CASE SERIES

The palliative efficacy of modified Mohs paste for controlling canine and feline malignant skin wounds

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ABSTRACT

In veterinary medicine, the management of malignant skin wounds is highly challenging. We conducted a study on seven case animals (four dogs and three cats) which presented with malignant skin wounds. All seven animals had signs and symptoms which were controlled following treatment with a modified Mohs paste. Upon obtaining informed consent from their owners, the animals requiring management of malignant wounds were enrolled in this study. The modified Mohs paste was prepared by mixing zinc chloride, zinc oxide starch powder, glycerin, and distilled water. The modified Mohs paste was topically applied to and left to remain on the malignant wounds for one hour, under controlled conditions. Once the paste was removed, the wounds were irrigated with a solution of sterile saline. At the first examination, the wounds of each animal were observed for signs of exudate, malodor, and bleeding. In every case, visible improvement was observed immediately after the modified Mohs paste treatment. Specifically, the size of the malignant wounds, and the number of times the dressing gauze required changing, significantly decreased ($p < 0.05$ and $p < 0.01$, respectively). The open malignant skin wounds caused by mammary gland tumors disappeared in two cases. The Mohs paste has been shown to be a viable option for the palliative treatment in canine and feline malignant skin wound management.

KEYWORDS

Cat; dog; wound management; Mohs paste; palliative treatment

1. Introduction

In veterinary medicine, complete surgical excision of skin tumors under general anesthesia is accepted as the gold standard (MacDonald et al. 2008). However, tumor excision is contraindicated in cases which are considered high risk regarding general anesthesia, such as those with the complications of heart failure, hepatopathy, and/or nephropathy. The animals’ owners may also refuse to authorize tumor resections due to the expenses which would be incurred with surgical treatment and laboratory work-up for general anesthesia. In these cases, as well as in terminally ill patients with skin cancer, the surfaces of the tumors gradually become ulcerative, hemorrhagic, and malodorous, developing into malignant skin wounds. This worsens the quality of life (QOL) of such patients and, in the case of animals, their owners as well. These malignant skin wounds are common problems in the life-long management of animals with unresectable skin tumors. In addition, due to the importance of companion animals in the nationalistic philosophy of the Japanese people, owners are rarely willing to authorize euthanizing their animals. These factors render a more cost-effective and non-invasive management of malignant wounds a necessity for animals with skin cancer in Japan.

Zinc chloride fixative paste (called Mohs paste) was developed by Frederic E. Mohs in the 1930s, and used for fixed-tissue micrographic surgery in accessible skin tumors (Phelan 1968; Mohs 1970,1971,1989; Brook 2010; Trost & Bailin 2011). Its mechanism of action is degeneration of protein by astringent of ionized zinc that is produced by chemical reaction of zinc chloride and the exudate from skin wound. The paste is cost-effective and non-toxic to medical practitioners (Mohs & Guyer 1941; Mohs 1989; Trost & Bailin 2011). It is experimentally associated with a decreased risk of metastasis (Mohs & Guyer 1941; Kalish et al. 1998; Brook 2010).

Human skin tumor patients who have a guarded prognosis are contraindicated from undergoing anesthesia, and/or have increased risk of metastasis, are generally deemed ineligible for surgery. Malignant skin wounds which are likely to appear in these patients are an issue which worsens the QOL of the patients. The modified Mohs paste has been applied in patients with malignant skin wounds whose skin tumors are considered unresectable (Shigeyama et al. 2005; Kakimoto et al. 2010; Uno et al. 2010; Tsukada et al. 2012; Komine et al. 2014; Nakai et al. 2015). The application of the Mohs paste had positive effects on the fixed-necrotic
tissues, alleviated the signs and symptoms of malignant wounds, and decreased tumor volumes, allowing their subsequent excision (Shigeyama et al. 2005; Kakimoto et al. 2010; Uno et al. 2010; Tsukada et al. 2012; Komine et al. 2014; Nakai et al. 2015). The efficacy of modified Mohs paste has been reported in pleomorphic adenoma (Shigeyama et al. 2005), adenoid cystic carcinoma (Shigeyama et al. 2005), malignant melanoma (Shigeyama et al. 2005), and squamous cell carcinoma (SCC) (Komine et al. 2014; Nakai et al. 2015), and for those with non-cutaneous skin tumors such as angiosarcoma and advanced breast cancer (Shigeyama et al. 2005; Kakimoto et al. 2010; Uno et al. 2010; Tsukada et al. 2012).

