Case Report

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Facial Paralysis and Myositis Following the H3N2 Influenza Vaccine in a Dog

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Abstract A dog (2-year old, female, Shih-Tzu) presented with hyperthermia and right-sided facial paralysis characterized by the inability to close the right eye and drooling from the right side of the mouth after H3N2 influenza vaccination [A/Canine/Korea/01/07(H3N2) strain; Caniflu-Max, Bionote, Hwaseong, Gyeonggi-do, ROK]. To determine the cause of the fever and neurological symptoms, physical examination, ophthalmic examination, thoracic and abdominal radiography, abdominal ultrasonography, complete blood counts, serum chemistry values, and electrolyte levels were determined. In addition, Cerebrospinal fluid analysis, antinuclear antibody test, fever of unknown origin polymerase chain reaction (PCR) panel, tick-borne pathogen PCR panel were performed. As a result, hyperthermia, leukocytosis, and elevated C-reactive protein were confirmed. In addition, neurological examination revealed decreased right eyelid reflexes, corneal reflexes, threat response, and facial sensation, it was possible to suspect problems with the trigeminal and facial nerves of the cranial nerve. Magnetic resonance imaging revealed a lesion suggestive of myositis in the right muscular lesion at atlanto-occipital junction level on site of vaccine injection. Therefore, right-sided facial paralysis was tentatively determined to be a secondary cause of nerve damage caused by myositis. The patient was treated with immunosuppressants such as prednisolone and mycophenolate mofetil. After 3 months of immunosuppressant therapy, the patient's symptoms improved.

Key words facial paralysis, influenza vaccine, myositis, magnetic resonance imaging, neurological complications.

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Introduction

Influenza virus infection can cause an acute febrile respiratory illness that necessitates treatment in dogs. H3N2 is the subtype of influenza virus that has been identified in the Republic of Korea (ROK) since 2007 (16). Therefore, annual H3N2 influenza vaccination is recommended for healthy young dogs in the ROK (15). Commonly occurring side effects of influenza vaccines in humans are redness, pain, and swelling at the injection site, which reportedly occurs in 20% of all vaccine recipients (14,28,29). Several neurological complications of influenza vaccination have been reported, such as Guillain–Barre syndrome (10) and chronic inflammatory demyelinating polyneuropathy (5), although they are uncommon and their association with the vaccine has not been adequately established. Facial paralysis is a neurological adverse effect of concern (24). However, there are limited case reports of neurological complications following influenza vaccination in dogs. Here, we describe the case of a dog with right-sided facial paralysis characterized by the inability to close the right eye and drooling from the right side of the mouth after influenza vaccination.

Case Report

A 2-year-old, female, Shih-Tzu presented with hyperthermia, weakness, and right eye blinking disorder. One month before admission, the patient received an influenza vaccine containing the H3N2 influenza virus [A/Canine/Korea/01/07(H3N2) strain; Caniflu-Max, Bionote, Hwaseong, ROK] by intramuscular injection into the back of the neck at a local animal hospital. Five days after vaccination, the patient was lethargic and had a fever. Nine days following vaccination, the patient developed additional symptoms, including right facial paralysis characterized by the inability to close the right eye and drooling from the right side of the mouth, which were duly verified.

To determine the cause of the fever and neurological symptoms, physical examination, ophthalmic examination, thoracic and abdominal radiography, abdominal ultrasonography, complete blood counts, serum chemistry values, and electrolyte levels were determined.

On physical examination, the patient's vital signs were as follows: heart rate, 120/minute; systolic blood pressure, 105 mmHg; respiratory rate, 24/minute; and body temperature, 40°C. A neurological examination was conducted, including assessment of mental status, posture, gait, cranial nerves, postural reactions, spinal reflexes, sensitivity to spinal palpation, and pain perception. Consequently, the examination disclosed reduced right eyelid reflex, corneal reflex, menace response, and facial sensation, with no abnormalities were observed in the remainder of the assessment. Blood test results showed a white blood cell count of 30.12 $\times$ $10^3/\mu L$ (reference range: 5.05-16.76 $\times$ $10^3/\mu L$), hemoglobin level of 10.0 g/dL (reference range, 13.1-20.5 g/dL), hematocrit concentration of 27.7% (reference range: 37.3-61.7%) and C-reactive protein level of 158.9 mg/L (reference range: 0-20 mg/L). Other blood tests showed no remarkable findings. Additional tests were also conducted to closely check the patient's condition. Antinuclear antibody test results were negative, and a fever of unknown origin polymerase chain reaction panel (IDEXX Laboratories, Inc. Seoul, ROK) showed negative results for DNA amplification of *Babesia* spp., *Anaplasma* spp., *Ehrlichia* spp., *Rickettsia* spp., *Hepatozoon* spp., *Histoplasma capsulatum*, *Brucella canis*, *Bartonella* spp., *Cryptococcus* spp., *Toxoplasma gondii*, *Blastomyces dermatitidis*, *Coccidioides* spp., *Neospora caninum*, *Leishmania* spp., *Leptospira* spp., and *Trypanosoma cruzi*. Additionally, a tickborne pathogens panel (Pobanilab Laboratories, Guri, ROK) preformed at a local hospital before the patient was brought to us showed negative results for DNA amplification of *Anaplasma* spp., *Ehrlichia* spp., *Babesia* spp., Lyme borreliosis, *Bartonella* spp., *Hemotropic mycoplasma*, *Rickettia* spp., *Leptospira* spp., *Hepatozytozoon* spp., and *Theilera* spp. This patient additionally underwent magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) tests at a local hospital. Fat-saturated T1-weighted MRI revealed hyperintense signal changes in the right muscular lesion at atlanto-occipital junction level, which was suggestive of myositis (Fig. 1). The right retropharyngeal lymph node was enlarged. In addition, slight meningeal enhancement at the posterior medulla oblongata and at the level of the atlas was confirmed. CSF was collected from the cerebellomedullary cistern though puncture; however, no significant abnormalities were observed on cytology. EMG and muscle biopsy could not be carried out as the patient owner did not give consent. Considering the overall neurological examination, there were abnormalities in the sensory and motor nerves of the right side of the face, and taking this together, it was possible to suspect problems with the trigeminal and facial nerves of the cranial nerve. Since EMG and biopsy were not performed, there are limitations in carefully diagnosing the nerve condition. However, when conducting an MRI examination, there were no abnormalities in the nucleus of the cranial nerve, and the area of the muscle that could cause problems with the projection of the cranial nerve suspected inflammatory findings were confirmed. Therefore, right-sided facial paralysis was tentatively determined to be a secondary cause of nerve damage caused by myositis.

