

Immune Thrombocytopenia: A Rare Complication of Rabies Vaccine

Sir,

Rabies is a very fatal disease and is transmitted through infected secretions that gain entry through animal bite or open wound. In India, >99% of human death from rabies are secondary to infected dog bites. Postexposure prophylaxis in the form of vaccines before the development of clinical signs and symptoms is almost 100% successful in prevention as opposed to 99% mortality in its natural course. Vaccines are usually free from any adverse effects, but vaccine associated thrombocytopenia (VAIT) is reported in approximately 2.6/100,000 of MMR doses.^[1] We report a patient who developed immune thrombocytopenia (ITP) following anti-rabies vaccination after a dog bite.

A 38-year-old male had minor scratches, without bleeding (category II wound) following stray dog-bite on the right leg. He received intramuscular injection of purified Vero cell culture vaccine (Abhayrab, Human Biologicals Inst). Within 12 h of vaccine administration, he developed generalized petechiae and oral wet bleeds. On physical

examination, he was afebrile and had no lymphadenopathy or hepatosplenomegaly. Hemogram revealed haemoglobin of 11.8 g/dL, total leukocyte count of $7.8 \times 10^3/\text{dl}$ (N70L25E5B0), and platelet count of $0.12 \times 10^9/\text{l}$. His previous hemogram, liver function test and renal function test was normal. Abdominal ultrasonography was normal. Serological tests by ELISA for HIV antibodies, HBsAg antigen, anti HCV antibodies, ANA and RA factor were negative. Prothrombin time and activated partial thromboplastin time were normal. The bone marrow examination report was consistent with the peripheral destruction of platelets. He was treated with 1 g injection methylprednisolone for 3 days and two units of single donor platelets. However, he did not improve clinically and thrombocytopenia persisted ($0.1 \times 10^9/\text{l}$) on day 4 of pulse steroids. Intravenous immunoglobulin (IVIG) was given at 1 g/kg/day on days 5 and 6. Platelet count improved to $0.37 \times 10^9/\text{l}$. He was discharged on tablet prednisolone at 1 mg/kg/day. On day 17 of follow-up, the patient had a repeat episode of bleeding manifestation and platelet count had fallen to $0.21 \times 10^9/\text{l}$. He received IVIG at 1 g/kg on day

18. Bleeding manifestations subsided and platelet counts improved to $0.39 \times 10^9/l$ and $0.78 \times 10^9/l$ on days 19 and 20, respectively. He was discharged on tablet eltrombopag 50 mg daily. He is maintaining his platelet counts more than $>1 \text{ lac/mm}^3$ for the past 4 months and is planned to taper and stop eltrombopag.

The only vaccine for which there is a demonstrated cause-effect relationship is MMR, with thrombocytopenia reported in approximately 2.6/100,000 of MMR doses.^[1] The binding of pathogenic autoantibodies to platelet and megakaryocytes may cause thrombocytopenia by different mechanisms, such as opsonization, direct activation of complement, or apoptotic pathways.^[2] In the anti-platelet antibody-negative cases, a complementary mechanism based on T-cell immune-mediated mechanism has been suggested.^[3] In particular, T-cell subsets seem dysregulated with an increased production of pro-inflammatory cytokines as interferon-gamma and tumor necrosis factor and chemokines as CXCL10.^[4] Usually, anti-rabies vaccines are safe and potent, few side effects of anti-rabies vaccine are pain and erythema at the local site, fever, stomach pain and myalgia. Thrombocytopenia is often severe, but responsive to IVIG or corticosteroids. More than 80% recover within 2 months, with $<10\%$ evolving into chronic ITP.^[5,6] Our patient developed thrombocytopenia shortly after the first dose of vaccine and responded well to IVIG and eltrombopag. Anti-rabies vaccine-induced thrombocytopenia has been rarely reported in medical literature. However, the possibility of VAIT should be considered, though life-saving potential of vaccine outweighs this rare side effect.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Sachin Bansal, Rahul Bhargava, Ayush Singh¹, Meet Kumar, Santosh Raut Kurmi, Prabhat Agrawal¹

Department of Hematology and BMT, Fortis Memorial Research Institute, Gurugram, Haryana, ¹Department of Internal Medicine, SN Medical College, Agra, Uttar Pradesh, India

Address for correspondence: Dr. Prabhat Agrawal, Professor, Department of Internal Medicine, SN Medical College, Agra, Uttar Pradesh, India.

E-mail: prabhatagrwal321@gmail.com

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