



The rabies early death phenomenon: A report of ineffective administration of rabies vaccine during symptomatic disease

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Abstract

It was reported that in some individuals who received postexposure rabies vaccine, clinical features of rabies developed at the shorter time compared to individuals who were exposed, but not received the vaccine, which called “early death” phenomenon. We reported an early death phenomenon in a 67-year-old woman who was bitten by a jackal, although receiving three dose of rabies vaccine. Results show that the immune response to rabies has a dual role, sometimes has a favorable effect on survival but sometimes amplification the disease.

Keywords: Early death, postexposure vaccine, rabies

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Introduction

Rabies is a fatal encephalomyelitis that transmitted most commonly through the bite of a rabid animal. Tens of thousands of people around the world die every year from rabies, mostly in developing countries.^[1] In a few study, it was reported that in some individuals who received postexposure rabies vaccine, clinical features of rabies developed at the shorter time compare to individuals who were exposed, but not received the vaccine. This phenomenon called “early death.”^[2] In this article, we report an early death in a patient infected with rabies.

Case Report

A 67-year-old woman was admitted to the hospital with shortness of breath, headache, fatigue, anorexia and

headache. The patient’s symptoms began gradually the day before admission and then were aggravated.

The patient had a history of bite of her finger by jackal about 10 days before admission, and three doses of rabies vaccine (Imovax[®] rabies, Sanofi Pasteur, Iran) was administered as an 1.0 ml injection in the deltoid muscle on days 0, 3, and 7 in conjunction with antirabies serum according to protocol, that is, prescribed by WHO Expert Committee on Rabies.^[3] On admission, her vital signs were as follows: Temperature 37°C, pulse rate 100/min, blood pressure 210/110 mmHg, and respiration rate 26/min. She was confused, disoriented, with slurred speech and had sialorrhea. Admission laboratory values included prerenal azotemia (blood urea nitrogen level of 54 mEq/L and serum creatinine

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of 1.9 mEq/L) with mixed respiratory alkalosis and metabolic acidosis. Results of blood tests were as follows: White blood cell count, 19.0×10^3 /dL with 86% neutrophils; hemoglobin, 13.0 g/dL; serum sodium, 143 mmol/L; serum potassium, 3.4 mmol/L; serum glucose, 232 mg/dL; and serum calcium, 8.6 mg/dL; serum phosphorus, 2.7 mg/dL; prothrombin time and partial thromboplastin time were normal and procalcitonin were <0.5 ng/ml.

The initial clinical diagnosis was rabies and ceftriaxone, and acyclovir was initiated. Moreover, sodium valproate, phenytoin, and clonazepam were administered according to the neurological consultation.

The third hour after admission, tachycardia, tachypnea, and sialorrhea were increased, blood pressure had dropped and cyanosis occurred in the distal parts of upper and lower extremities. The patient level of consciousness was decreased gradually, and myoclonus had started. In the 4th h of admission, the patient developed respiratory and cardiac arrest and were transferred to Intensive Care Unit after intubation. On the 3rd day of hospitalization, she died despite treatment. To confirm the diagnosis, an autopsy was performed giving more attention to the brain. There were many punctuate hemorrhages and multiple infarcts involving the cortex, basal ganglia, and hippocampus. An acute encephalomyelitis characterized by a lymphohistiocytic infiltrate, perivascular lymphocytic infiltration, and neuronophagia was reported in the cortical gray matter, along with patchy changes in the white matter. Eosinophilic intracytoplasmic inclusion bodies indicative of Negri bodies are present within Purkinje cells, and larger neurons of the brainstem.

Conclusion

Rabies is a fatal viral disease of carnivorous animals, but warm-blooded animals, and human are believed to be susceptible and is spread by the bites of mammals. The importance of disease due to the high fatality rate, mortality and economic losses that can cause disease in animals, high vaccine cost.^[4] Rabies is endemic in the wildlife of Iran and infection frequently transmitted from wildlife hosts to domestic animals.^[5] The incubation period of rabies is usually 3–12 weeks. Rabies immune globulin and the first dose of rabies vaccine should be given as soon as possible after exposure since delays in initiating a postexposure prophylaxis reduce its effectiveness, and the disease is almost always fatal. Rabies prophylaxis is very effective documented for

correctly completed vaccination series in the USA since cell-purified vaccines have been utilized.^[3] However, in recent years, there have been doubts about the safety of rabies vaccines.

It has been proposed that administration of rabies vaccine during symptomatic rabies could be ineffective, and there are concerns about the “early death” phenomenon reported in animals that develop rabies with shorter incubation period after rabies vaccine administration.^[2] Early death could be developed during symptomatic rabies by rabies vaccine rabies or transfer of effector cells or antibodies, and cause dominant symptoms and earlier death.^[6] It has been shown that infection with replication-deficient rabies viruses, in some animals with a low level of rabies-induced antibody lead to earlier death compared with those without antibody. Similarly, in humans exposed to rabies, individuals who received postexposure immunization develop clinical rabies with shorter incubation period than patients who did not receive the vaccination.^[7]

The pathophysiology of early death is unknown. This phenomenon can be transferred via spleen cells or plasma of vaccinated animals into infected recipients.^[6] It has been proposed that the immunity of the rabies virus during the active disease may lead to immune response convert from noncytotoxic antibody-mediated clearance to antibody-dependent cytotoxicity. Significant neuronal loss and demyelination may occur due to the extension of the immune response to the brain.^[8] Andral in his study shows that lack of thymus in the mouse prevents early death, but the reduction of B lymphocytes with cyclophosphamide administration has not had any effect on this phenomenon.^[6] Results show that the immune response to rabies has a dual role, sometimes favorably on survival but sometimes with amplification of the disease.

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Conflicts of interest

There are no conflicts of interest.

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