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Application of local anaesthesia and cryosurgery for eyelid masses in dogs

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Abstract

Background: Eyelid mass removal and cryotherapy application using only local anaesthesia and restraint may benefit patients with high anaesthesia risks.

Objective: To evaluate and validate cryosurgery application using the CryoPen XL® on palpebral masses under local anaesthesia for patients not suitable for general anaesthesia.

Methods: Thirty patients underwent the procedure between November 2015 and April 2020. The procedure steps were as follows: skin preparation and local anaesthesia of the affected eyelid; debulking by resection and/or squeezing out the inspissated material; cryosurgery and post-operative care using topical medication, antibiotics and anti-inflammatory ointment. The medical records of the patients who underwent the operation were evaluated. Moreover, a telephonic survey with the pet owners was performed to determine recurrence, time to recurrence, survivability and side effects.

Results: Among the 30 owners, 29 responded to the survey. Ten (10/38, 26.3%) masses recurred with an average time to recurrence of 6.0 months. The estimated average depths for all, non-recurred, and recurred masses were 1.89, 1.88 and 1.90 mm, respectively. The average recurrence rate and time to recurrence were higher and earlier, respectively, than previously reported values. However, no patient presented intra- or post-operative complications.

Conclusion: These findings suggest that local anaesthesia and cryosurgery using the CryoPen XL® can be used in patients with eyelid masses who are not suitable for general anaesthesia. Compared with the surgical eyelid mass removal and blepharoplasty procedure, the reported procedure is time- and cost-effective, with the additional benefit of not requiring general anaesthesia.

KEYWORDS
CryoPen XL®, cryosurgery, eyelid mass, local anaesthesia

1 | INTRODUCTION

Eyelid tumours are common in older dogs, with most being benign (Aquino, 2008). Resection and restoration of the eyelid structure are essential for maintaining long-term ocular surface health; moreover, the tumour may become problematic if it is left untreated and becomes sizable. Further, alterations in eyelid structural function result in ocular surface irritation and may even become ulcerative (Aquino, 2007). Generally, the gold standard for eyelid tumour treatment is surgical mass resection and blepharoplasty to allow complete mass removal with a clean margin. However, cryosurgery is a useful treatment for a superficial, small and non-invasive lesion or when definitive surgery cannot be performed due to limitations resulting from regional anatomy or owner reluctance (De Queiroz et al., 2008). Cryosurgery or cryotherapy is a technique involving the use of cryogens, including carbon dioxide, nitrous oxide and liquid nitrogen, to rapidly freeze the local tissue and to cause ice crystal formation to rupture the cells. Subsequently, the tissue is slowly thawed for more complete destruction (Yiu et al., 2007). Previous studies have evaluated debulking and cryotherapy application to palpebral masses (Zibura et al., 2019), as well as evaluation of cryosurgery efficacy for canine and feline skin/subcutaneous tumours (De Queiroz et al., 2008). Additionally, studies have reported clinical and experimental results of cryosurgical treatment of palpebral neoplasms (Holmberg & Withrow, 1979). However, all these studies on the efficacy of cryotherapy and surgery on palpebral masses employed general anaesthesia. Moreover, palpebral masses may occur at any age but are most often encountered in older dogs (Roberts et al., 1986), which is suggestive of potential risks of general anaesthesia.

Eyelid mass removal and cryotherapy application using only local anaesthesia and restraint may benefit patients with high anaesthesia risks and those whose owners are reluctant towards general anaesthesia. This study aimed to evaluate the efficacy of cryotherapy for small eyelid masses under local anaesthesia, as well as to determine the complications, recurrence rates and time to recurrence.

2 | MATERIAL AND METHODS

Between November 2015 and April 2020, 30 canine patients were treated using mass resection procedures at the tumour base using Westcott scissors and/or squeezing out of the inspissated materials after local anaesthesia, followed by cryotherapy application using the cryopen (CryoPen XL®, H & O Equipment nv/sa, Belgium). Patients treated using cryotherapy alone and/or put under general anaesthesia were excluded from this study. The study was approved by the Institutional Animal Care and Use Committee of Konkuk University (protocol #KU20182). All the dog owners provided written informed consent.