In veterinary medicine, only two case reports exist which demonstrate the efficacy of modified Mohs paste on hemostasis and the reduction of malodor in Japanese animals. However, these animals died within one month after the treatment was completed (Hara 2012; Yamada 2011). To address the relative scarcity of veterinary studies on this topic, the objective of this case series was to examine whether or not modified Mohs paste would prove to be a viable option for the palliative treatment of the signs and symptoms of malignant wounds in terminally ill dogs and cats with cutaneous and non-cutaneous skin tumors. The modified Mohs paste treatment (MPT) significantly decreased the number of times dressing gauze required changing, and resulted in reduction of tumor size. In the observation of two feline cases of mammary gland tumors, open malignant wounds were completely closed by MPT. In addition, MPT was shown to extend the animals’ lifespan by at least one month.

### 2. Materials and methods

#### 2.1. Cases

Seven cases admitted to our Veterinary Teaching Hospital were observed from August 2012 to May 2013. All seven animals had unresectable malignant tumors and malignant skin wounds. Informed consent was obtained from all owners prior to the animals’ enrollment in the MPT study. The World Health Organization (WHO) staging system described by Owen (1980) was applied to all enrolled animals. Their profiles (species, breed, sex, age, tumor location, and pathology) are presented in Table 1. None of animals had responded previously to single antibiotic treatments. The dogs were enrolled for at least one of the following purposes: to arrest intermittent hemorrhaging from their wounds; for palliative treatment; to reduce tumor volume, if the animals were terminally ill with skin cancer; and/or for the management of exudate and malodor occurring in the wounds of patients in which health and/or owner finances contraindicated other treatment options. These criteria for participation in the MPT study were based on the report described by Shigeyama et al. (2005).

| Cases | Species | Breeds | Sex | Age (year) | Tumor location | Need for sedation | Pathology |
|-------|---------|--------|-----|------------|----------------|------------------|-----------|
| 1     | Dog     | Doberman Pinscher Mix | Spayed female | 13 | On the outside of the tarsal joint of the right hind foot | No | Soft tissue sarcoma |
| 2     | Dog     | Chihuahua | Female | 15 | Ventral aspect of the chest wall | No | Mammary gland tumor |
| 3     | Dog     | Shi Tzu | Spayed female | 9 | Cutaneous of head and neck region | Yes | Squamous cell carcinoma |
| 4     | Cat     | Domestic cat | Castrated male | 12 | Right pinna of ear | No | Squamous cell carcinoma |
| 5     | Dog     | Labrador Retriever | Castrated male | 15 | Zygomatic process of frontal bone | Yes | Osteosarcoma |
| 6     | Cat     | Domestic cat | Spayed female | 18 | Lower abdominal wall | No | Mammary gland tumor *a |
| 7     | Cat     | Domestic cat | Spayed female | 13 | Left chest wall | No | Mammary gland tumor |

*aButorphanol tartrate, 0.1 mg/kg body weight (BW) intramuscularly.
*bDue to its aggressive behavior and the site of the wound.
*cAs the body temperature elevated and the patient was perceived to be distressed.
*dTentative diagnoses were made by cytology. Epithelial characteristics of tumor cells were observed.
2.3. Modified Mohs paste preparation and treatment

