REVIEW ARTICLE

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RABIES IN NIGERIA: A REVIEW OF LITERATURE

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ABSTRACT

Rabies, also known as hydrophobia is an acute, viral disease of all warm blooded animals including man. It is caused by the rabies virus (RABV), a bullet–shaped, enveloped RNA virus, 45-100 nm in diameter & 100-430 nm in length with projections and helical nucleocapsid, one of the better known encephalitis viruses of the family *Rhabdoviridae* and genus Lyssavirus type 1

It is a major public-health problem in most parts of the developing world. The domestic dog (*Canis familiaris*) plays a principal role (accounting for over 99%) as a reservoir and transmitter of the disease to humans. Developing countries account for almost all the reported human deaths (99.9%) and most cases of human post-exposure treatments. Rabies is an important public health problem especially in the developing countries and this articles aims to draw attention to this neglected disease.

Key words: *rhabdoviridae*, rabies

LA RAGE AU NIGERIA: UNE REVUE DE LA LITTERATURE.

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RESUME:

La rage , également connu sous hydrophobie, est une maladie virale aiguë de tous les animaux a sang chaud y compris l'homme. Elle est causée par le virus de la rage (RABV), une forme de balle, virus enveloppé à ARN,45 – 100nm de diamètre et 100 – 430 nm en longueur avec des saillies et des nucléocapsidehélicoïdale, l'un des virus encéphalite mieux connu de la famille *Rhabdoviridae* et le genre *Lyssavirus* type 1.

C'est unproblème majeur de Sante Publique dans la plupart des régions du monde développant. Le chien domestique (*Canis familiaris)* joue une rôle majeur (représentant plus 99%) comme une réservoir et émetteur de la maladie aux humains. Les pays en voie de développementreprésentent presque tous les décèsrapportés des humains (99,9%) et la plupart des cas de traitement post – exposition de l'homme. La rage est un problème important de Santé publique particulièrement dans les pays en voie de développement et cet article vise à attirer l'attention sur cette maladie négligée.

Mots – clés: *rhabdoviridae*, la rage.

INTRODUCTION

Rabies has existed for more than 4,300 years making it one of the most typical zoonoses known through the ages (1). The antiquity of rabies is illustrated by the ancient origins of terms describing the disease. For instance, the word "rabies" is a Latin word derived from the Sanskrit "rabhas" meaning "to do violence."

Early recognition of the infectivity of the saliva of rabid dogs led Roman writers to describe the infectious material as a poison, for which the Latin word was "virus" (2). Lyssa virus, the genus to which rabies and rabies-related viruses belong, owes its name to the Greek "lyssa" or "lytta," meaning "madness." The first recorded description of canine rabies apparently was made by Democritus in 500 B.C. In his Natural History of Animals, Aristotle's writings on rabies described dogs suffering from a madness causing irritability and how following their bite other animals became diseased. Little has changed in the epidemiology of rabies, as dogs and other carnivores remain the common sources of human infection in most areas of the world where the virus is enzootic.

In the 1930s it was thought that if dog rabies were eliminated, the human problem would be solved and by the late 1950s it appeared that rabies had indeed lost much of its potential as a public health problem, having been significantly reduced by mass dog vaccination programs. A turning point was reached in 1958, when rabid canine cases had been reduced by such a degree that they were surpassed by the increasing number of cases in wild animals but it was discovered that rabies in wild animals is equally a threat to the human populace as it is in dogs. The situation continued to improve until 1960s; when"only" 16 human rabies related deaths were recorded as against 113 in the previous decade (3).

Rabies in Nigeria

Rabies was first reported in Nigeria in 1912 and about 10,000 annual human cases are reported in Nigeria (4) making the disease a persistent endemic problem. Despite efforts to control rabies, the disease continues to be a major scourge of dogs and cats in plateau state and in Nigeria in general (4).

AETIOLOGY

Rabies is caused by a single stranded, negative-sense RNA virus of the order *Mononegavirales,* family *Rhabdoviridae* and genus Lyssavirus (5). It is a neurotropic virus that is generally transmitted through bites from infected animals to susceptible host species including humans (6).

