bio Safety Level-4 (BSL-4) for other countries and a group 3 risk pathogen for India. KFDV is regarded as a potential biowarfare agent.[26] During investigative procedures, over 100 laboratory persons got infected and suffered with the disease. Majority of the infections occurred in field during investigations on etiological agent, arthropods and mammals in nature.

CONCLUSIONS

More studies would be required to understand the geographic extent or spread of KFD, along with its role as a biowarfare agent in South India. Incidences of human fever cases and unnatural monkey deaths in KFD epidemic area have to be monitored and detail information be communicated to health authorities.

REFERENCES

1. Banerjee K. Kyasanur Forest disease. In Arboviruses: Epidemiology and Ecology. Edited by Monath TP. CRC Press, Boca Raton, Florida;1990:93 -116.
2. Work TH, Roderiguez FM, Bhatt PN. Virological epidemiology of the 1958 epidemic of Kyasanur Forest disease.Am J Public Health Nations Health. 1959; 49(7):869-74.
3. Chambers T.J, Hahn C.S, Galler R, Rice C M. Flavivirus genome organisation, expression and replication. Annual Reviews of Microbiology.1990 ;44 :649-88.
4. Kasabi GS, Murhekar MV, Yadav PD, Raghunandan R, Kiran SK, Sandhya VK, et al. Kyasanur Forest disease, India,2011–2012.Emerg Infect Dis. 2013;19(2):278-82.
5. Mourya DT, Yadav PD, Sandhya VK, Reddy S .Spread of Kyasanur Forest disease, Bandipur Tiger Reserve, India,2012–2013.Emerg Infect Dis. 2013;19:1540-41.
6. Yadav PD, Shete AM, Patil DY, Sandya VK, Prakash KS, Surgihalli R, et al.Outbreak of Kyasanur Forest disease in Thirthahalli, Karnataka, India, 2014.Int J Infect Dis.2014; 26:132-4.
7. Mourya DT, Yadav PD, Patil DY. Highly infectious tick borne viral diseases: Kyasanur forest disease and Crimean-Congo hemorrhagic fever in India.WHO South-East Asia J Public Health. 2014;3(1):8-21.
8. The Hindu (News Paper). Youth gets Kyasanur disease in Wayanad. [http://www.thehindu.com/news/national/kerala/youth-gets-kyasanur-disease-in-wayanad/article4712468.ece]. Accessed 6 Jun 2014.
9. Abiliyababu, Jayakrishnan S.S. Viral hemorrhagic fever: new health challenge to south Indians. Int.J.Inv.Pharm.Sci. 2015;3(2);976-78.
10. PriyabrataPattnaik. Kyasanur forest disease: an epidemiological view in India.Rev. Med. Virol. 2006; 16: 151–65.
11. Work TH, Trapido H. Summary of preliminary report of investigations of the virus research centre on an epidemic disease affecting forest villagers and wild monkeys in Shimoga district, Mysore. Indian J. Med. Sci. 1957;11:340–41.
12. Nichter, Mark. Kyasanur Forest Disease: Ethnography of a Disease of Development. Medical Anthropology .1987; 1(4): 406–23.
13. Lewis, Michael. Scientists or Spies?Ecology in a Climate of Cold War Suspicion. Economic and Political Weekly. 2002 ;37 (24): 2324–332.
14. Pavri K. Clinical, Clinicopathologic features of of Kyasanur forest disease. Rev Infect Dis. 1989; 11:854-59.
15. Bhat W R. Kyasanur forest disease and decimation of monkeys in Malnad area of Karnataka. BiolIndica. 1991,1: 59-67.
16. Devndra TM, Pragya D , Sandhya ,Shivanna R. Spread of Kyasanur Forest Disease, Bandipur Tiger Resrve. India, 2012-13. Emerg infect Dis. 2013; 19:1-7

17. Adhikari PMR , Prabhu MG, Raghuuveer CV. Clinical study of 100 cases of Kyasanur Forest Disease with clinicopathological correlation. Indian J Med Sci.1993;47: 124-30.

18. Pattnaik P. Kyasanur forest an epidemiological view in India. Rev Med Virol 2006, 16: 51-65 |

19. Mourya DT, Yadav PD, Mehla R, Barde PV, Yergolkar PN, Kumar SR et al. Diagnosis of Kyasanur Forest Disease by nested Rt-PCR, real time Rt-PCR and IgM CAPTURE Elisa. J.Virol Methods 2012; 186: 49-54 .

20. Dandawate CN, Desai GB, Achar TR, Banerjee K. Field evaluation of formalin inactivated Kyasanur Forest disease virus tissue culture vaccine in three districts of Karnataka state. Ind. J. Med. Res. 1994;99:152-8.

21. Sarkar JK, Chatterjee SN. Survey of antibodies against arthropod-borne viruses in the human sera collected from Calcutta and other areas of West Bengal. Indian J Med Res. 1962;50:833–41.

22. Directorate of Health and Family Welfare Services, Government of Karnataka, 2005 manual on Kyasanur Forest disease. (unpub. data)

23. Gambel JM, Brundage JF, Kuschner RA, Kelley PW. Deployed US army soldiers' knowledge and use of personal protection measures to prevent arthropod-related casualties. J. Travel Med. 1998;5:217–20.

24. Ho-Pun-Cheung T, Lamarque D, Josse R, Perez-Eid C, Niel L, Martenot G et al. Protective effect of clothing impregnated with permethrin against D. reticulatus and D. marginatus in an open biotope of central western France. Bull. Soc. Pathol. Exot.1999;92:337–40.

25. Ergonul O, Whitehouse CA. Risk groups and control measures for crimean-congo hemorrhagic fever. In: Ergonul O, Whitehouse CA. Editors. Crimean-Congo hemorrhagic fever: a global perspective. Dordrecht: Springer, 2007. pp. 273-80.

26. Borio L, Ingleshy T, Peters CJ. Hemorrhagic fever viruses as biological weapons-medical and public health management. JAMA 2002; 287: 2391– 405.