The surgical procedure was performed as described below. First, the surgical site was prepared as follows: sterilisation of the eye globe and peripheral region using 0.2% povidone-iodine, and washing and wiping with sterile eyelid wipes (EyeLike Lid Cleanser®, Koryo Eyetech, Korea). Subsequently, 0.3 ml of the local anaesthetic (Lidocaine HCl 2% Injection®, Daihan, Korea) was subcutaneously injected around the surgical site. A topical anaesthetic (0.5% proparacaine, Alcaine®, Alcon, Belgium) and antibiotic eye drops (Ofloxacin, Tarivid®, Santen Pharmaceutical Co. Ltd., Japan) were then applied. Two patients required light sedation (case 24: 0.2 mg/kg intravenous butorphanol; Butophan®, Myung Moon, Korea and case 26: 6 mg/kg intravenous propofol; Anepol®, Hana Pharm, Korea) during the preparatory local anaesthetic injection step; the respiration rate and heart rate of both patients were monitored throughout the whole procedure. The subsequent surgical procedures were performed while the patient was firmly strained. The mass was cut using Westcott scissors and/or squeezed out of the inspissated sebaceous debris to achieve a fine surface eyelid margin (Figure 1). Haemostasis was managed before cryotherapy application since the interposed frozen blood layer could act as an insulator for the targeted tissues (Withrow 1980). Cryotherapy was performed using cryopen to provide an ideal temperature between −60°C and −80°C for tissue destruction on application. According to the guidelines of H & O Equipment User Manual,[1] liquid N_2O spray was applied to the lesion. The application duration was dependent on the lesion depth (referred to as 'size' henceforth). For all patients, the size was evaluated and estimated by a single operator and was dependent on the operator's clinical experience. The freezing penetration rate using the cryopen is approximately 1 mm per 5 s with a maximum freezing depth of 3–6 mm depending on the used applicator. Further, the blue dot applicator alone was used since all mass lesions had a size of ≤3 mm. Two cycles of the freezing-thawing procedure were performed to allow the best opportunity for therapeutic success. After the first freezing cycle, the tissue was allowed to thaw for approximately 30 s before the second freezing cycle. Notably, the second freezing causes the tissue to freeze faster than the first one. Topical antibiotics (Tarivid®) were applied at the end of the procedure. For post-operative care, all the patients received prescriptions of topical ophthalmic neomycin, polymyxin B and dexamethasone ointment (Maxitrol®; Alcon-Couvreur, Belgium), or oxytetracycline hydrochloride with polymyxin B ointment (Terramycin®; Pfizer, United States) for 7–14 days. A follow-up was recommended to all patients, with weekly monitoring for 4 weeks.

Recurrence and time to recurrence were determined through owner-driven follow-up using a telephone survey. Recurrence was defined as either diagnosed by a veterinary ophthalmologist or the owner observing a mass on the same eyelid location, which was treated using the aforementioned procedures. During the survey, we determined the breed, age (current age, age when treated), sex, affected eyelid, mass size, time of cryopen application, recurrence status, known or estimated time to recurrence and severe side effects such as permanent functional/structural eyelid damage. If the patient was deceased, we calculated the time from treatment to death.

To confirm the correlation between the mass size and recurrence rate, the significance was tested using the chi-square test. The results for case 5 were excluded from this analysis because we did not receive a response to the survey in this case (both eyes). A p value of <0.05 was considered statistically significant. All statistical analyses were per-

[1] CryoPen® and CryoProbe Series User's guide, H & O Equipment.

FIGURE 1 (a) After surgical site preparation, the mass was cut using Westcott scissors. (b) The mass base is squeezed to remove inspissated materials; simultaneously, haemostasis was achieved before applying cryogen to the surgical site. (c) Cryogen application onto the mass base. Note that the bleeding from the mass is completely controlled beforehand since the blood and clots may act as an insulator and not allow proper temperature control

formed using SPSS software (Statistical Package for the Social Sciences version 25 for a window; IBM).

