A Retrospective Study on Adverse Reactions to Canine Vaccines in Japan

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ABSTRACT. Adverse reactions to vaccines were examined in 311 canine cases reported to the Ministry of Agriculture, Forestry and Fisheries in Japan during the period of 6 years from April of 1994 to March of 2000, and classified according to their clinical symptoms. There were 27 cases of adverse reactions to rabies virus vaccines. Gastrointestinal symptoms were the most frequently observed (26%), followed by respiratory and/or cardiovascular symptoms (22%) and dermatologic symptoms (11%). There were 284 cases of adverse reactions to non-rabies monovalent vaccines and mixed vaccines. Dermatologic symptoms were the most frequently observed (53%), followed by gastrointestinal symptoms (16%) and respiratory and/or cardiovascular symptoms (14%). Of the total 311 cases, 11 (3.5%) died of adverse reactions to vaccines.

KEY WORDS: adverse reaction, canine, vaccine.

NOTE Internal Medicine

During the past 40 years, canine vaccines have been developed and have successfully reduced the incidence of infectious diseases in dogs, such as canine distemper, canine parvoviral infection and infectious canine hepatitis [1]. Furthermore, canine vaccines against zoonosis such as rabies and leptospirosis allow people to have and contact their dogs without being anxious of the diseases. In Japan, the law obliges that dogs should be vaccinated against the rabies virus once a year [11]. Canine vaccines, therefore, are considered to play a very important role not only in small animal veterinary practice but also in public health.

Like other drugs, it is possible that vaccines induce various adverse reactions [2, 8]. In previous epidemiological reports, vaccines used in veterinary medicine caused various adverse reactions in dogs [4, 7, 13]. The adverse reactions frequently observed in canine vaccination were allergic reactions such as urticaria, edema of the face and itching [4, 7, 13]. Although canine vaccines are widely used in small animal veterinary medicine in Japan, there has been no retrospective literature on the adverse reactions to canine vaccines. In the present study, we retrospectively reviewed the cases of adverse reactions to canine vaccines based on the reports of Animal Hygiene Weekly by the Ministry of Agriculture, Forestry and Fisheries [12].

During the period of 6 years from April of 1994 through March of 2000, 311 cases of adverse reactions to canine vaccines were reported in Animal Hygiene Weekly by veterinarians who had been selected as monitors [12]. We classified the 311 cases into five groups according to the clinical symptoms: respiratory and/or cardiovascular symptoms (dyspnea, tachypnea, cyanosis, circulatory collapse, bradycardia, hypotension and hypothermia), dermatologic symptoms (urticaria, angioedema, swelling of face, flush, pruritus and eczema), gastrointestinal symptoms (vomiting, diarrhea and nausea), neurologic symptoms (convulsion and paralysis) and others (insufficient symptoms such as hypodynamia and anorexia to classify).

Vaccines that induced adverse reactions in this study were inactivated rabies virus vaccines, non-rabies monovalent vaccines (attenuated or inactivated parvovirus vaccines) and mixed vaccines (combination of the attenuated or inactivated vaccines against canine distemper virus, canine adenovirus type 2, canine parvovirus, canine parainfluenza virus, canine coronavirus and 2 or 3 kinds of leptospira bacteria). Of the total 311 dogs, 27 dogs were inoculated with the rabies virus vaccine, 5 were non-rabies monovalent vaccine and 253 were mixed vaccine. The remaining 26 dogs were inoculated with two kinds of vaccines (one non-rabies monovalent vaccine and one mixed vaccine) at the same time.

Table 1 shows the 27 cases of adverse reactions to the rabies virus vaccines. Gastrointestinal symptoms were the most frequently observed (26%), followed by respiratory and/or cardiovascular symptoms (22%) and dermatologic symptoms (11%). Two dogs that received the rabies vaccination showed neurologic symptoms. Of the 27 cases, 5 (19%) died of respiratory and/or cardiovascular symptoms. Table 2 shows the 284 cases of adverse reactions to non-rabies monovalent and mixed vaccines. Dermatologic symptoms were the most frequently observed (53%), followed by gastrointestinal symptoms (16%) and respiratory and/or cardiovascular symptoms (14%). In this group, only 1 dog showed neurologic symptoms. Of the 284 cases, 6 (2.1%) died of adverse reactions to vaccines. Two cases died of respiratory and/or cardiovascular symptoms and 4 died of gastrointestinal symptoms. The overall incidence of
death for all types of vaccines was 3.5% (11 of 311 dogs).

The incidence (2.1%) of deaths in 284 cases of non-rabies monovalent and mixed vaccines was clearly lower than that found for rabies virus vaccines (19%). However, it is unclear why deaths should be more likely to occur in dogs inoculated with the rabies vaccines than with other vaccines. It is necessary to investigate more clinical cases of adverse reactions to rabies virus vaccines in order to clarify this issue.

Among the clinical symptoms observed in this study, severe allergic reactions such as respiratory and/or cardiovascular symptoms are considered to be anaphylaxis, while dermatologic symptoms are considered to be allergic reactions. Among many clinical symptoms of adverse reactions to vaccines, systemic anaphylaxis is the most dramatic symptoms [2, 8]. Anaphylaxis refers to a systemic and immediate hypersensitivity caused by allergen-specific IgE antibodies, which mediate release of immune mediators from mast cells [6]. It is reported that some cases of anaphylaxis can progress to death [2]. In the previous epidemiological study, of 26 cases of adverse reactions to live vaccines in the UK in 1989, 10 showed hypersensitivity such as subcutaneous edema, urticaria or vomiting, and 3 showed anaphylaxis, with 2 of the latter cases resulting in death [4]. In the present study, we found 46 cases (15%) with anaphylaxis such as respiratory and/or cardiovascular symptoms after injection of vaccines, and 7 of these cases died.

It was demonstrated that the allergen causing anaphylaxis in human vaccines was gelatin as a stabilizer [5, 9]. Likewise, it can be suspected that components of vaccines induce allergic reactions in dogs, however, no allergen in canine vaccines has yet been identified. Therefore, identification of allergens in canine vaccines will be needed in order to reduce the incidence of adverse reactions to canine vaccines. In addition, techniques of DNA vaccines may make it possible to induce protective immunity without anaphylaxis and allergic reactions to canine vaccines in a safer manner.

There has been no retrospective study on the incidence of adverse reactions to canine vaccines. The mean incidence of adverse reactions such as anaphylaxis to vaccines in humans was reported as 0.5 cases per million doses in the US in 1990–1995 [3] and 7 cases per million doses in Japan in 1994–1996 [10]. In this study, we were unable to calculate the total incidence of adverse reactions to canine vaccines because we could not obtain information of the total vaccine doses. However, in this study, 311 cases were reported to show adverse reactions for 6 years, suggesting that the incidence of adverse reactions in dogs should be higher than that in humans. It will be necessary to study adverse reactions to canine vaccines not only from pathological aspects but also further epidemiological aspects including breeds, onset time of clinical symptoms after vaccination, number of times of vaccination and the incidence of adverse reactions.

REFERENCES