

RABIES, Fatal yet preventable

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ABSTRACT

Rabies is a viral zoonotic disease that proves highly fatal in its neurological form. However, a few cases have also been reported regarding recovery but with brain disabilities. As the disease progresses, signs and symptoms also get crucial (from non-specific to highly specific). Numerous transmission routes can be seen but dog bite is the most common among all. Multiple preventive measures can be used to lower the impact of disease, but all are effective up to certain limits. Moreover, effective treatment of this disease is still under study due to multiple challenges such as lack of resources and pathogenic mechanisms.

1. Introduction:

For centuries, humans felt terror after being bitten by a rabid dog. Until the 19th century, there were not any accurate diagnostic, therapeutic, and prevention techniques for this fatal disease. Increased mortality rate put a massive pressure on scientific thoughts which influenced them to make it more curable and preventable. So, from the 19th century, scientists started to achieve multiple milestones from diagnostics to preventive techniques for this

Rabies is derived from the Latin word rabere which means "mad". Rabies is caused by the virus belonging to the Rhabdoviridae family consisting of more than 100 viruses, with a wide host range. There are numerous genera among which lyssavirus has high pathological importance because of the presence of highly significant rabies virus in it. Structurally they are single-strand, negative sense, enveloped RNA viruses [2]. It has high zoonotic potential and is highly lethal. Dogs, cats, ruminants, and even rodents can also be affected by this virus. It is a cosmopolitan virus found in the world infecting animals and humans of all age groups. It is mostly transmitted by the bite of a rabid animal. An increase in the population of free-roaming infected animals makes it a serious threat to humans. Awareness regarding prevention and control is necessary to avoid rabies infection [3].

2. Route of transmission

Diseases have multiple routes of transmission, some need interruption in skin integrity (Rabies) while some can be transmitted without interruption (mange). The most common cause of the transmission of rabies virus is dog bite. Exposure to the mucus membranes and the oral route is ineffective while the nasal route is significantly important due to the olfactory nerves which are directly linked to the brain.

Human-to-human transmission is rare, but cases are reported during organ transplantation in which donor tissue was infected with the virus. Moreover, exposure to urine, blood, and feces does not cause the disease [4]. No transplacental transmission has been reported while transmission from mother to offspring through breastfeeding is reported. Transmission also occurs from rabies zones to rabies-free zones by the movement of stray dogs [5].

3. Pathogenesis

Depending upon the age and site of the bite to the patient, it has a highly variable incubation period ranging from 5 days to as long as 6 years. The infected patients shed the virus in their saliva which is deposited through multiple routes (such as bites or skin abrasion) into the subcutaneous tissue and muscles of the host. After crossing the skin barrier, the virus starts to bind with the cell receptors and replicates in striated muscles. After successful replication, it enters the peripheral nervous system through the neuromuscular junction and causes infection in neuronal cells. After this virus reaches to spinal cord, brain, and ganglion. Till that stage, no signs of disease will show due to insufficient viral antigen which is required to trigger an immune response of the host body [6].

By the time the virus reaches the CNS Central nervous system, it starts extensive replication. At this stage, clinical signs can be seen. The virus starts to disseminate into different body parts and eventually reaches nervous to non-nervous tissues such as taste buds, salivary glands, thymus, etc. Along with all these, the virus causes damage to brain cells which leads to the paralysis of the body [7].

4. Clinical Significance

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Signs and symptoms of rabies depend upon the amount of viral load, form of disease, and the site of infection. Once the patient has started to show signs and symptoms, it becomes incurable. Generally, the disease is divided into multiple stages such as the incubation period, prodromal period, neurological period (furious and paralytic form), coma, and death. In earlier stages, signs are non-specific such as fever, fatigue, ptyalism, restlessness, signs related to

the respiratory system, and GIT is also present. More prominent and differential signs can be seen in the neurological form such as psychiatric disturbance, agitation, photophobia, encephalitis, and priapism which often lead to death [8].

5. Diagnosis

A rough diagnosis can be made based on history, signs, and symptoms. It can also be diagnosed by taking a little part from an infected brain which must include tissues from the brain stem and cerebellum. Moreover, there are multiple tests for the diagnosis of rabies such as DFA (Direct Fluorescent Antibody Technique), MIT (Mouse Inoculation Technique), Tissue Culture Infection technique (TCIT), PCR/RT-PCR, virus isolation, histopathology [9]

6. Treatment

Once clinical signs have been obvious no treatment will remain effective and it becomes difficult to cure the disease. As it is anti-viral there is not any specific treatment available. The anti-viral drugs such as ribavirin and favipiravir fail to reach enough efficacious levels [10]. It can only be controlled through supportive treatment and multiple prevention strategies vaccinations. Moreover, combining the antiviral neuroprotective drugs could provide better results. There are also multiple challenges while dealing with the prevention of rabies such as limited global will, fewer resources, and a lack of enough information regarding the pathogenesis of the virus [11].

7. Control and Prevention

It can only be prevented through prophylactic measures. WHO stresses the immediate and thorough washing of wounds through water and disinfectants as it decreases the viral load. However, awareness campaigns within societies may also have positive outcomes regarding the control and prevention of disease [12]. Another effective method to control the disease is the dog neutering campaign which started in 2022. In this campaign, free-roaming dogs have been caught and neutered [13]. Since 2007, every year Rabies Day has been celebrated on 27 September to provoke awareness in society and to eliminate the disease globally.

Massive vaccination and proper surveillance are another way to control the disease. In humans, vaccination is recommended as pre and post-exposure to the virus. Pre-exposure vaccination is scheduled at 0, 7, 21, and 28th day while post-exposure is scheduled at 0, 3,7, 14, and 28th day [14].

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