3 | RESULTS

This study included 30 canine patients (38 masses); among them, 29 responded to the owner-driven follow-up survey. The average age of the patients at the treatment point was 11.0 ± 3.57 years [mean ± standard deviation (SD), range: 3–16 years]. The dogs comprised 11 breeds, 14 castrated males, 1 intact female and 15 spayed females. Table 1 shows the specific data. Among the 38 masses removed, two tissue samples underwent histopathological assessment with one being meibomian adenoma and the other being granulomatous with plasmacytic inflammation. Table 2 provides details regarding risk factors and owner consent status. Owner-driven follow-up through a telephone survey and/or recurrence verification from the ophthalmologist revealed that 10 of the 38 masses had recurred (26.3%). The average time to recurrence was 6.0 ± 6.72 months (mean ± SD; range: 1–24 months). Further, eight (26.7%) patients were confirmed as deceased. The average time from surgery to death was 16.5 ± 10.8 months (range: 1–32 months). The mass sizes were estimated by a single operator; the application time duration was selected accordingly. The average mass size was 1.89 ± 0.71 mm (range: 1–3 mm). The sizes of the recurred and non-recurred masses were 1.90 ± 0.70 mm (range: 1–3 mm) and 1.88 ± 0.75 mm (range: 1–3 mm), respectively. One patient (case 5) with 2 mm masses on both eyelids did not respond to the survey; however, the medical history confirmed that the mass did not recur for at least 7 post-operative months. None of the followed-up patients showed complications other than depigmentation, local hair loss and mild inflammation, regardless of whether there was a recurrence. Immediately after treatment (Figure 2), the mass removal site and peripheral region became erythematous, with some patients showing temporary local chemosis. Upon mass resection, the eyelid margin was finely shaped and almost comparable to that after surgical removal with general anaesthesia. Case 24 (Figure 3) showed a typical wound scab at the resection site, depigmentation and local hair loss during 7 post-operative days. The histopathologic results showed meibomian adenoma and no recurrence. Case 19 (Figure 4) presented with typical depigmentation and local hair loss without other complications on day 14; however, it recurred at 2 post-operative months. Case 29 showed non-neoplastic inflammatory masses (Figure 5) without other complications; in this case, on day 27, the surgical site was fully healed without discolouration at the site and with only depigmentation being noticed. Hair started growing around the surgical site. Recurrence rates according to the mass size (1, 2 and 3 mm) are shown in Figure 6; no significant difference was observed ($p = 0.917$).

4 | DISCUSSION

Generally, surgical excision and blepharoplastic procedures are considered the gold standard treatment for palpebral masses, especially masses that could cause large defects upon removal (Stades & Woerdt, 2013). Moreover, for smaller masses involving one-third or less of the eyelid margin, a full-thickness wedge resection has been traditionally recommended, while those involving one-fourth to one-third of the eyelid length can be removed without blepharoplastic procedures (Bettenay et al., 2018). The prevailing recurrence rate after debulking and cryotherapy application on dogs is reportedly 15.2% (Zibura et al., 2019); however, the recurrence rate in this study was 26.3%. This could be attributed to differences between general and local anaesthesia, with the restraint procedure resulting in fluctuation of surgery precision, depending on the compliance of each patient. Notably, the local anaesthesia with restraint procedure was more cost- and time-efficient than the general anaesthetic procedure, without the risk of general anaesthesia complications. In this study, when general anaesthesia was not possible for some reason (Table 2), the subcutaneous injection anaesthetic method was used to remove the protruding mass, after which cryotherapy was used. Although our results indicate that recurrence rate may be higher than when surgery is performed after general anaesthesia, our method has the advantage of having at least a far higher treatment effect than in the event of the procedure not being performed at all. Patients who received additional treatment other than the conducted procedure or skipped part of the procedure, such as those who underwent cryogen application without tumour resection, were excluded from the study, as the recurrence rate could have depended on whether or not the masses were resected. This ensured