The original Mohs paste consists of stibnite (antimony ore ground), Sanguinaria canadensis (powdered root of the bloodroot plant), and saturated zinc chloride solution. Although stibnite and S. canadensis are used as a vehicle due to their suitable viscosity, these products are not available in Japan. The preparations of original (Mohs & Guyer 1941) and modified Mohs paste used in this study are described in Table 2. The dosages and formulations of the chemicals and the procedure were based on methods described by Kakimoto et al. (2010) and Tukada et al. (2012). First, zinc chloride (Sigma-Aldrich Japan K.K., Tokyo, Japan) and distilled water were placed in a beaker, and then homogenized by stirring. Once an exothermic chemical reaction had occurred, the mixture was cooled to room temperature. Next, zinc oxide starch powder (Maruishi Pharmaceutical Co., Tokyo, Japan) was added to adjust the viscosity of the paste. Finally, glycerin (Nichi Iko Pharmaceutical Co., Tokyo, Japan) was added to adjust the viscosity of the paste. The Mohs paste cannot be stored for any length of time, due to a rapid loss of its adhesive properties. The modified Mohs paste was applied to the animals only once a day. The procedure for applying Mohs paste consists of several steps. First, the animals were kept under controlled conditions, with sedation only if necessary, using butorphanol tartrate, 0.1 mg/kg body weight (BW), administered intramuscularly (Butorphanol, Meiji Seika, Tokyo, Japan). The wound was maintained in an upward position, so as not to spill or disturb the placement of the paste. The second step was the application of petroleum jelly (White Petrolatum, Taiyou Pharmaceutical Co., Tokyo, Japan) to the surrounding healthy skin to protect it from the paste. The third step was the application of a uniform layer of the paste, 1–3-mm-thick, to the surface of the malignant wound. Following the application of the modified Mohs paste to their wounds, the animals rested in a cage. Elizabethan-style collars were placed on their necks to prevent them from licking the paste. In the fourth step, the paste was removed one hour after application. Finally, a sterile saline solution was used to irrigate the wound. In treating an open malignant wound, MPT should be administered 1–2 times per week.

3. Results

Any changes which occurred in the malignant wounds are described in Table 3. The size of the malignant wounds after the last MPT significantly decreased when compared to the size of the wounds at the first MPT ($p < 0.05$). Four of the seven case animals showed a decrease in the size of the malignant wounds after MPT. In two of the four cases in which a decreased wound size was observed, the wounds had been completely eradicated by the MPT. None of the cases treated showed any visible increase in wound size. In addition to the reduction in wound size, the number of times the animals’ gauze dressing required changing significantly reduced compared to that before the MPT ($p < 0.01$). In all of the seven cases, the malodor and bleeding were no longer markedly noticeable after MPT. Two cases (Cases 3 and 5) required sedation for the administration of MPT. All of the animals’ owners were satisfied with the results after MPT had been completed.

Case 1: A dog presented with a malignant wound developed on the lateral tarsal joint of the right hind foot due to soft tissue sarcoma (T4N0M1) (Figure 1(a)).

### Table 2. Formulation of the modified Mohs paste in this study.

| Materials                        | Mohs (1941) | Kakimoto et al. (2010) | Tukada et al. (2012) | This studya |
|----------------------------------|-------------|------------------------|----------------------|-------------|
| Saturated zinc chloride          | 34.5 mL     | 30 g                   | 10 g                 | 5 g         |
| Zinc chloride                    | 60 g        | 10 g                   | 2.5 g                |
| Purified water                   | 30 mL       | 10 mL                  |                      |
| Stibnite                         | 40 g        | 10 g                   |                      |
| Powdered Sanguinaria canadensis  |             |                        |                      |
| Zinc oxide starch powder         | 30 g        | 5 g                    | 2.5 g                |
| Glycerin                         | 15 mL       | 5–10 mL                | 1 mL                 |

*aThe paste must be applied to the surface of the malignant wound in a uniform layer, 1–3-mm thick, depending on the size of the wound. This is a sufficient amount of paste to cover a wound measuring 10 cm × 10 cm.

