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Rabies: The Deadly Dilemma

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Introduction

Rabies is a rapidly progressive, acute viral encephalomyelitis caused by a neurotropic RNA virus that belongs to the genus Lyssavirus in the family Rhabdoviridae and is transmissible to all warm-blooded animals including humans.

The disease is prevalent in almost all areas of the world and the burden of the disease is very high in Africa, Asia, and Latin America. Globally, around 55,000-60,000 human rabies deaths occur every year of which about 20,000 (as per the 2003 survey) are reported from India alone. More than 97% of human rabies cases are caused by the bite of rabies-infected dogs. Children under the age of 15 living in rural settings are victims in most instances, where awareness of the disease and access to appropriate post-exposure prophylaxis (PEP) is limited or non-existent. Nonetheless, human rabies of dog origin is completely preventable. Public awareness, health education, dog vaccination, and accessibility of pre-and post-exposure prophylaxis are key for rabies prevention and control.

Transmission

People and animals can get rabies if they are bitten, licked, or scratched by a rabid animal. The infection is commonly transmitted following the bite of a rabid dog (~97%), cat (~2%), and other animals (~1%) i.e., mongoose, fox, jackal, and other wild animals. Sometimes the virus appears in the saliva even before the onset of clinical signs in the infected animal. Person-to-person transmission of rabies has never been documented other than few cases resulting from organ/ tissue (cornea) transplant; however, the aerosol transmission of rabies has occurred in laboratory settings.

Symptoms of rabies

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In humans, the symptoms usually start after an incubation period of typically 3 to 8 weeks but can range from 5 days to several years. The incubation period varies in different animals; dogs (10 days to 6 months), cats (2 weeks to even years) & cattle (15 days to 5 months). Humans: Initial symptoms may include headache, fever, malaise, paraesthesia (abnormal dermal sensation), and pain at the site of the bite (prodromal phase). Subsequently neurologic symptoms viz., seizures, dysphagia, hydrophobia, delirium, agitation, and paralysis occur. Neurological deterioration is rapid and death is often due to cardio-respiratory failures. Death usually occurs on an average 10 days after the onset of symptoms.

(1) Dogs may show irritability, restlessness, excessive salivation, unusual aggression, attack/bite without provocation, eat unusual objects like wood, stones, and paper. Sometimes, dogs may look depressed and hide away or may have paralysis or a drooping head.

(2) In the case of cat irritability, restlessness, hitting paws in the air, aimless jumping, and aggressiveness are more commonly observed. Affected dogs and cats usually do not survive for more than ten days.

(3) In ruminants (cattle, buffalo sheep, and goat) excessive salivation, behavioural change, muzzle tremors, vocalization (bellowing), aggression, hyperaesthesia, hyperexcitability, ataxia, lameness, and pharyngeal paresis/paralysis is observed. The furious form of rabies is seen in 70% of the ruminants in experimental settings; however, cattle and buffaloes do not bite when they are rabid.

(4) Horses and donkeys get aggressive and bite ferociously when they are rabid.

Samples for diagnosis

In the case of human saliva, serum, spinal fluid, and skin biopsies of hair follicles at the nape of the neck (nuchal skin biopsy) are the best ante-mortem samples for rabies diagnosis, and brain tissue can be collected at post-mortem. Saliva can be used for RT-PCR/virus isolation. Serum and spinal fluid can be used for testing antibodies to the rabies virus. Skin biopsy specimens are examined for rabies antigen in the cutaneous nerves at the base of hair follicles. From animals, brain stem, cerebellum, thalamus, medulla oblongata are generally collected after death/euthanasia for diagnosis of rabies. In India four regional

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laboratories have been strengthened for rabies diagnosis including National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru; Disease Investigation Unit Lab, Directorate of Animal Husbandry and Veterinary Services, Goa; AIIMS, Jodhpur; and National Centre for Disease Control (NCDC), Delhi. In addition, various medical colleges, Veterinary colleges and Regional Disease Diagnostic Laboratories (RDDL) have expertise in rabies disease diagnosis.

Diagnostic tests

The most widely used and gold standard test for post-mortem rabies diagnosis is the fluorescent antibody test (FAT), which is recommended by both WHO and OIE. Rapid Fluorescent Focus Inhibition Test (RFFIT) is considered the gold standard method to assess rabies virus-neutralizing antibodies. Histological techniques such as Seller's staining (for detection of Negri bodies) are no longer recommended for rabies diagnosis.

