A CASE OF ERYTHEMA MULTIFORME DEVELOPING AFTER H1N VIRUS VACCINE

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ABSTRACT

A 12-year-old male patient presented at our hospital complaining from eruptions that occurred 7 days after being inoculated with a single-dose monovalent H1N1 virus vaccine. Dermatological examination of the patient showed papules and occasional targetoid plaques particularly in the acral areas. The patient who did not have mucosal involvement did not have an infection or history of drug use in the last one month. Laboratory examinations did not reveal any pathology. Although its pathophysiology has not been fully understood yet, erythema multiforme is described as keratinocyte damage caused by the cell-mediated immune response to an antigenic stimulus. Infections play the major role in the etiology of erythema multiforme, but drugs, malignancies and vaccines, though rarely, are also held responsible. We are presenting the second literature case of EM that occurred secondary to monovalent influenza A/H1N1 vaccine.

Key words: Influenza A H1N1 virus, erythema multiforme, vaccine

INTRODUCTION

Erythema multiforme (EM) is an acute and self-restricted hypersensitivity reaction that occurs against various antigenic stimuli and is generally associated with infections and drugs. Infectious agents, among which herpes simplex virus has the leading part, drugs, collagen tissue diseases and malignancies have been held responsible in the etiology of the disease. EM has been occasionally reported to develop after Bacillus-Calmette-Guerin (BCG), diphtheria-pertussis-tetanus (DPT), oral polio, varicella, hepatitis, human papilloma virus and measles vaccines. The most common side effects encountered in association with influenza A/H1N1 virus vaccine in the literature include pain and rash at the injection site, fever, headache, myalgia and rarely urticaria and/or angioedema. We present the second case of EM that developed secondary to monovalent influenza A/H1N1 virus vaccine.
CASE REPORT

A 12-year-old male patient presented at the Dermatology Clinic of Etimesgut Military Hospital complaining from rash on his body. Anamnesis of the patient showed that this complaint occurred a week after being vaccinated with monovalent influenza A/H1N1 virus vaccine, started on the hands and feet and spread to the upper and lower extremities. The patient did not have a history of infection or drug that could trigger the current clinical manifestation in the last month. Systemic questioning and physical examination of the patient did not reveal any additional pathology.

Dermatological examination demonstrated erythematous papules, plaques and a small number of bullae containing occasional targetoid lesions located bilaterally on the upper and lower extremities, but more intensively in the acral areas in particular (Figures 1, 2). The patient did not have mucosal involvement. Whole blood count, routine biochemical analyses, whole urine analysis and pulmonary radiography did not show any pathological signs. There was not any bacterium or neutrophil in the Gram staining examination of the material taken from the lesion.

Figure 1. Erythematous papules, plaques and a small number of bullae containing occasional targetoid lesions on bilateral legs of the patient.
The patient who was diagnosed as EM on the basis of clinical signs was put on 20 mg/day (1mg/kg) systemic corticosteroid therapy. The treatment was continued for a period of 2 weeks and then gradually interrupted. The lesions regressed after therapy.

**DISCUSSION**

Although its pathogenesis is not known for sure, erythema multiforme is thought to be an immune-mediated disease. The most widely accepted hypothesis about EM is apoptosis and keratinocyte necrosis induced by mediators like interleukin (IL)-2, IL-6 and tumor necrosis factor-α (TNF-α) secreted from the cytotoxic T lymphocytes. Vaccines or the adjuvant substances they contain probably lead to the development of EM by increasing the production of these cytokines.

The pandemic influenza A/H1N1 vaccine used in our case, which had A/California/7/2009 (H1N1) and a similar strain and was produced from chicken egg, contained 7.5 micrograms Hemagglutinin. The vaccine has been produced against the influenza A pandemic in accordance with the recommendation of the World Health Organization (WHO) and European Union (EU) resolutions. It contains sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, sodium citrate, citric acid, thiomersal and injection water as adjuvant substances.
The most common side effects that arise due to influenza A/H1N1 virus vaccine include pain and rash at the injection site, and more rarely, fever, headache, myalgia, Guillain-Barre syndrome, facial paralysis, idiopathic thrombocytopenic purpura or autoimmune thrombocytopenia, transverse myelitis, optic neuritis, still birth and urticaria/angioedema (9-11). Urticaria/angioedema associated with the vaccine is observed more commonly in individuals who are allergic to eggs (as the vaccine is produced from chicken egg) 12. The incidence of anaphylaxis is extremely rare (0.1-1/100000). Development of EM as a reaction to a vaccine is an extremely rare situation. EM has been reported to develop after Bacillus-Calmette-Guerin (BCG), diphtheria-pertussis-tetanus (DPT), oral polio, varicella, hepatitis, human papilloma virus and measles vaccines in the literature 3-8. Karincaoğlu et al. 4 reported a case of EM that developed 10 days after the first dose of DPT and oral polio vaccine and was characterized by targetoid bullae on the hands, feet, eyelids and perioral area. They noted that the first dose of the vaccine contained cellular pertussis, diphtheria-tetanus toxoid and thiomersal as the preservation agent, while the second dose contained acellular pertussis, diphtheria-tetanus toxoid and 2-phenoxethanol as the preservation agent and that this second vaccination did not cause any reaction in the patient. It was emphasized in the concerned article that cellular pertussis, diphtheria-tetanus toxoid and thiomersal content used as the preservation agent could be responsible for the development of EM 4. Samad I et. al. 13 reported a case of EM that developed 2 days after the H1N1 virus vaccine.

CONCLUSION

We present the second case of EM that developed secondary to influenza A/H1N1 virus vaccine.

REFERENCES

9. The Public Health Agency of Canada identified a higher-than-normal rate of anaphylaxis (4.1/100 000 doses distributed) linked to one particular lot of the adjuvanted pandemic (H1N1) 2009 vaccine. Pending further investigation of adverse event reports linked to the lot, unused vaccines from this lot were withdrawn from use on 24 November 2009.