Rabies Virus Characteristics

Based on antigenic characterization of panels of Lyssaviruses, seven genotypes (GTs) have been identified (7). These are Classical rabies (RABV) GT1, Lagos bat Virus (LBV) GT2, Mokola virus (MOKV) GT3, Duvenhage virus (DUVV) GT4, European bat Lyssavirus type-1 (EBLV-1) GT5, European bat Lyssavirus type-2 (EBLV-2) GT6 and Australian bat Lyssavirus (ABLV) GT7. There are several emerging Lyssaviruses recently identified in Eurasia and these include Aravan (ARAV), Khujand (KHUV) (Kuzmin et al., 2005), Irkut (IRKV) and West Caucasian bat virus (WCBV) (8). These were incorporated into the genus as putative species including Rochambeau virus (RBUV), but no phylogenic relatedness to Lyssaviruses (9)

The virus is contained within a bullet-shaped bilayered envelope. The genome encodes five structural proteins viz:Viral nucleocapsid protein (N), Phosphoprotein (P), Envelope matrix protein (M), Glycoprotein (G), RNA polymerase (L). The Polymerase, Nucleoprotein and Phosphoprotein form a complex with the genome to form an inner nucleocapsid. The matrix protein forms the inner side of the bilayered lipid envelope and the glycoprotein forms the outer layer and spike-like projections, the target of virus neutralizing antibody (Wunner et al, 1988)*

The Lyssavirus genus is separable into two distinct phylogroups based on genetic analysis of the G gene, and sequences of representative virus isolates, immunogenicity and their virulent properties [11]. Phylogroup I comprises of GTs 1, 4, 5, 7, ARAV, KHUV and IRKV, whereas phylogroup II is composed of GTs 2 and 3. Recent reports suggest that WCBV does not reside in either of the two phylogroups[12] based on genetic distances and the absence of cross-reactivity, hence the proposal to place WCBV in a newly formed phylogroup III (12).

EPIDEMIOLOGY

Rabies is a worldwide threat of which the domestic dog (*Canisfamiliaris*) is the main source of exposure and primary vector for this important human disease (13). Global estimates indicate that approximately ten million persons are bitten by animals around the world yearly and considered for prophylaxis and treatment against rabies. The disease causes 55,000 annual mortalities with 56% (30,800/55,000) and 44% (24,200/55,000) occurring in Asia and Africa respectively (14).

In spite of its endemic nature, the true picture of the disease burden has not been well understood. The disease recently gained tremendous public interest of which several efforts were made by government to assess the magnitude of the problem through surveillance approach, mass vaccination programmes and awareness campaigns in hot zones of high rabies activities. Despite all efforts made by health authorities nationwide to curb increasing preponderance of the disease, reports of cases still

persist (15). However, myriads of factors have been highlighted by some studies to be responsible for the persistent increase in cases both in animal and human populations in Nigeria. These factors include; socio-economic disposition, awareness and knowledge of the disease, vaccine and vaccine related factors, weak surveillance system, game activities involving dogs, slaughter dog meat consumption, lack of accurate data on the true impact of the disease and finally lack of government commitment to control measures amongst others

TRANSMISSION

The virus is transmitted in most cases by bites and to a lesser extent by contamination of cuts, wounds and mucous membranes with saliva from rabid animals. Non-bite related exposures to the virus of apparent highest risk are those from large amounts of aerosolized rabies virus, organs (i.e., corneas) transplanted from patients who died of rabies, and contact of saliva or nervous tissue from a rabid animal with mucous membranes or scratches (16).