TABLE 1 Characteristics of patients receiving CryoPen XL® treatment

Case	Breed	Age[a](years)	Sex	Mass location	Cryogen application duration(second)	Whether the mass was recurrent (months)[b]
1	Shih Tzu	16	SF	OS	5	O (6)
2	Shih Tzu	16	SF	OS	10	O (3)
3	ECS	15	SF	OD/OD[c]	5/5[c]	O (2)[d]
4	Mixed	15	SF	OS/OS[c]	5/5[c]	X
5	Shih Tzu	14	CM	OU	10/10	Unknown[e]
6	Shih Tzu	14	CM	OU	10/10	X
7	ECS	14	CM	OD	15	O (1)
8	Shih Tzu	13	CM	OS	10	X
9	Shih Tzu	13	SF	OS	15	X
10	Dachshund	12	SF	OS	5	X
11	Shih Tzu	12	SF	OS	15	X
12	Schnauzer	12	CM	OU	5	X
13	Shih Tzu	12	CM	OD	10	X
14	Pekingese	11	CM	OS	15	X
15	Shih Tzu	11	SF	OS	5	O (24)
16	Schnauzer	10/11[f]	CM	OD/OS[f]	15/ 10[f]	X
17	Schnauzer	11	CM	OS	10	X
18	Shih Tzu	11	SF	OS	10	O (3)
19	Maltese	11	CM	OD	10	O (2)
20	Schnauzer	10	SF	OD	10	X
21	Maltese	10	SF	OD	5	X
22	Pomeranian	10	SF	OS	10	X
23	YT	10	SF	OS	15	O (5)
24	Bichon Frise	9	CM	OD	15	X
25	Poodle	7	CM	OD	10	O (12)
26	Shih Tzu	6	SF	OD/OD[c]	5/15[c]	X
27	Maltese	5	SF	OU	10/10	X
28	Pomeranian	4	CM	OD	10	O (2)
29	Maltese	4	CM	OD	10	X
30	Shih Tzu	3	IF	OS	5	X

[a]The age of the patient when the treatment was performed.
[b]The duration when the recurrence was detected.
[c]Same eye but two sites.
[d]Two sites were treated and one recurred.
[e]Unsuccessful owner-driven follow-up.
[f]Onset on OD at 10 years of age and on OS after 1 year.
SF; spayed female, CM; castrated male, IF; intact female. OS; left eye, OD; right eye, OU; both eyes, ECS; English cocker spaniel, YT; Yorkshire terrier. Twenty-nine cases responded to the survey and case 5 did not.

that our results reveal the recurrence rate only of cases in which the protruding masses were resected before cryotherapy.

Cryosurgery or cryotherapy involves tissue destruction under controlled freezing, with its main advantages being less invasiveness and lower morbidity compared with surgical resection (Grahan, 2001). The cryogen applicator used in this study (CryoPen XL®) sprays liquefied N_2O to freeze the target site; the temperature of −60°C to −80°C destroys the tissues by forming intracellular ice crystals (Kuflik, 1994). Cell organelles and protein matrices are destroyed, and vascular stasis occurs after thawing. The destruction is selective to the tissue, and the remaining stroma provides a structural framework for later wound repair. Collagen fibres and cartilages are resistant to the damage and play a role in favourable healing (Kuflik, 1994). Cryotherapy techniques in human and veterinary medicine include the continuous freeze technique and intermittent freezing until thermocouple needles register −50°C or a 5-mm halo of frozen tissue around the tumour is achieved.

TABLE 2 Details regarding patient risk factors and/or owner consent for general anaesthesia

Case	Owner Consent	Risk factors
1	No	Advances age (16 years)
2	No	Advanced age (16 years)
3	Yes	Advanced age (15 years), hepatopathy
4	Yes	Advanced age (15 years), hepatopathy
5	Yes	Advanced age (14 years), hepatopathy
6	Yes	Advanced age (14 years), anaemia, hepatopathy
7	Yes	Advanced age (14 years), chronic heart failure
8	Yes	Hepatopathy
9	No	–
10	Yes	Lymphoma, renal failure, pancreatitis
11	Yes	Bronchial collapse, chronic kidney disease
12	Yes	Hepatopathy
13	No	–
14	Yes	Adrenal tumour, renomegaly
15	Yes	History of cardiac arrest under general anaesthesia
16	No	Hepatopathy
17	No	Hepatopathy
18	No	–
19	Yes	Hepatic tumour, hepatopathy
20	No	Hepatopathy, recent general anaesthesia
21	No	–
22	Yes	Hepatic tumour, partial hepatectomy
23	No	Tracheal collapse, hepatopathy
24	No	–
25	Yes	Chronic kidney disease, hepatopathy
26	Yes	Hepatopathy
27	Yes	Anaemia, hepatopathy
28	Yes	Pancreatitis, inflammatory bowel disease, aspiration pneumonia
29	No	–
30	No	Anaemia, hepatopathy