### Table 3. Results in the categories evaluated before and after modified Mohs paste treatment.

| Cases | Size of the malignant wounds | Number of times gauze dressing required changing per day | Number of times patients receive MPT | Median interval days (range) | Durations (days) patients receive MPT | Survival time after the last MPT (days) |
|-------|------------------------------|---------------------------------------------------------|-------------------------------------|----------------------------|----------------------------------------|----------------------------------------|
| 1     | 8.0 cm × 6.0 cm              | Before MPTb: 5                                          | After MPTb: 2                       | 14                        | 14 (2–35)                             | 210                                    | 205                                    |
| 2     | 3.0 cm × 3.0 cm              | Before MPTb: 4                                          | After MPTb: 2                       | 2                         | 5                                      | 6                                      | 95                                     |
| 3     | 2.3 cm × 2.0 cm              | Before MPTb: 2                                          | After MPTb: Not determinedd         | 2                         | 7                                      | 8                                      | 655                                    |
| 4     | 4.0 cm × 3.0 cm              | Before MPTb: 2                                          | After MPTb: Not determinedd         | 2                         | 7                                      | 8                                      | 655                                    |
| 5     | 20 cm × 20 cm                | Before MPTb: 2                                          | After MPTb: 2                       | 2                         | 7                                      | 22                                     | 64                                     |
| 6     | 2.5 cm × 2.0 cm              | Before MPTb: 2                                          | After MPTb: Not determinedd         | 2                         | 7                                      | 7                                      | 112                                    |
| 7     | 4.3 cm × 1.4 cm              | Before MPTb: 2                                          | After MPTb: Not determinedd         | 2                         | 31                                     | 31                                     | 30                                     |

*aLast visiting before MPT.  
*b2–3 weeks after the final MPT.  
*cFinally, the tumor was surgically resected.  
*dThe cat did not use dressing gauze for the exudate.
Presumptive metastatic nodules were detected on the caudal lobe of the right lung after examination by a thoracic radiograph. Amputation of the right foot was proposed because sustained bleeding from the wound would shorten the dog’s lifespan. The owner refused to authorize the amputation due to the poor prognosis of the dog. An Elizabethan collar was placed to prevent the animal from licking the wound. An antibiotic drug (cephalexin, 15 mg/kg BW twice daily; Syncl Tablets, Asahi Kasei Pharma Corp., Tokyo, Japan) was administered orally to prevent further infection of the wound. The dog exhibited exercise intolerance and mild anemia (hematocrit, 27.5%) when reevaluated in one week. The dog was then enrolled in the study for MPT. After the application of Mohs paste, its wound exudate and malodor showed improvement immediately upon removal of the paste (Figure 1(b)). On day 14, the dog’s hematocrit had increased to 37.0%, and the dog showed increased vigor. The dog received MPT a total of 14 times, requiring no antibiotics throughout the rest of its lifespan. The animal died 205 days after the final administration of the MPT.

Case 2: A dog presented with a malignant wound from a mammary gland tumor (T2cN0M0) on the ventral aspect of the chest wall (Figure 2(a)). The animal’s owner refused to authorize surgical excision of the tumor on the basis of poor financial circumstances. The owner enrolled it in the study for MPT. After the application of Mohs paste, its wound exudate and malodor showed improvement immediately upon removal of the paste (Figure 1(b)). On day 14, the dog’s hematocrit had increased to 37.0%, and the dog showed increased vigor. The dog received MPT a total of 14 times, requiring no antibiotics throughout the rest of its lifespan. The animal died 205 days after the final administration of the MPT.

Case 3: A dog presented with multiple ulcerated malignant wounds on the head and neck from cutaneous SCC (T2N0M0). The carcinoma had extended over a broad area of the skin. The animal showed enlargement of both superficial cervical lymph nodes, a possible indication of metastasis, and severe inflammation from the malignant wounds. The owner chose MPT from the available treatment options. The dog required sedation due to its aggressive behavior and the location of the malignant wounds. On day 7 after the start of MPT, the exudate and bleeding from the wounds disappeared, and decrease in the size of both the tumor and lymph nodes was observed. This provided evidence of a controlled disease progression. The positive results of MPT allowed surgical resection of the tumor and lymph nodes to be performed. Metastasis to the lymph nodes was not shown by histopathological examination. The dog received MPT two times, the second MPT on the day of its surgery. The animal died 655 days after the final MPT.

