NOTE *Surgery*

A case of acute postoperative transitory sialadenosis of the submandibular glands in a healthy dog

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ABSTRACT. A 1-year-old healthy female cross-breed dog, weighing 4.5 kg, was scheduled for elective neutering. Fentanyl (5 μg/kg) and propofol (4 mg/kg) were administered intravenously (IV) to induce anesthesia, which was maintained with isoflurane and a constant fentanyl infusion rate (10 μg/kg/hr). During the recovery from the anesthesia, the presence of bilateral dense submandibular masses was recognized, as was the excessive secretion of saliva. An ultrasound examination was performed and revealed bilateral abnormally-diffused enlargement of the submandibular salivary glands. A cytology examination was conducted, and no signs of abnormality were found. The size of the swellings subsequently diminished, completely subsiding after 2 hr, as did the hyper-salivation. To the authors' knowledge, this represents the first case report of an acute transient swelling of submandibular glands after general anesthesia in a dog.

KEY WORDS: acute sialadenosis, anesthesia, dog, postoperative, salivary gland swelling

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The acute transient swelling of one or more salivary glands in the early postoperative period is a rare phenomenon in human anesthesia practice. Nevertheless, several papers have described this finding [1, 2, 7, 9, 12, 14, 16, 21], which has been reported as occurring 1 in 600 times following endotracheal intubation and anesthesia [12]. The condition is almost always painless and is typically self-limiting, resolving spontaneously within a few hr to a few days without leaving any sequel. In a retrospective study, Sozmen *et al.* (2000) [20] reported 13 cases of dogs where there was bi- or unilateral submandibular salivary gland swelling. Possible mechanisms for such enlargements remained unclear for these authors, and none of the cases of idiopathic salivary gland enlargement had an acute onset and spontaneous resolution within a few hr. The example that we report here, based on onset and duration, seems to be more akin to the cases, described in human medicine, of acute, transient salivary gland swelling in anesthetized patients, also known as "anesthesia mumps" [16].

A 1-year-old, 4.5 kg female cross-breed dog was scheduled to undergo elective neutering at the University's veterinary teaching hospital of Padua. Her medical history and preoperative examination were unremarkable. Food, but not water, was withheld overnight. After placement of an intravenous catheter in the right cephalic vein and clipping of the ventral abdominal wall, 5 μg/kg of fentanyl (50 μg/m*l*, Fentanest; Pfizer, Latina, Italy) and 4 mg/kg of propofol (10 mg/m*l*, Propovet; Esteve, Milano, Italy) were administered IV to induce anesthesia. After the trachea was intubated, the dog was placed in the dorsal recumbent position and connected to a circle breathing system. Pressure controlled mechanical ventilation was started with a peak airway pressure of 10 cm H_2O, while the respiratory rate was changed to maintain normocapnia (35–45 mmHg). Anesthesia was maintained with isoflurane (IsoFlo; Esteve) (end-tidal 1–1.3%) in an oxygen-medical air mixture (1:3) and a constant rate infusion of fentanyl at 10 μg/kg/hr. Ringer's solution was infused IV at 5 m*l*/kg/hr. During anesthesia, the dog was kept warm using a heating pad (Petmat; Dale Ecotech, Milsons Point, Australia). Monitoring (Datex-Ohmeda S3 Monitor; Datex-Ohmeda, Milano, Italy) was conducted using electrocardiography, non-invasive blood pressure, body temperature and inhaled gas concentration measurements, lingual pulse oximetry, sidestream capnography and spirometry. Cardiovascular and respiratory variables were manually recorded at 5-min intervals. During the surgery, 0.3 m*l* of a 2% lidocaine solution (Lidocaina Cloridrato; Galenica Senese, Siena, Italy) was splashed on to each ovarian ligament. After removal of the ovaries, the constant rate infusion of fentanyl was reduced to 5 μg/kg/hr. However, the heart rate progressively fell to 50 beats per min, so the fentanyl infusion was stopped and 15 μg/kg of atropine (1 mg/m*l*, Atropina Solfato; Galenica Senese) were administered IV. After an initial, transient, paradoxical bradycardia with Mobitz type II second-degree atrioventricular blocks (probably due to atropine), the heart rate rose to over 100 beats per min. The surgery ended after about 10 min, and the inhalation anesthetic was stopped. Seventy minutes had elapsed from the induction of anesthesia at this point. At the end of the surgery, the dog was put in the lateral recumbent position, weaned from the mechanical ventilation and, once extubated, transferred to the recovery room. At this point, the presence of bilateral dense submandibular masses was recognized (Fig. 1), as was the excessive secretion of saliva.

