ISSN: 2577 - 8455

Case Report

Archives of Infectious Diseases & Therapy

Deadly Rabies Diagnosis Post One Year of Viral Transmission from Dog's Bite: A Case Report from Sikka, East Nusa Tenggara, Indonesia

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Submitted: 25 Oct 2019; **Accepted**: 30 Oct 2019; **Published**: 08 Nov 2019

Abstract

Introduction: *Rabies is an invariably deadly zoonotic viral infection transmitted mostly from rabid dog's bite. This infection is targeting CNS with no cure once clinical symptoms had occur. Typically, the incubation period range from 20 to 90 days. In this case, it was approximately 1 year, proven that atypically long period of rabies incubation period is possible.*

Case presentation: *Presenting an atypically long incubation period of rabies, approximately one year post transmission.*

Conclusion: *Possible long incubation period of rabies and suspected diverse viral behaviour affecting its incubation period. Thus, needs further investigation on how and what determinants underlie the condition.*

Keywords: Rabies, Deadly, Dog's bite, Long incubation period, Atypical, Post one year of transmission

Introduction

Rabies is an invariably deadly zoonotic (transmitted from animals to human) viral infectious disease. The virus is a single-stranded RNA virus belongs to the *Lyssavirus* genus of the *Rhabdoviridae* family. It is transmitted to humans through the saliva of infected animals. The common mode of transmission is by bites or the contamination of scratch wounds with saliva. The virus invade Central Nervous System (CNS) and causing acute CNS infection [1]. Until now, there is no medication to treat rabies and almost always (99.9%) causing death when the virus has successfully reached CNS and showed clinical manifestations. The time needed for the virus to infect CNS from inoculation is usually 20-90 days although it can be varied up to 3 years according to previous reported cases. The disease can only be prevented and 100% preventable by vaccine, pre and post-exposure injection [2].

Rabies disease is especially harming people in Asia and Africa (more than 95% of these deaths). According to the WHO global vaccines research forum, statistic can be over 30.000 people die every year due to rabies in Asia. South East Asia (SEA) alone contributes to 45% of human deaths due to rabies worldwide. Assuming the actual numbers are bigger since not all rabies cases are very well reported [3]. Indonesia as a country in SEA reported 118 rabies death cases at the year of 2015. The country has 25 rabies endemic provinces, including Flores of East Nusa Tenggara [4]. The province is somewhat behind compared to others in Indonesia. For years, Sikka region of Flores, East Nusa Tenggara has examined suspicious dog's brain with unstably positive number every year. In mid 2018 alone, 45% of the sample were positively infected meaning that the virus infection rate is still high and threatened many people in the area.This case reporting an atypically long incubation period of rabiesdisease in Sikka, East Nusa Tenggara, Indonesia.

Case Presentation

On September 2017, a 51 years old woman (native in the area) was referred from primary healthcare to the emergency room of TC Hillers General Hospital Maumere, Sikka as brought by her husband complaining of change in his wife's behavior. She tend to be agitated and easily got angry although still capable of taking care of herself, taking a bath, eating, and else by herself. Along the way in the ambulance, she was fidgety every time the wind touched her skin. The symptoms suddenly showed since 2 days prior to admission and were not accompanied with fever, convulsion, vomiting, or headache. She had no history of hypertension, type 2 diabetes mellitus, renal or liver disease, and no previous trauma. Turning out she had history of unknown dog bite on her left calve one year prior and didn't seek for any vaccine injection or medical assistance. She only washed the wound with running water and soap then tied the surrounding wound with a rope. She thought the dog is her neighbour's but was not quite sure as the dog has not been seen since then. Until approximately one year post bite, she started to show symptoms. Although the patient and family member are all aware of the importance of vaccine injection after dogs bite, she just didn't go for it without a single reason.

From physical examination: she was compos mentis although seemed to be restless. Every words she said were still in the right sense and in accordance with the questions. On the vital sign examination she was tachypnea (24x/min) and tachycardia (117x/min) with no fever

(37°C) and normal blood pressure (100/60 mmHg). Other physical examination: conjunctivas were not anemic, no edema in any part of her body, from auscultation vesicular breathing sound on both sides of her lungs, ronchi (-/-), wheezing (-/-), her heart sound was regular with no abnormal sound. No abnormalities on abdominal and extremities. Neurological examinations also showed no abnormalities with positive results on pathognomonic signs of aerophobia and hydrophobia test. Informative laboratory examination: leukocytosis (23.340 cells/mm^3), elevated serum uremic level (164 mg/dL) and creatinine (1.9 mg/dL). Strong diagnosis for this patient is rabies and treated symptomatically with intravenous fluid (ringer lactate), analgetic (paracetamol drip), and sedation if necessary (diazepam 1 amp slow intravenously) then observe with other possibilities. Twelve hours after admission, the patient apnea and didn't survive.