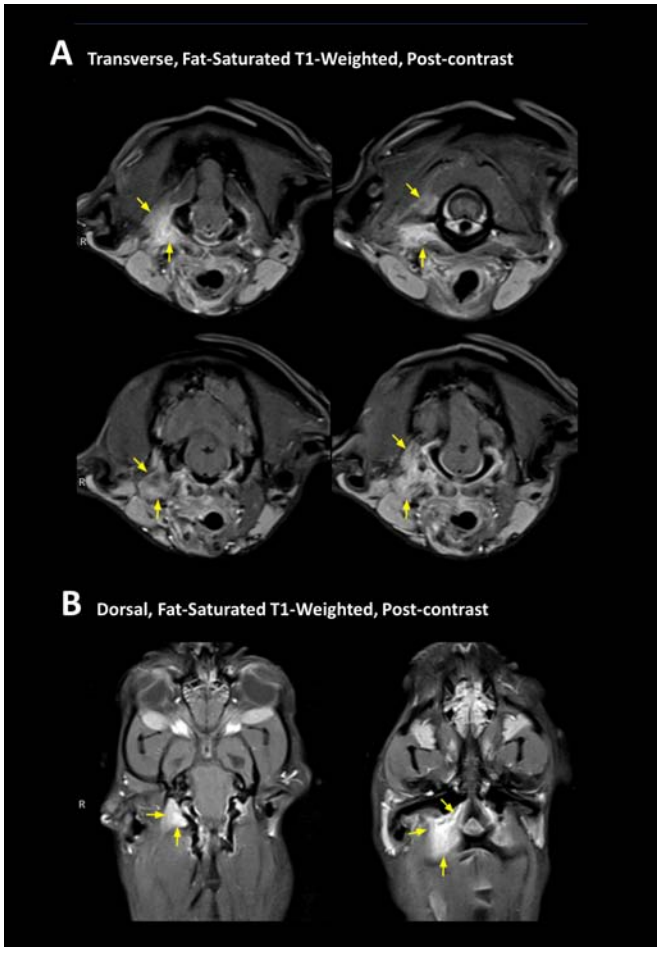

Fig. 1. Hyperintense signal changes on the fat saturated T1 weighted image with GAD in the right muscular lesion at atlanto-occipital junction level in MRI scan. (A) View of transverse, fat-saturated of T1-weighted, post contrast. (B) View of dorsal, fat saturated of T1 weighted, post-contrast. GAD, gadolinium.

Because the patient had shown temporary improvement with prednisolone (PDS, 0.5 mg/kg, orally, twice a day) therapy, which had been prescribed at a local hospital and immune-mediated myositis was considered preferentially, the steroid dose was increased (1 mg/kg, orally, twice a day). Additionally, because systemic infection was tentatively ruled out, the antibiotics (amoxicillin clavulanate, 22 mg/kg PO bid; marbofloxacin, 2 mg/kg PO sid; metronidazole, 15 mg/kg PO bid) prescribed at the first visit were discontinued. 10 days after admission, the patient's body temperature was maintained at 39.5°C, and the appetite and vitality were good. The C-reactive protein level was within the normal range. However, the inability to close the right eye persisted. Therefore, a secondary immunosuppressant was added (mycophenolate mofetil [MMF], 12 mg/kg, orally, twice a day). 24 days after admission, the disclosed reduced right eyelid reflex, corneal reflex, menace response, and facial sensation had improved. Therefore, PDS and MMF were gradually tapered over 3 months. Three months after treatment cessation, the patient is doing well and has no initial neurological symptoms.

