CASE REPORT

Serum Sickness should not rule out Equine Rabies Immunoglobulin Administration - A Case Study

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ABSTRACT

A forty years old Hindu male presented to the Anti-Rabies Clinic of a tertiary care hospital with rashes all over the body associated with myalgia and mild fever following treatment with Anti-Rabies vaccine and Equine Rabies Immunoglobulin (ERIG) for Category III dog bite injury. On seventh day of vaccination, the person developed generalized rashes all over the body. He was primarily given anti-histamines, antibiotics and analgesics for 5 days from the 1st day of vaccination in which period he didn't develop these rashes. The rashes were present more on face, shoulders, arms and forearms, thighs and sparse over the back. He was then treated with Inj Pheniramine maleate (2 ml) 1 ampule and tab Hicope 25 mg (Hydroxizine Hydrochloride), Tab Paracetamol 500mg and was completely cured after three days. The adverse reaction following ERIG administration was diagnosed as a case of Serum Sickness and reported to the Adverse Drug Reaction Monitoring Centre of the College. The purpose of this case study is to create awareness about the adverse drug reactions following ERIG administration among the health care personnel, importance of prompt management of such Serum Sickness cases and timely reporting to the ADR Monitoring centres.

Keywords: Serum Sickness, Equine Rabies Immunoglobulin, Adverse Drug Reaction Monitoring, Rabies, Anti-Rabies Vaccination

INTRODUCTION

Rabies is a zoonotic disease caused by Lyssavirus. It mainly affects the CNS and cause fatal encephalomyelitis in humans and animals. It is a 100% fatal disease and hence deserves utmost importance in slightest of injury from animal bite/ scratch; else a small negligence could cost a human life. This deadly disease can be prevented with just timely and appropriate anti rabies prophylaxis. [1] Modern medical science with its fast evolution has gifted mankind with products from animals which are life-saving for humans. One such is the Equine Rabies Immunoglobulin (ERIG) which is administered to humans upon any bite/ scratch from warm-blooded animal. Heterologous serum administration is associated with a number of adverse effects. So, skin sensitivity test is performed in order to know the clinical safety of the immunoglobulin. Howsoever, as the sensitivity and specificity of skin sensitivity is very low, so testing will be of little help in predicting anaphylaxis or serum sickness. [2] WHO even recommends that there is no scientific background for performing a skin test before administration of ERIG in the present era as the current available ERIG are pure.

Serum sickness in humans is a reaction to proteins in antiserum derived from a non-human animal source, occurring 5-10 days after exposure. It is a type III immune complex hypersensitivity disorder. It usually presents

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 Submission Date : 17/09/2019 Acceptance Date : 26/11/2019

with symptoms such as rashes, arthralgia, fever, malaise, headache and gastrointestinal symptoms. [3] The human immune system mistakenly treats the serum proteins as antigen and start producing antibodies, which form immune complexes and precipitate in the walls of the blood vessels. Proper treatment with anti-histamines, analgesics and corticosteroids, would completely cure the patient else it could lead to as serious a condition as shock to cause death of the patient. [3]

CASE PROFILE

A forty years old male from Cuttack district of Odisha presented to the Anti-Rabies Clinic (ARC) of SCB Medical College hospital Cuttack Odisha on 9th of Nov 2019 with the chief complaints of eruption of rashes all over the body for last one day. It was associated with mild degree of fever, malaise and generalized pruritus. The patient had a history of Category III dog bite over the left leg (Tibial shin) on 2nd of November 2019.

He had washed the wound with soap and water and came to the ARC on 2nd November 2019, where he was administered with Inj. Tetanus Toxoid 0.5 mL Intramuscular, Injection Purified Vero Cell Rabies Vaccine (PVRV, Injection Abhayrab, manufactured by Human Biologicals Institute, TamilNadu, India Batch No. - 18URAB089, Mfg date October 2018, Expiry Date September 2021 with a potency of ≥ 2.5I. U. per vial), 0.1 mL over both arms intra dermally. He weighed 88 Kg and hence was advised to be infiltrated with Equine Rabies Immunoglobulin (ERIG, Inj Equirab manufactured by Bharat Serums and Vaccines Limited, Mumbai, India Batch No. A02719007, Mfg date February 2019 Expiry Date January 2021 with a potency of 300 IU/ml) i. e. 10 mL after the skin sensitivity test. The intra dermal skin test was done using 0.1 ml of ERIG diluted with 0.9 ml(1:10) of normal saline provided by the manufacturer over left forearm and with 0.1ml normal saline on right forearm as control. A positive test result is not a formal contraindication for the use of sero therapy, but it should be considered as a warning. In such cases Equirab should be administered only after ensuring the facility to overcome the anaphylactic shock. A negative test is not an absolute guarantee for the absence of an immediate allergic type reaction[4]. He was observed for any induration after 15 minutes but only a wheal of 5 mm was seen on left forearm and 3mm was seen on right forearm. Hence the test was read as negative.