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Fig. 1. Photograph of a 1-year-old female cross-breed dog in the recovery room with acute submandibular swelling.

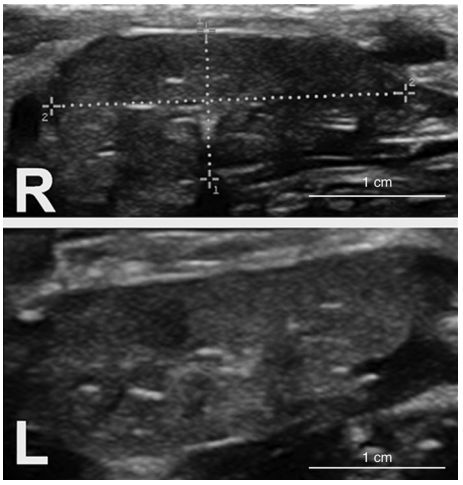

Fig. 2. Ultrasound image of the right (R) and left (L) submandibular salivary glands in longitudinal axis showing bilateral abnormally diffused enlargement.

The masses were warm and apparently painless on palpation. The body temperature was 37.4°C.

An ultrasound examination was performed and revealed bilateral abnormally-diffused enlargement of the submandibular salivary glands. Both the glands appeared to be diffusely hypoechoic, with patchy hypoechoic spots in the parenchyma (Fig. 2). A cytology examination was performed, and no signs of abnormality were found. The size of the swellings subsequently diminished and completely subsided after 2 hr, as did the hyper-salivation. No other problems were observed during the recovery, and the patient was therefore discharged from the hospital on the same day.

It is very difficult to provide a convincing explanation of why the subject in our paper developed acute bilateral swelling of the submandibular glands, which has never been reported in animals as a consequence of anesthesia. However, some suggestions can be made. The secretions, blood flow and growth of the salivary glands are mostly controlled by the two branches of the autonomic nervous system. Parasympathetic stimulation through the liberation of acetylcholine activates both acinar activity and the ductal transport mechanism that is mediated by myoepithelial cell contraction. Stimulation of the sympathetic nervous system by the binding of norepinephrine to adrenergic receptors produces thicker and less abundant secretions and the contraction of myoepithelial cells [3, 11, 19]. Afferent stimuli from taste, mastication, smell, sight and thought modulate the neural control of salivation [6, 19]. Moreover, a wide variety of drugs are also capable of increasing or decreasing salivary flow by mimicking autonomic nervous system actions or by indirectly affecting blood flow to the glands or the electrolyte balance [17].

Our dog received atropine towards the end of the anesthesia. Atropine, which exercises a competitive antagonism against acetylcholine on the muscarinic salivary receptor site, reduces salivation [15]. Lung (2003) has shown that atropine (0.5 mg/kg) can eliminate the flow of saliva in dogs and the parasympathetic nerve-induced contraction of myoepithelial cells, confirming what was reported by Emmelin *et al.* (1969) [4]. The drug's administration has been reported as a possible contributing factor to postoperatory salivary gland swelling in humans [7, 16]. The timing of the atropine administration in our subject was unusual and may have meant that some residual effects of the drug were still present during the immediate post-anesthetic period. This drug is well known for its antisialagogue effect. Nevertheless, hyper-salivation was present during the recovery from anesthesia in this dog. It should be born in mind that the antisialagogue effect of atropine is dose-dependent [4, 15] and can therefore be overcome by more intense stimuli. In addition, as already mentioned, the sympathetic nervous system, which is not affected by atropine, could elicit salivation.