Treatment

There is no specific treatment once rabies develops. In rabid animal bite suspected cases, efforts should be focused on preventing the disease development and treatment should be started immediately after exposure. Treatment comprises four components: (a) Wound management, (b) Vaccination, (c) Rabies immunoglobulin (RIG) infiltration and (d) Counselling.

a) Wound management: Wound washing greatly eliminates the risk of rabies and all animal bite victims are advised to thoroughly flush the wound/s with running tap water, when appropriate for 15 minutes to remove the traces of saliva from the wound. Then wash the wound/s with soap to inactivate the virus. Povidone-iodine or 70% ethanol or any other antiseptics/ virucidal may be then applied on all the wounds. If the wound/s is gaping, then the edges can be brought together by application of a pressure bandage (after careful infiltration of Rabies Immunoglobulin, RIG), and delayed (after 72 hours) suturing may be done. Antibiotic prophylaxis/ tetanus toxoid may also be given if required to prevent sepsis in the wound(s).

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b) Post-exposure prophylaxis (PEP): Intradermal / Intramuscular rabies vaccination (IDRV/IMRV) can be given to the bite victims. The recommended regimen for intradermal vaccination (given on deltoids and suprascapular region) consists of injecting 0.1mL of the reconstituted vaccine at two sites on days 0,3,7 and 28 post-exposure. This is known as the updated "Thai Red Cross (TRC)" regimen. The PEP can also be given by intramuscular (IM) route using five doses Essen regimen given on days 0, 3, 7, 14, and 28.

c) Rabies Immunoglobulin (RIG): RIG provides passive immunity to the patients. RIG administration is recommended after category III exposures of individuals who have not been previously vaccinated against rabies. The dose of the ERIG is 40 IU per kg body weight with a maximum of 3000 units.

d) Human Rabies Immunoglobulin (HRIG): HRIG is of homologous origin and is relatively free from side effects. The dose of the HRIG is 20 IU per kg body weight with a maximum of 1500 units. Care should be taken not to administer RIG and anti-rabies vaccine at the same site.

Prevention and control

Mass dog vaccination and vaccination of wild animals (using vaccine baits); providing improved access to pre- and post-exposure prophylaxis in humans and animals; stray animal population control programs (reducing population density through sterilization); creation of public awareness on rabies; education of people on management of animal bites; and increased surveillance of the disease are the effective methods for prevention of rabies. Rabies control programs are aimed at elimination of canine rabies (urban rabies), control of wildlife rabies, and also by avoiding/reducing infection of humans from animal sources. As >95% of human rabies occur as a result of rabid dog bites, control programs targeting canine rabies can effectively reduce the risk of rabies to humans. Various analyses indicate that vaccinating 70% of dogs should be enough to break the rabies transmission cycle and thereby eliminate endemic infections. However, in many countries due to the complex nature of rabies control activities and other public health priorities, this target is often not achieved. A multi-disciplinary approach involving Government, local bodies, medical professionals, veterinary professionals, public health workers, ecologists, vaccine producers, and the general

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public is required make to this vision a reality. Government should have a national action plan for control of rabies and regularly monitor, control, and evaluate the program at regional and national levels. In India, the Ministry of Health & Family Welfare, Govt of India is implementing the "National Rabies Control Program" to prevent human deaths due to rabies & to prevent transmission of rabies through canine rabies control. Local government authorities (Panchayat/ Municipality/Corporation) who are responsible for the development and enforcement of legislation relating to dog ownership (e.g., registration, microchipping, vaccination, abandonment) and control of stray dogs (e.g., dog catching and shelters) and environmental hygiene should act promptly. Regular and proper actions from local bodies that limit the availability of food, water, and shelter to stray dogs (e.g., proper removal of municipal waste as it is the main food for stray dogs) will have a huge impact on rabies control.

Veterinarians have an important role to play in rabies control in coordinating animal birth control (ABC) programs and mass vaccination in their locality. In addition, veterinarians can also play role in reproductive control in stray dogs (capture, sterilization, microchipping, return, and rehoming), registration of dogs (licensing), control of dog movement national/international, and educating pet owners to regularly vaccinate their animals. Medical professionals can educate people on bite prevention and immediate care measures after a bite. Dog owners/public should accept that 'responsible dog ownership is key to the successful implementation of any rabies control program. Non-governmental organizations (NGOs) that have expertise in handling and kennelling dogs can help in the implementation of dog sterilization programs. Low-cost vaccines with adequate efficacy, safety, and potency from vaccine manufacturers would also help in the successful implementation of the rabies control program.