Discussion

Patient was admitted with a chief complaint of agitation. There should be several Differential Diagnosis (DD) proposed for her condition: psychological, metabolic, neurological disease and finally infectious disease. Although she had history of an unknown dog bite led to rabies, physician should eliminate other DD. From anamnesis, she was coherent and had no history of illness or trauma. General physical and neurological examination only showed patient's restlessness with tachypnea and tachycardia, therefore laboratory examinations were performed. Abnormal laboratory results were not supported with patient history of illness and physical examination. Specific tests for rabies pathognomonic: hydrophobia and aerophobia were then performed with positive results. Our strong diagnosis was rabies and treat her symptomatically with observation. Twelve hours after admisssion the patient apnea then died. Patient immediate death strenghtened our diagnosis for rabies.

Based on the clinical manifestations, the disease can be classified into 2 forms: encephalitic (furious) and dumb (paralytic) form, where believed brainstem is involved in both clinical forms. Furious type is characterized by irritability, agitation, hyperaesthesia, autonomic disturbances with pathognomonic symptom of hydrophobia due to a triad of inspiratory muscle spasm, painful laryngospasm, terror (fear of swallowing), and aerophobia. Just like what we have seen in this patient. Where as the paralytic form characterized by generalized flaccid paralysis. Each of these forms evolve through five general stages: incubation, prodromal, acute neurological, coma, and death. Prodromal symptoms of rabies includes itching, pain, or parasthesia at the wound site [5].

Pathomechanism of rabies can be briefly described as the following: when the rabies virus successfully inoculated into human body, it replicates in the striated or connective tissue at the site of entry, then enters the peripheral nerves through the neuromuscular junction. The virus spreads via retrograde axonal transport to reach CNS in the endoneurium of the Schwann cells to cause functional damage. It usually took 20-90 days for rabies virus to migrate from inoculation area to CNS but it can be varied up to 3 years according to reported cases. In humans, the incubation period of rabies is influenced by: i) location, extent and depth of the wound; ii) distance between the location of the wound and the CNS; iii) concentration of inoculated virus particles and iv) virus strain.The virus then moves from the CNS via anterograde axoplasmic flow within peripheral nerves, leading to infection of some of the adjacent non-nervous tissues, for example, secretory tissues of salivary glands [6].

Rabies virus (RABV) has defining characteritics of neuroinvasiveness, neurotropism, and neurovirulence. These pathology were all related with virus uptake, axonal transport, trans-synaptic spread and the rate of virus replication. The virus itself has a relatively simple modular genome organization and encodes a nucleoprotein (N), a phosphorylated protein (P), a matrix protein (M), a single external surface glycoprotein (G), and an RNA dependent RNA polymerase (L). Fixed and street RABV strains differ significantly from each other in their ability to invade the CNS from a peripheral site and cause a lethal encephalitis.There were studies conducted to investigate the role of G protein/gene in the invasiveness and velocity of RABV invade human cells. The mechanisms by which RABV G mediates neuroinvasion include the facilitation of fast virus entry and fast trans-synaptic spread, and regulation of viral RNA synthesis. G gene (1674 bases) encodes the transmembrane glycoprotein (495 amino acids residue with 3 ectodomains), which is located in lipid bilayer envelope as spikes. Biologically, it is responsible for binding target cell receptors (myocytes, neurons, acini of salivary glands) mediating the binding of envelope of virus with host endosomal membrane (pH-dependent) so it enhances the entry of virus from the peripheral area into central nervous system (CNS). Both the Neuronal Cell Adhesion Molecule (NCAM) and the p75 neurotrophin receptor (p75NTR) in the neurons have been identified as RABV glycoprotein G binding receptors [6]. There was also a study focusing on p75NTR-dependent transport of RABV which conclude those specific transport is faster and more directed than p75NTR-independent RABV transport. It has been estimated that RABV migrates within the axons at the rate of 3 mm/h, by this transport the virus can travel faster [7]. These studies suggested G protein role in RABV hostile characteristics.

Conclusion

Although atypical, long incubation period of rabies is possible. Physician shouldn't ruled out rabies diagnosis for patient with history of rabid animal bite. Also suspected, rabies virus has a diverse behaviour affecting its incubation period. Thus, needs further investigation on how and what determinants underlie the condition.

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