CASE REPORT

Moh's micrographic surgery for the management of a periocular mast cell tumor in a dog

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Abstract
A 3-year-old neutered male boxer dog presented with a 6-month history of a waxing and waning mass of the left dorsotemporal eyelid margin. Cytology and biopsy confirmed a diagnosis of mast cell neoplasia. Systemic staging of the dog failed to reveal any evidence of metastatic neoplasia. Owing to the location of the tumor within the eyelid margin and the wide surgical margins recommended for excision of mast cell tumors, Mohs micrographic surgery (MMS) was chosen for its potential to conserve tissues while providing intraoperative confirmation the tumor was completely excised. Utilizing MMS horizontal sectioning technique, 100% of the surgical margins were assessed prior to closure of the surgical wound. This represents the first time a comprehensive MMS protocol was used in a veterinary patient under general anesthesia.

Key Words: dog, eyelid, horizontal section, mast cell tumor, Mohs micrographic surgery, veterinary

INTRODUCTION
Mohs micrographic surgery (MMS) is the gold standard for the excision of locally invasive, high-risk, cutaneous malignancies in human dermatology.1–3 MMS utilizes a horizontal sectioning technique, which enables 100% surgical margin assessment and provides the lowest recurrence rates for locally invasive cutaneous tumors.2 Intraoperative mapping of excised tissues and examination of the entire margin allow removal of insidious tumor extensions.1 In a previous pilot study, the authors established the feasibility of Mohs technique for margin assessment in veterinary cutaneous oncologic surgery.5 Subsequently, there was a report of the application of MMS for the management of a horse with a penile squamous cell carcinoma (SCC) under sedation and local anesthesia.6

Malignant neoplasms of the periocular adnexa are challenging because of the tendency for these neoplasms to extend along embryonic fusion planes of the orbit. MMS was chosen in this case because the intraoperative microscopic assessment permits localization and a directed excision of tumor extensions in this compressed anatomic location. In addition to minimizing the risk of incomplete excision of the neoplasm, the technique enables tissue conservation in an area where normal function of the organ may be severely compromised by the demands of wide margins.7

Canine eyelid masses are very common in older dogs and usually benign (75%) and of epithelial origin. Typical clinical management of these masses includes excisional biopsy with narrow margins followed by histopathology to confirm the benign nature of the mass. When histopathology of these initial excisional biopsies identifies a malignant eyelid neoplasm, a more aggressive surgical approach, one that frequently requires intricate reconstructive techniques, is employed. MMS is an alternative surgical approach that will prevent taking wider surgical margins than are required for the individual neoplasm. The density of sensory organs and their highly differentiated tissues makes MMS particularly appropriate for neoplastic lesions of the face.

Mast cell tumors (MCT) represent 2.5% of total canine eyelid neoplasms and are among the most frequently reported malignant neoplasms of the canine eyelid along with sebaceous adenocarcinoma, melanoma, basal cell carcinoma and SCC.8 Among malignant eyelid neoplasms in the dog, MCT are reportedly more likely to metastasize and
therefore carry a worse prognosis. Complete surgical excision with wide margins remains the standard recommendation in the clinical management of well-differentiated, focal canine MCT.

With the prior validation of the use of MMS in veterinary medicine, the technique was applied intraoperatively for the first time under the constraints of general anesthesia in the case of a dog with a periocular MCT. To our knowledge, this is the first report of the application of a comprehensive Mohs technique under general anesthesia in veterinary medicine.

CASE REPORT

Physical exam
A 32 kg, 3-year-old neutered male boxer dog presented to the Louisiana State University, School of Veterinary Medicine with a 6-month history of a waxing and waning mass of the left dorso-temporal eyelid margin. Previous cytology suggested mast cell neoplasia, but a small incisional biopsy was inconclusive. At presentation, physical examination was unremarkable with the exception of a 1 cm by 1.5 cm raised dermal mass at the dorsolateral lid margin and lateral canthus (Fig. 1). Neuro-ophtalmic examination was normal. Schirmer tear test values were 26 mm/min OD and 27 mm/min OS. Applanation tonometry revealed the intra-ocular pressures were 17 mm Hg OD and 20 mm Hg OS.

Fluorescein stain uptake was negative OU. Biomicroscopic examination was normal with the exception of the 15 mm by 10 mm raised, mildly erythematous, alopecic mass in the dorsal eyelid adjacent to the lid margin and lateral canthus. Binocular indirect ophthalmoscopic examination was normal.

