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Unresolved Issues concerning Inadequate Immune Response after Rabies Post-Exposure Prophylaxis in an Immunocompromised Patient

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Abstract

We present an immunocompromised patient with inadequate immune response to the rabies post exposure prophylaxis (PEP), and our management strategy after this inadequate response. Currently, evidence based strategy for action after failure of PEP is partial. Since the prevalence of immunocompromised patients is increasing, further studies and guidelines are necessary.

Keywords

Rabies, Post exposure prophylaxis, Immunosuppression, Immune response

Introduction

Rabies is a fatal viral disease caused by neurotropic viruses in the Rhabdoviridae Family, Genus Lyssavirus. It is mainly transmitted from rabid animals through a bite. There is no proven therapy for rabies but the infection can be prevented with proper wound care and vaccine post exposure prophylaxis. It is assumed that immunocompromising conditions may prevent adequate immune response to the rabies vaccination. Therefore, it is recommended that if post exposure rabies prophylaxis is needed in an immunosuppressed person, antibody titers should be measured 1-2 weeks (US Advisory Committee on Immunization Practices) or 2-4 weeks (World Health Organization) after completion of immunizations [1,2].

In this case study we report an inadequate immune response of an immunocompromised patient to the recommended rabies post exposure prophylaxis regimen, as well as presenting the management strategy we performed after this failure of response.

Case Report

A 69-year-old man was bitten by a stray cat in Haifa district, Israel, which is considered a low risk region of rabies. He had a category III injury on his right calf. In his medical background, a chronic lymphocytic leukemia has been in remission since 2013. Currently, he is being treated with replacement IVIG once a month due to secondary hypogammaglobulinemia.

On the same day of exposure, the immediate treatment included cleaning of the wounds and prophylactic antibiotics. In addition, he started the rabies PEP regimen as recommended for immunocompromised patients according to the guidelines of the Israeli Ministry of Health and in accordance to the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) recommendations [1-3]. This included 5 doses of purified vero cell rabies vaccine (Verorab 0.5 ml, Sanofi Pasteur) administered by the intramuscular route, in the deltoid muscle on days 0, 3, 7, 14 and 28. Human rabies immunoglobulin (HRIG) 20 IU/kg was infiltrated into and around the bite at the same time as the first rabies vaccine (day 0). HRIG and the rabies vaccine were given in distinct anatomical sites using different syringes, as required. Seven days after completion of the immunization series; we tested for virus neutralizing antibodies (VNA) in the serum. The test analysis was performed by using the fluorescent focus inhibition test. No detectable levels of VNA titer were measured (< 0.07 IU/ml). This indicated an inadequate immune response (Acceptable level, 0.5 IU/ml). After consultation with our public health experts, we decided to administer a second series of rabies vaccine. This included 4 doses of active vaccine (Verorab 0.5 ml, Sanofi Pasteur) administered in the deltoid muscle at the appropriate time intervals (on days 0, 3, 7 and 14).Two weeks after completion of the second series, the VNA titer was 1.74 IU/ml. This level indicated an adequate immune response. No additional doses of the vaccine were recommended and no further antibody tests were performed.

Discussion

Currently, there are no evidence based data to support a specific strategy of management after failure of post exposure rabies vaccination in the immunocompromised patient. In the literature, there are a limited number of brief reports describing immunocompromised patients who had unacceptable immune response after the first PEP regimen. Some of them were followed by administration of varied post exposure vaccination courses, including distinct injection routes and vaccine dosage. Nevertheless, that did not necessarily ensure an acceptable antibody response [4-9]. The rabies PEP guidelines of CDC and of Public Health England (PHE) do not include any specific guideline relating the inadequate immune response after the first series and only recommend consulting with public health officials [1,10]. On the other hand, the WHO guidelines for rabies PEP [2], recommend administering one single dose while The Public Health

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Agency of Canada recommends receiving additional series [11].

In our case, we decided to administer a second series containing 4 doses of the available rabies vaccine, and an adequate antibody response was finally achieved as indicated by the VNA titer levels determined 2 weeks after completion of the second series.

In conclusion, the current rabies PEP recommendations for immunocompromised patients are neither sufficient nor consistent. The guidelines after inadequate immune response to the first rabies vaccine series vary widely and the best course of action has yet to be determined. In addition, there are other unresolved questions. For example, after a failure of a second series, should the immunocompromised patient get a third series or only one more dose? Is it appropriate to re-evaluate the original decision to give PEP? When and for how long should rabies antibody titers be monitored?

In the meantime, decisions are taken on an individual basis by consulting with the public health experts. Since the prevalence of immunocompromised patients is increasing, further discussions and studies in order to publish more appropriate guidelines are necessary.

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