This study adopted the continuous freezing and slow thawing technique following the product manual of the cryopen. This technique allows rapid freezing of the targeted tissue and minimal damage to local tissue. Furthermore, the intermittent freezing technique requires thermocouple needle placement at the target location, which is difficult in most conscious canine patients. Overall, two cycles of continuous freezing–slow thawing were effective on 71.1% of the masses treated using our procedure; moreover, the masses did not recur, with only minimal, previously reported cryosurgery complications (Holmberg & Withrow, 1979; Rickards, 1980). Notably, among eight patients (11 masses) who were confirmed dead during the survey, only one (9.01%) showed mass recurrence.

Periocular neoplasms may impair vision and cause ocular discomfort; therefore, they must be excised if they cause irritation or inflammation of the ocular structures or impair eyelid function (Klopfleisch, 2016). In general, the clinical considerations for performing eyelid mass removal are patient physical status, neoplasm size and the surgical procedures appropriate for the mass. Considering the average age of patients with primary eyelid neoplasms is over 10 years (Stades & Woerdt, 2013), a considerable number of patients are likely to be unsuitable for general anaesthesia due to advanced age. The procedure used in this study could aid such patients who are not amenable to general anaesthesia but have small eyelid masses that can be removed without any blepharoplastic procedures. The recurrence rate of our procedure was 26.3%, which is higher than the prevailing rate – the recurrence rates for surgery, cryotherapy and debulking followed by cryotherapy are 15%, 11% and 15.2%, respectively (Zibura et al., 2019). However, this procedure could not only provide an alternative to surgical intervention under general anaesthesia, but could also emerge as a cost-efficient and repeatable treatment option for owners, ultimately resulting in an improvement in patient quality of life.

We attempted to determine the correlation between the mass size (1, 2 and 3 mm) and recurrence rate, as shown in Figure 6, and did not find any significant correlation ($p = 0.917$). Similarly, Zibura et al. (2019) stated that the size of a palpebral mass did not appear to be a major factor for recurrence. However, we could not perform histopathological analyses because the owners did not provide consent for the same,

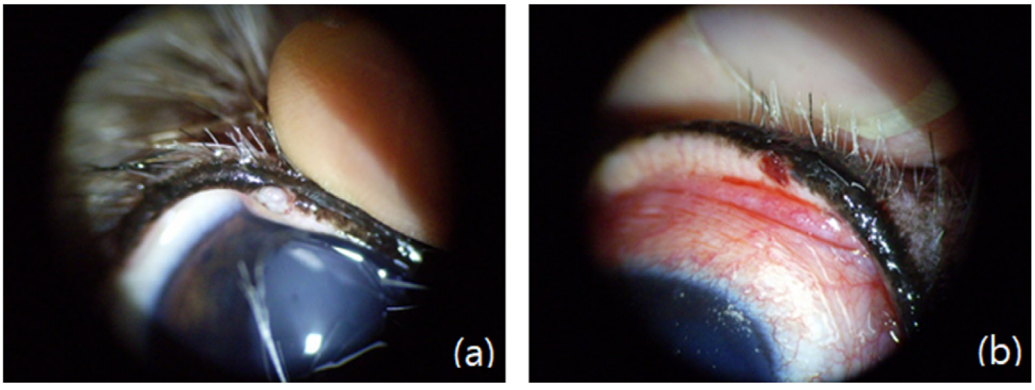

FIGURE 2 Case 13, pre-operative (a) and post-operative (b) image of the affected eyelid and mass. The picture was taken immediately after the procedure. The active bleeding was easily controlled with compression; the bleeding stopped after cryogen application