Differentials for eyelid masses include sebaceous adenomas, squamous papilloma, sebaceous adenocarcinoma, benign and malignant melanomas, histiocyтома, mast cell tumor, basal cell carcinoma, SCC, fibroma, fibropapilloma, lipoma and others. On the basis of these findings and the previous cytology, a tentative diagnosis of mast cell neoplasia was made. Preliminary diagnostics included a complete blood count, serum chemistry profile, urinalysis, buffy coat, thoracic and abdominal radiographs, bone marrow aspirate and skin punch biopsy. Prior to the bone marrow aspirate and biopsy, torbutogesic (0.2 mg/kg) was provided for analgesia and anesthesia was achieved with propofol given IV to effect (up to 5 mg/kg).

Diagnostic results
The complete blood count revealed only mild changes including a slightly elevated hematocrit 57.4 (upper limit 54%), mild thrombocytopenia 127 (lower limit 220 $10^3/\mu L)$, elevated mean platelet volume 14.2 (upper limit 12.5 $\mu L$) and mild lymphopenia 0.9 (lower limit 1.0 $\times 10^3/\mu L$). On a manual differential evaluation, a few Howell–Jolly bodies were noted. Serum chemistry profile and urinalysis were unremarkable. A buffy coat analysis of six slides did not demonstrate any mast cells. Thoracic and abdominal radiographs were unremarkable. A bone marrow aspirate revealed normal bone marrow with normal ratios and orderly maturation of megakaryocytes and erythrocytes and no mast cells. A skin punch biopsy harvested from the lateral margin of the left dorsal eyelid mass revealed large, densely cellular, poorly demarcated mass of neoplastic mast cells. The tumor was classified as an intermediately differentiated grade II MCT based on the Patnaik grading system. The cells were well differentiated and mitotic figures were infrequent, but there was infiltration into the subcutis and skeletal muscle (Fig. 2).

On the basis of the original cytology and the histopathology of the second biopsy, a diagnosis of MCT was confirmed. Based on the lack of evidence of metastasis in the
diagnostic evaluation, it was determined this mass was probably a primary tumor and excision of the mass was recommended. Given the anatomic location, the margins typically recommended (2–3 cm peripherally and one fascial plane deep)\textsuperscript{11–13} were unfeasible without enucleating or exenterating the orbit. Owing to the need for tissue conservation, the location of the tumor on an embryonic fusion plane, and the locally infiltrative nature of the tumor on histopathology, MMS was determined to be the treatment of choice.

\textit{Surgical technique}

Two weeks after the confirmatory biopsy was completed, the dog was catheterized with a 20-guage catheter in the right cephalic artery, premedicated with butorphanol (0.2 mg/kg) IV, acepromazine (0.01 mg/kg) IV and glycopyrrolate (0.1 mg/kg) IV, induced to general anesthesia with propofol (<5 mg/kg) IV and maintained on isoflurane inhalant anesthesia. He was prepared aseptically for surgery with three scrubs of 1:40 dilute betadine solution rinsed with warm sterile saline. The planned excision was delineated with 5-mm lateral margins and a two dimensional map (Mohs map) (Fig. 3) was drawn for reference. The excision was made using the scalpel at a shallow angle, approximating \(45^\circ\), to the tissue surface. The beveled incision was continued around the entire mass (Fig. 4). Unique to MMS, this angled incision is necessary to enable the histopathology technician to flatten the tissues, permitting the entirety of the deep and peripheral margins to be sectioned in a horizontal plane. Maintaining the orientation of the tissues with respect to the Mohs map, the sections were numbered and cut edges dyed with different colors (Davidson Marking System\textsuperscript{®}, Bradley Products Inc., Bloomington, MN, USA) (Fig. 3). Color coding on the map corresponded to the color dyes on the tissue edges.

\textit{Tissue handling – frozen technique and histopathologic assessment}

Tissues were immediately processed according to accepted Mohs protocol and as elaborated in the authors’ previous report.\textsuperscript{5} Briefly, the cryostat was used to obtain frozen horizontal sections intraoperatively. Peripheral edges were teased or pressed into the same plane as the deeper margin, thus flattening the tissue. Each specimen was mounted upside down on a cryostat chuck allowing the entire deep and peripheral margins to be cut. Serial sections 8 \(\mu\)m in thickness were cut from the deep borders for evaluation.