PATHOGENESIS

The Lyssaviruses have a predilection for neural tissue (neurotrophism) where they migrate to the central nervous system and cause severe signs. Following a bite wound, the virus may remain inactive or replicate in local nervous tissues (and possibly skeletal muscle). The virus then spreads to neuromuscular junctions and neurotendinal spindles after a variable period (days or weeks). By retrograde (centripetal or axoplasmic) flow in peripheral nerves, transport of the virus to the central nervous system (CNS) needs a minimum of 21 days. After progression in CNS, the virus moves rapidly to the brain. The virus enters the spinal cord or brain stem ipsilateral to the initial inoculated site. The infection then spreads to contralateral neurons and ascends bilaterally in the spinal cord or brain stem to the forebrain. The damaged motor neurons can cause typical flaccid paralysis and ascending paralysis. Viral invasion leads to inflammation and degeneration of nervous tissue. From the CNS the virus spreads centrifugally to other tissues such as heart, cornea, adrenal glands, etc via peripheral, sensory and motor nerves. Visceral and somatic portions of cranial and spinal cord nerves and the autonomic nervous system are affected. The virus spreads via cranial nerves to salivary glands which indicates that the brain has been already infected. Viremia is not detectable; the virus affects the neural system and results in mental status changes and respiratory failure which is fatal (17).

DIAGNOSES

The confirmation of suspected rabies cases involveslaboratory tests. Rabies diagnoses based on clinical presentation is unreliable as there are no truly pathognomonic symptoms of the disease (18) Definitive diagnosis of rabies in the laboratory usually requires various histological and virological techniques (19).

Direct Rapid Immunohistochemstry Test (DRIT)

The DRIT is a biotin streptavidin-HRP system of immunohistochemical test that detects rabies virus antigen in fresh frozen, glycerol preserved and other archived brain tissues. It is an unlicensed procedure designed by the CDC for consideration as a potential confirmatory measure of the direct fluorescent antibody test, according to the national standard operating procedure for the diagnosis of rabies in animals. In addition, the RIT may be used to enhance field surveillance among suspect wildlife, particularly in support of national, regional, state, or local oral vaccination programs

A study carried out by Lembo et al., 2006, in Tanzania result in the conclusion that DRIT showed a sensitivity and specificity equivalent to those of the DFA. The test is simple, requires no specialized equipment or infrastructure, and can be successfully performed on samples preserved in glycerol solution for 15 months or frozen for 24 months and in variable conditions of preservation. These qualities make it ideal for testing under field conditions and in developing countries. Although further laboratory and field evaluations are required, results are promising and highlight the potential value of the DRIT for countries with limited diagnostic resources. First, this technique could greatly enhance epidemiologic surveillance in remote areas where rabies incidence data are difficult to obtain. Second, the test could improve the ability to respond to outbreaks with effective management decisions. Third, it could be extremely valuable in guiding decisions regarding rational use of rabies PEP.

Histopathology

As described by Adlochi Negri in 1903, definitive diagnosis for rabies include demonstration of intracytoplasmiceosinophilic inclusions which are round or oval in shape, eosinophilic with basophilic granules in rabies infected tissues. These granules now referred to as negri bodies can be demonstration in histological sections or fresh bilateral smears of samples from hippocampus (Ammon's horn), brain stem and the cerebellum after staining with seller, haematoxylin& eosin or Mann. This method which

has been proven to have 50-80% reliability in detecting antigens in infected animals (20) has been superseded by other methods.

Fluorescent antibody test (FAT)

This is the current OIE and WHO prescribed method for rabies virus detection (21) because of its reliability and sensitivity. It is a quick test with result of test being obtainable within two hours but the expensive nature of equipments such as fluorescent microscope and the expensive antibody conjugate makes its usage a challenge in Africa.

PREVENTION AND CONTROL

Pre exposure immunization

In humans, especially high-risk groups such as rabies laboratory workers, animal control facilities workers and veterinarians, pre-exposure immunization is recommended. Persons living in or traveling to areas of the world where rabies in dogs is poorly controlled and post-exposure treatment may be difficult to obtain should also receive pre-exposure immunization against rabies. Although it almost certainly confers some degree of protection against an in apparent contact with rabies virus, the intent of preimmunization is to eliminate the need for immune serum and reduce the number of vaccine doses to two booster injections should the worker or traveler sustain a bite or wound exposure to rabies virus.

Post exposure immunization

Post exposure immunization comprise of administration of anti-rabies immune globulin and vaccine. When indicated, treatment should begin within 24-48 hrs of an animal bite.

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