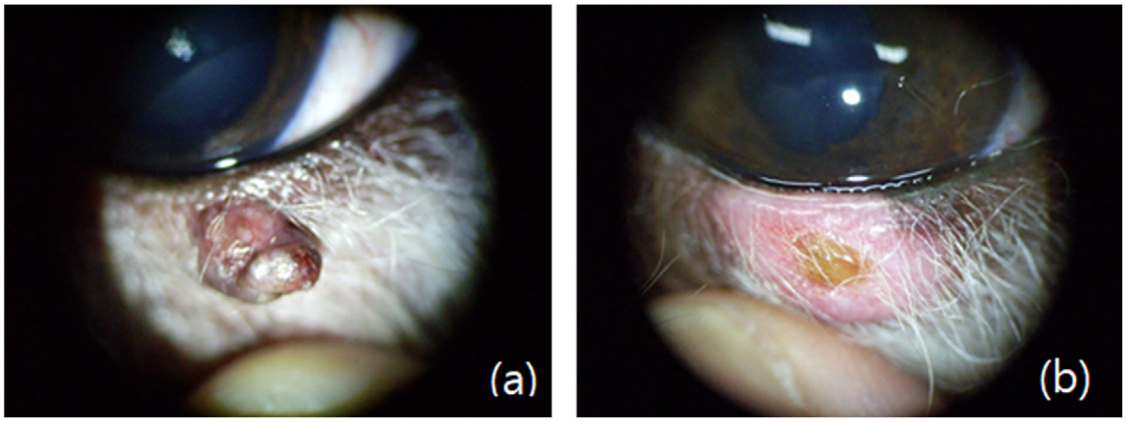

FIGURE 3 Case 24, pre-operative (a) and 7-day post-operative (b) images of the affected eyelid and mass. The surgical site shows scab formation, local depigmentation and discolouration. The removed mass was histopathologically diagnosed as a meibomian adenoma. The mass was completely resected and did not recur

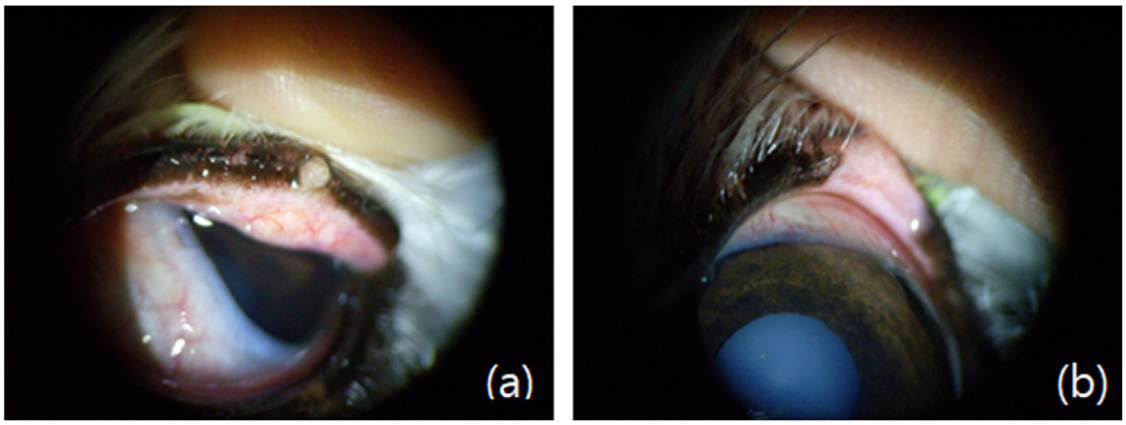

FIGURE 4 Case 19, pre-operative (a) and 14-day post-operative (b) images of the affected eyelid and mass. Depigmentation, discolouration and hair loss at the local site are noted. The mass recurred 2 months after cryosurgery