Even if hyper-salivation pathophysiology is controversial, nausea, pain and drug administration have been suggested as the most common causes [18, 22]. Some authors have reported nausea as a side-effect of fentanyl administration in dogs [5, 8, 13]. Tsai *et al.* (2007) [23], meanwhile, reported hyper-salivation as a postoperative symptom, with an incidence of around 20% in dogs undergoing general anesthesia with propofol induction and maintenance with isoflurane; no dogs received opioids in that study and, according to the manuscript, the majority of the hyper-salivation was not associated with signs of nausea. In our case, propofol, isoflurane and fentanyl were used, and we cannot exclude the possibility that the dog had nausea, although the quality of the recovery was good. The excessive saliva secretions may have been an important predisposing factor for the submandibular gland swelling in this case, favoring saliva accumulation within the salivary duct system.

Chronic stimulation of the sympathetic innervation of the submandibular glands in rats has been shown to cause glandular enlargement [24]. Bilateral submandibular salivary gland swelling has also been reported in humans by Pirat *et al.* (2009) [14], who suggested that the use of vasopressors can play a role in salivary gland enlargement due to an increase in saliva production mediated by sympathetic stimulation. In our case, the rising of the sympathetic tone may

have been caused by the regaining of consciousness, possibly followed by fear and/or pain, during the recovery from anesthesia. This stimulation by endogenous catecholamine may have played an important role in the genesis of the sialadenosis. It has been shown in dogs that superimposed sympathetic stimulation can retard parasympathetic-induced salivary flow [10]. Indeed, myoepithelial cell contraction, which is fundamental step in the physiology of salivation, requires an appropriate balance between the sympathetic and parasympathetic systems to occur [11]. Experimental evidence suggests that the contraction serves not only to aid the flow of saliva through the duct system, but to also counteract the backflow of fluid into the gland tissue [4]. It may be that the residual atropine, blocking the contraction of the myoepithelial cells, led to an accumulation of saliva within the glands until the appropriate balance between sympathetic and parasympathetic systems was regained to generate overt fluid secretion. As already noted, the sympathetic saliva is highly viscous compared with the watery parasympathetic saliva [11]. This could have been a contributing factor in delaying the saliva excretion.

One mechanism suggested in the literature for the development of acute salivary gland swelling is the retention of secretions due to salivary-duct occlusion as a consequence of the pressure exerted on the submandibular region by the laryngeal mask airway cuff or as a result of patient positioning [2, 21]. The mandibular ducts leave the medial surface of the respective glands and run rostromedially in the intermandibular space up to a small sublingual papilla beside the lingual frenulum on the floor of the mouth. In this case, although improbable, we cannot exclude the possibility that an occlusion or partial occlusion of the ducts occurred during anesthesia, for example, due to an excessive pressure on the tissues of the submandibular region by the lace used to secure the endotracheal tube or an indirect pressure on the sublingual tissues by the tube itself.

The postoperative sialadenosis observed in this case lasted about two hr. A similar quick resolution is reported also in humans [16, 21], although, often healing time of several days is reported [1, 2, 7, 9, 12, 14]. However, perioperative salivary gland swelling in human should be taken very cautiously as term of comparison for other species. Difficult intubation, prolonged anesthesia time, frequent use of neuromuscular blocking agents and body weight are all conditions much more frequent in humans that in dogs, these factors can predispose humans to prolonged salivary gland swelling. Predisposing factors to submandibular salivary gland swelling, such as subclinical conditions affecting this dog, can not be excluded, nevertheless, it is highly unlikely.

To the best of the study authors' knowledge, this is the first paper to describe the acute transient swelling of salivary glands after general anesthesia in a dog. The aetiology and pathogenesis remain unclear, but some considerations have been made. Similarly that for humans, salivary glands swelling seems to arise in certain conditions as postoperative complication even in dogs. We believe it is important for veterinary anesthesiologist to be aware of this.

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