Discussion

Post-vaccination complications generally occur due to procedure-related local trauma, irritant vaccine constituents, inappropriate injection techniques, or injection of intramuscular medication in the artery and veins (18), which can result in bleeding, persistent pain, abscess and scar formation, surrounding tissue necrosis, muscle fibrosis, and development of malignancy at the injection site (6). In addition to these, there have also been documented instances of uncommon and severe adverse responses, such as thrombosis with thrombocytopenia syndrome (8), Guillain-Barré syndrome (12), vasculitis (7), autoimmune hepatitis (21), inflammatory myopathies, and myocarditis (30). These are now believed to result from immune-mediated mechanisms.

Our patient developed right facial paralysis characterized by the inability to close the right eye and drooling from the right side of the mouth after H3N2 influenza vaccination. Unfortunately, the owner does not agree, an EMG test was not conducted. In addition, while IDEXX FUO PCR, ANA test, and Pobanilab tick-borne pathogen panel were administered, no tissue examination, such as biopsy or culture testing, was undertaken. Consequently, the possibility of infections and immune-related diseases affecting the lesion site could not be completely excluded. However, MRI revealed myositis at the injection site, which could have caused facial nerve irritation.

In this case, although this idiopathic facial paralysis cannot be completely ruled out, considering that myositis was confirmed at the injection site and facial paralysis was confirmed after injection, facial paralysis accompanied by myositis after vaccine injection is most suspected. In addition, after receiving a vaccine at a local hospital, she visited our hospital with symptoms of facial paralysis that persisted for a long time, and needed medication.

There are a few reports of vaccine-induced neurological disorders and myositis in humans. Chou et al. (4) reported two cases of right facial neuropathy after influenza vaccination, diagnosed based on facial nerve conduction studies and blink reflex testing. Cases of acute disseminated encephalomyelitis and transverse myelitis with acute motor axonal neuropathy after influenza vaccination have been reported (19). Although these reports discuss several possible causes of myositis (22) such as viral infection (12) and autoimmunity (10), the relationship between influenza vaccination and neuro-

logical complications such as facial paralysis and neuritis has not been clearly established (23). Additionally, a 60-year-old man developed polyarthropathy, orbital myositis, and posterior scleritis 10 days after receiving the 1993 Fluvirin vaccine. Because there was ocular involvement, he was prescribed oral prednisolone and acetazolamide, with dramatic improvement over four months (27). Belliveau reported the case of a patient with orbital inflammation and posterior scleritis hours after receiving Arepanrix (GlaxoSmithKline, Quebec, Canada), an H1N1 influenza vaccine. The patient was treated with oral and topical steroids and showed complete symptom resolution within 2 weeks (2). Although the mechanism of vaccine-related autoimmune disease is unclear, several studies report a correlation between vaccine administration and inflammatory myopathy, a rare phenomenon presumed to be due to an autoimmune reaction (3,20,25,27).

However, it is unclear whether our patient's symptoms were due to the adverse effects of the vaccine itself or to reactions to antigens or adjuvants. Adjuvants such as adsorbent aluminum hydroxide gel are often used with vaccines (9,11). They enhance the antigen-specific immune response, ideally without triggering an immune reaction, and are commonly used to boost the immune response to vaccination (17). In previous reports, side effects of adjuvants have been reported (1,13). There have been cases of myositis, myocarditis, and rhabdomyolysis after administration of the seasonal influenza vaccine, possibly due to the immunogenicity of the vaccine adjuvant. This has been termed "adjuvant-induced autoimmune/inflammatory syndrome" (1).

Considering everything, it was determined that this patient's facial paralysis was most likely secondary to myositis caused by vaccination, and PDS and MMF treatments were performed to treat vaccine-induced myositis. In veterinary medicine, there is still insufficient evidence for treatment guidelines for vaccine-induced myositis. In human medicine, there have been cases of vaccine-induced myositis that were treated with glucocorticoids and immunosuppressants (26). All these cases were treated with immunosuppression, including glucocorticoids, intravenous immune globulin, cyclophosphamide, methotrexate, hydroxychloroquine, MMF, and tocilizumab. However, it has not yet been studied which of these immunosuppressants has better results, and further research is needed.

Conclusions

We report a rare case of facial paralysis and myositis after influenza vaccination in a dog. Vaccination may cause neurological symptoms in dogs, and these symptoms can be effectively managed with immunosuppressive drugs such as PDS and MMF.

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Authors' Contributions

JHA, YIO, SHK, SMP, THK, KYS and HYY analyzed and interpreted patient data. JHA was a main contributor in writing manuscript. JHA, YIO, SHK, SMP, THK, KYS and HYY performed imaging evaluation and contributed to imaging descriptions and discussions in this manuscript. All authors read and approved the final manuscript.

Ethics Approval

Not applicable.

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Written informed consent for publication of the clinical detail was obtained from the dog's owner.

Conflicts of Interest

The authors have no conflicting interests.

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