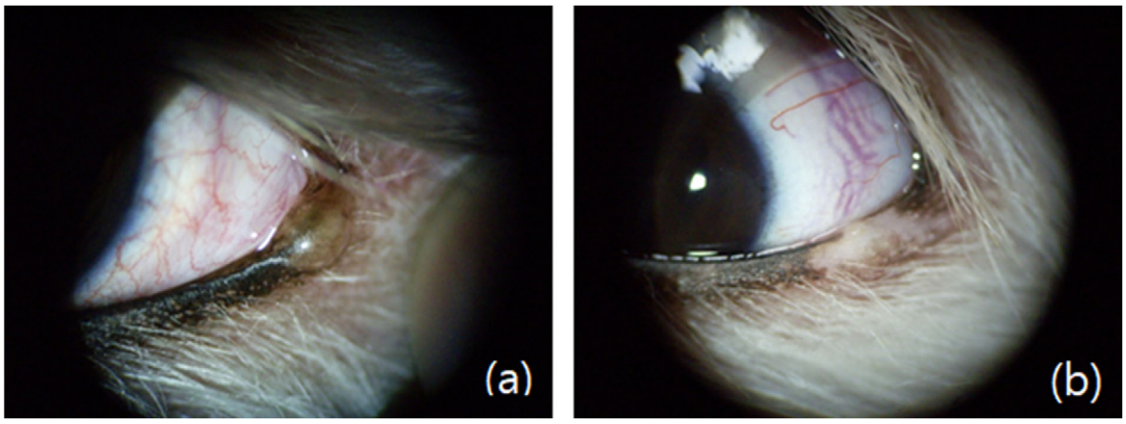

FIGURE 5 Case 29, pre-operative (a) and 27-day post-operative (b) images of the affected eyelid and mass. The mass was completely resected and did not recur

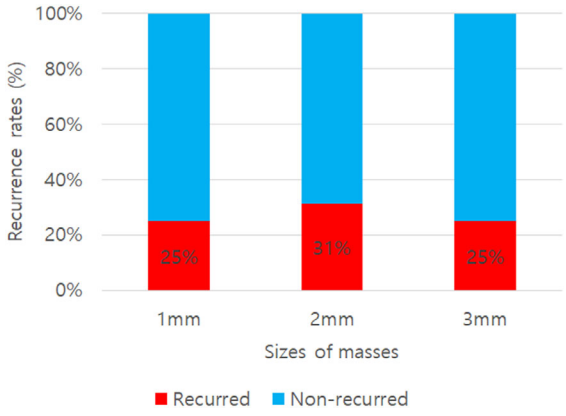

FIGURE 6 The recurrence rates according to the mass size (1, 2 and 3 mm) are shown by the red bar graphs. Data for case 5, wherein the patient was lost of follow-up with no survey response, were excluded. The chi-square test did not yield a statistically significant difference ($p = 0.917$)

and analysis of the correlation between the mass size and recurrence rate in the absence of histological findings could have limitations.

To the best of our knowledge, this is the first study on cryotherapy using the cryopen as a cryogenic instrument for canine patients. The advantages of using the cryopen, other than instruments requiring nitrous oxide cryoprobe, include the lack of contact with the eye or associated anatomic structures and easy manipulation of the cryotherapy degree by adjusting the distance between the applicator and treated lesion. This allows a safer method without contacting unnecessary structures and causing eye damage.

5 | CONCLUSION

Most cases of eyelid tumours are encountered in older patients, which makes the general anaesthetic procedure challenging. The general anaesthetic procedure could provide higher efficacy for patients; however, geriatric patients under general anaesthesia are at an increased risk of mortality. In this study, we conducted a procedure for patients not suitable for general anaesthesia due to various reasons. Therefore, this procedure could be performed on geriatric patients with systemic illness, which provides a safer therapeutic approach compared with surgical removal under general anaesthesia.

CONFLICT OF INTEREST

The authors have no competing interests to declare.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to and that no ethical approval was required for this particular case report.

AUTHOR CONTRIBUTIONS

MGH performed the survey and drafted the manuscript. JYK participated in the study design and manuscript review. All authors have read and approved the final manuscript.

PEER REVIEW

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