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Case Series

Allergic Manifestations to Equine Rabies Immunoglobulin: A Case Series

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I N F O

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A B S T R A C T

Introduction: Rabies is a vaccine preventable zoonotic disease, however, if not prevented in time, it may become 100% fatal. Combining vaccine-immunoglobulin therapy with proper wound care is advised for effective rabies prevention. Equine rabies immunoglobulin is cheaper than human rabies immunoglobulin, but there is an increased chance of hypersensitivity reaction following its administration.

Method: A case series study has been presented in this article consisting of three different presentations of hypersensitivity reactions after the administration of equine rabies immunoglobulin.

Results: Two cases developed an immediate allergic reaction after desensitization. The third case showed a delayed local reaction and did not develop any allergy during the skin test before administering the full dose.

Conclusion: In a poor resource setting like India, skin sensitivity testing may be continued to identify high risk patients, and provide desentization, but still allergic reactions may be anticipated for them.

Keywords: Rabies, ERIG, Skin Test, Test Dose Hypersensitivity

Introduction

Rabies is a vaccine-preventable, but fatal zoonotic disease. Globally, the aim is to eliminate dog-mediated rabies by 2030, which is emphasized by the goal "Zero by 30."[1] Yearly about 20,000 rabies deaths occur in India accounting for 35% of the total rabies deaths worldwide.[2]

Combining vaccine-immunoglobulin therapy with proper wound care is advised for effective rabies prevention. Currently available, Equine rabies immunoglobulin (ERIG) is cheaper than Human Rabies Immunoglobulin (HRIG), but there is an increased chance of hypersensitivity reaction following its administration. Hypersensitivity reactions can be of immediate or delayed variety. The immediate reactions are wheezing, stridor, urticaria, hypotension, and dyspnea. Inflammatory reactions, fever, pruritis, urticaria, and serum sickness are examples of delayed reactions. Anaphylaxis has been reported for every one in 1.5 lakh ERIG-administered cases.[3]

The following case series consists of three different presentations of hypersensitivity reactions after the administration of ERIG.

Case Reports

Case I

A 72-year-old male presented with a lacerated wound (2 cm × 1 cm) and two abrasions on the dorsal aspect of his right hand from a domestic dog bite. The patient had no previous history of drug or food allergies. This category III

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wound was managed with the intradermal rabies vaccine (purified chick embryo cell vaccine), ERIG and tetanus toxoid injection. A skin sensitivity test was done intradermally on the ventral aspect of the left forearm with 0.1 ml of one-tenth dilution of ERIG in normal saline and found sensitive with induration of > 6 mm size. Full-dose ERIG was administered after desensitization with an injection of pheniramine maleate 25 mg intramuscularly (IM) and hydrocortisone 100 mg intravenously (IV).

While administering ERIG, the patient collapsed, blood pressure (BP) was not recordable, and the chest was clear with bilaterally equal air entry. No rash or angioedema was observed. Injection adrenaline 0.5 ml IM, hydrocortisone 100 mg IV, and pheniramine maleate 25 mg IM were given following the anaphylactic reaction. The patient became symptomatically better. He was discharged with antihistamines and steroids after observation for two days.

Case 2

A 43-year-old female reported with category III domestic dog bite over the dorsal aspect of the right ring finger of size 1 cm × 0.5 cm. She had no known comorbidities or allergies. The patient was managed with intradermal rabies vaccination (IDRV) and ERIG. The ERIG test dose was sensitive. Full-dose ERIG was administered after desensitization.

The patient developed itching all over her body about 30 minutes after the administration of the full dose. On examination, there was generalized erythema with urticarial lesions. Her vitals were stable and chest was clear with bilaterally equal air entry. The patient was symptomatically managed. She was kept for 24-hour observation and then discharged with oral medication of steroid tablets and antihistamine.

Case 3

A 25-year-old female presented with a history of itching over the site of infiltration of ERIG. She had a history of a domestic cat scratch over the ventral aspect of her left arm. She had no known comorbidities or any allergies. This category III exposure was treated with anti-rabies vaccine and ERIG. As the patient was not sensitive to the test dose, a full dose of ERIG (40 IU/kg) was administered around the wound. She was discharged after observation for 60 minutes.

The following day, she reported pruritus over the site of the administration of ERIG. On examination, her vitals were found to be stable. There was a local rise in temperature and an erythematous plaque of size 2.5 cm × 0.5 cm over the site. She was managed with topical steroids and antihistamines.

Discussion

Skin sensitivity tests were positive in the first two cases and after desensitization, ERIG was given, however, they developed allergic reactions. One must anticipate an allergic reaction even if the patient has been sufficiently desensitized. Moreover, ERIG should be administered in a setting where adequate facilities are available for managing anaphylactic reactions.

The third case was a delayed local reaction in a patient who did not develop any allergy during the skin test on administering the full dose. This shows that adverse events can present late even in patients who did not show any skin sensitivity.

The earlier guidelines recommended skin sensitivity testing of ERIG, and it is done in our clinic to identify those at risk of allergic reactions. A wheal > 10 mm diameter, with or without flare, or a wheal of 5–10 mm diameter with flare is considered a positive reaction.[4] The current guidelines of WHO do not recommend skin sensitivity testing before ERIG administration,[5] but in a poor resource setting like India, skin sensitivity testing is still helpful for identifying patients at a high risk of adverse reactions following ERIG administration, and desensitization using antihistamines and steroids will definitely reduce the chance of anaphylaxis.

In developing countries like India which accounts for the major burden of rabies cases in the world, the use of ERIG is an important cost-effective strategy to manage category III animal exposures.[2] The price of HRIG ranges from about 300 rupees per kilogram weight of the patient, whereas ERIG costs only about 12 rupees per kilogram weight of the patient. ERIG is made available free of cost in government hospitals. Many patients are reluctant to take ERIG due to fear of allergic reactions, which also hampers the confidence of the treating physician in administering ERIG, if they do not have an intensive care unit.[6,7] This also leads to more referrals of patients to higher centres. These issues must be also addressed by sensitization of the public, infrastructure strengthening, and capacity building of the peripheral health institutions.

Judicious use of HRIG can be made by scoring the reaction following the ERIG test and for high-risk scores, HRIG can be made available. Further studies are required to study the economic implications of the adverse events following the ERIG administration.

This case series describes three different manifestations of allergic reactions after the administration of ERIG. It shows the importance of proper counseling and informed consent before the ERIG administration. The drugs to manage anaphylaxis should be made available at the site where ERIG is administered.

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Conclusion

Allergic manifestations following ERIG administration are rare but still may range from milder forms like itching to more severe forms like anaphylaxis. Therefore, skin sensitivity tests may be continued and should be observed carefully to avoid any serious anaphylaxis. Adequate precautions should be made available to manage such cases at the earliest opportunity.

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