He was infiltrated 2mL of ERIG at the site of bite as that much of amount was possible to infiltrate locally over the bite site and rest 8 ml was administered as 4 ml each over the antero lateral aspect of both thighs, intra muscularly. He was further advised to take Tablet cetirizine (10mg) 1 tablet for 5 days in empty stomach in evening and Tablet Paracetamol 500mg three times for 3 days. He was advised to attend the ARC for completion of rest PVRV doses as scheduled on 5th Nov, 9th Nov and 30th Nov 2019.

Figure: Rashes over face, Shoulder and Upper Limb

The person was apparently alright from the initiation of treatment but on 8th Nov (i. e. 7th day of treatment) he presented to the ARC with rashes all over the body. The rashes first appeared on the bite site where ERIG was administered locally followed by both thighs, both upper limbs, shoulders and face. They gradually increased in size. It was associated with very mild degree of fever, malaise, and generalized pruritus, more over the rashes. He denied of having any previous allergy to any food items or drugs neither he took any unusual foods in the recent days. He was then diagnosed to be a case of Serum Sickness following ERIG administration. On examination, vitals were stable with pulse 78 /min and BP 122/78 mmHg. The person was administered inj Pheniramine Maleate (Avil) 1 amp IM to start, cetirizine 10 mg before food for 7 days. The person was then followed up over telephone and he reported decrease in the size of rashes by the next day. He was called after 2 days for clinical evaluation and was found to be completely cured of the rashes. He was further advised to complete his last scheduled Anti-Rabies Vaccine (ARV) on 30th Nov without any fear which he had completed. This case was reported to the Adverse Drug Reaction monitoring Centre of the institution.

DISCUSSION

In our study, the patient was a male of 40 years of age. He was working in a transport agency. Transport personnel are at more risk of animal bites probably due to their outdoor travelling and parcel delivery at costumer doorstep by their pet dogs and even by stray dogs. Cases attending ARC with history of dog bites/ scratches are more in comparison to other animals. Dogs are a major cause of rabies as also assessed by a national multicenter survey where dogs (96.2%) were mainly responsible for human rabies deaths. [5] We noticed a good practice in the case i. e. washing the wound immediately with soap and water. A study on "Effectiveness of child to child method of education regarding Rabies and its prevention" by Shwetha et al[6] showed only 21.5% of subjects knew of washing wound with soap and water prior to education which was followed by 100% of them knowing it after education. Serum sickness is a rare complication occurring in response to ERIG administration. Among the local adverse effects cited in Tripathy RM et al[2] urticaria, dizziness, redness, vomiting, localized swelling and headache were common. However, in our case there was no such symptom on the day of initiation of treatment. The person complained of various systemic adverse effects such as generalized pruritus, malaise, mild fever and rashes. He was diagnosed to have Serum Sickness as also found in other studies by Behera TR et al in Odisha and Wilde et al in Bangkok where the incidences were 3% and 1.6% respectively. [7,8] Another study by Maharana S et al[9] found rashes to be the most common symptom in 97.82% of cases following ERIG administration in the same setting which was similar to our case. Our case reported of rashes on seventh day after administration of ERIG which was a rare occurrence as only 12% of cases following ERIG infiltration reported symptoms of serum sickness on tenth day. [9] Only one case among 48 cases observed for serum sickness by Maharana S et al[9] required corticosteroids, however this patient was being treated with only antihistaminic and did not required corticosteroids for management.

CONCLUSION

Reactions following immunoglobulin such as Serum sickness though a rare adverse effect yet awareness regarding its symptoms among the patients and proper guidelines to manage such cases is of utmost importance. Adverse effects following immunization has been a hindrance for successful outcome of any immunization program. The fear of serum sickness following use of ERIG need to be addressed with timely management with simple antihistamines and keeping in hand with Anaphylaxis Kit among Doctors treating animal bite cases. So, it is very necessary to make people aware of different adverse effects that could follow vaccination and create a sense of urgency to seek timely treatment. It is also recommended that all immunization centers to be fully equipped with Adverse Effects Following Immunization (AEFI) kits or anaphylaxis kits as well as protocols for management of such cases. The life-saving drugs should be properly labelled, its usage made very clear to all the staff dealing with vaccination. In this era, where immunization has been a great step in averting disease and deaths, AEFI must be properly managed and reported to ADRM Centers on regular basis. This can surely be a step, safe enough, towards achieving the goal of "Dog-mediated Human Rabies free India by 2030".

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