The prepared sections were stained with toluidine blue. Each section was assessed for the presence and location of neoplastic mast cells based on the mapped orientation. Microscopic findings and the location of residual tumor were denoted on the Mohs map and communicated to the surgeon guiding further resection (Fig. 3).

\textbf{RESULTS}

The first excision (Stage 1) was divided into three sections (A, B and C) for microscopic assessment (Fig. 3). Foci of neoplastic mast cell were noted in all three specimens.
necessitating a second excision (Stage 2) (Fig. 5a,b). This tissue was divided into two sections (A and B). Histopathologic evaluation revealed all margins of Stage 2 were free of neoplastic cells.

After the second excision, a large defect dorsolateral to the eye was present (Fig. 6a). Closure was accomplished by advancing skin dorsal to the eye ventrolaterally and advancing the skin ventral to the lower eyelid in a dorsolateral H-plasty to meet the opposing advancing skin. The lateral canthus conjunctiva and lid margins were closed first shortening the eyelid fissure by 5 mm. Walking sutures were used to reduce the tension in the dorsal skin, and a simple skin fold resection was required at the medial aspect of the dorsal incision (Fig. 6B). The facial nerve was preserved and functional, with appropriate eyelid function noted at anesthetic recovery. The time from the initial incision to the histopathologic determination from Stage 1 was 1 h, and total operative time was 2 h 15 min.

Follow-up
No recurrence of neoplasia was noted in the dog over a 1-year follow-up.

DISCUSSION
Developed by Dr. Frederic E. Mohs in the mid-twentieth century and popularized in the 1970s and 1980s, MMS became the standard of care in human dermatologic surgery for locally invasive cutaneous malignancies. Indications for the use of MMS include the following: (i) tumors with poorly defined local invasion, (ii) tumors in anatomic locations associated with greater subclinical invasion, that is, embryonic fusion planes of the face (preauricular, eyelids, nose, nasal labial, philtrum and temple), (iii) tumors in areas where tissue conservation is required and (iv) tumors with...
known perineural invasiveness (i.e. SCC).\textsuperscript{1,3,7,15-19} Excision with traditional margin assessment is performed by examining representative vertical sections (‘breadloafing’) at intervals through the specimen. This typically results in $<1\%$ of the margin being assessed.\textsuperscript{1,20} This can result in missing subclinical extensions in tumors with irregular local invasiveness. MMS, with its ability to assess $100\%$ of the margin, allows the surgeon to precisely map such extensions for subsequent removal.

Mast cell tumors are the most common cutaneous malignancy in dogs, and the boxer breed is over-represented.\textsuperscript{21} The authors have previously utilized MMS horizontal sectioning to assess the margins of MCT.\textsuperscript{5} The biologic behavior of MCT remains poorly understood, and the prognostic value of histopathologic margin evaluation has been called into question.\textsuperscript{22} Despite this, wide surgical excision remains the treatment of choice for cutaneous MCT that are judged as nonmetastatic by staging and are in an amenable anatomic location.\textsuperscript{21} The extent of surgical margins required has been a subject of much research and debate.\textsuperscript{13,23-26}

In this patient, the conventional wide surgical margins were not achievable without sacrificing the associated globe and vision. MMS offered an alternative means to achieve and confirm clean margins while preserving tissue and function.

CONCLUSION

In human dermatology, physicians who perform MMS are specialized in dermatology, dermatologic surgery, dermatopathology and Mohs surgery. Advanced training is required with fellowships accredited by the American College of Mohs Surgery. Mohs surgeons have surgical and laboratory facilities with a cryostat and specially trained histotechnicians. The authors established that MMS in veterinary medicine was feasible and reliable in a previous report but recognize and openly acknowledge the inherent limitations of the application of MMS in veterinary dermatologic surgery.\textsuperscript{5} This project represented the culmination of several years of training and surgical trials. While acknowledging the practical limitations of the training and equipment as well as the requirement for general anesthesia in most small animal veterinary patients, the complete margin assessment provided by MMS with its higher cure rates for locally invasive cutaneous malignancies make this procedure highly desirable.

Ultimately, MMS was successfully employed in the resection of a canine periocular MCT. It was subsequently utilized for the removal of a SCC in a horse under sedation and local anesthesia,\textsuperscript{6} but this is the first report of the use of MMS in a patient maintained under anesthesia while surgical revision was performed. In this case, the initial resection was inadequate and tumor extensions were successfully identified, mapped and targeted in a subsequent intraoperative revision.

REFERENCES


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