Case 4: A cat presented with a malignant wound from cutaneous SCC (T2N1bM0) on the right pinna. Fine-needle aspiration indicated metastasis of the tumor cells to the right parotid lymph nodes. After MPT, bleeding and malodor improved immediately. The initial size of the large extended wound which measured 5 cm × 4 cm in diameter decreased after MPT to 5 cm × 1 cm in diameter, when reevaluated on day 28. The cat received MPT four times, and died 64 days after the final MPT.

Case 5: A dog presented with a nasal osteosarcoma (T3N1M0) developed on the zygomatic process of the frontal bone. Although the dog received radiation therapy, the tumor grew rapidly. Malignant wounds gradually appeared on the left eye socket. Bleeding and malodor followed self-destruction of the tumor and

Figure 1. Appearance of malignant wounds in Case 1 before and after MPT. (a) An ulcerated soft mass was present on the outside of the tarsal joint of the right hind foot; the wound was hemorrhagic. (b) On the day after MPT, the surface of the wound was chemically fixed, was allowed to dry, and immediate cessation of bleeding occurred.

Figure 2. Appearance of malignant wounds in Case 2 before and after MPT. (a) A firm, fixed tumor was attached to the ventral wall of the chest and had erupted through the skin. Necrotic tissue was present in the tumor. (b) On day 32 after MPT, the open skin wound was epithelialized and disappeared.
the prognosis of the dog was clearly considered to be grave (Figure 3(a)). Informed consent for euthanasia was proposed to the owner. MPT was performed to prevent infection and to decrease malodor and exudate from the wound. After MPT, the infection, bleeding, and malodor were controlled. However, the body temperature elevated and the patient was perceived to be distressed. Erosion of the nasal mucosa was observed, which was caused by some of the Mohs paste that had dripped on to the tumor during application (Figures 3(b) and 3(c)). CT examination one day after MPT revealed an area measuring approximately 1.0 cm where the Mohs paste had migrated from the surface of the malignant wound (Figure 4). Pathological examination was performed before MPT, and at 14 days while under sedation. Histopathology revealed that MPT markedly increased areas of necrosis in the neoplasm when compared with the pretreatment findings. The dog received MPT 13 times, and died 3 days after the final MPT. The owner was satisfied that all options had been committed to extend the life of the dog.

Case 6: A cat presented with a malignant wound which appeared apparently from the presence of a suspected mammary gland tumor (T3N0M0) on the ventral aspect of the chest wall. The cat had a previous history of severe nephropathy and cardiac myopathy, which rendered anesthesia, required for surgical excision, an unacceptable option. After two applications of the MPT, the malignant wound gradually decreased in size and the open wound closed on day 21. No recurrence of the malignant wound was observed, and further wound management was unnecessary. The cat died 112 days after the final MPT.

Case 7: A cat presented with a malignant wound. It was suspected that a mammary gland tumor (T3cN1M1) was present on the first and second mammary gland ventral aspects of the chest wall. Fine-needle aspiration from the enlarged axillary lymph nodes (1.6 cm × 1 cm) confirmed metastasis of the tumor cells. A thoracic radiograph confirmed multiple pulmonary metastases. Due to the poor prognosis of the cat, its owner refused to authorize surgical treatment. After one application of the MPT, the bleeding, exudate, and malodor from the wound decreased immediately. The effects of the MPT lasted for one month. One month later, another application of MPT was made with repeated efficacy. The cat died from respiratory failure 30 days after the final MPT.

4. Discussion

In the present case series, we demonstrated the efficacy of MPT as a viable treatment option for malignant
skin wounds. MPT produced the effects of showing visible improvement in malignant wounds. MPT has been proven effective in terminally ill animals with unresectable skin tumors and tumors that surgical excision is not desired by the animals’ owners. In humans, MPT has been documented as an effective treatment to decrease bleeding, decrease frequency of wound dressing changes, decrease odor and degree of pain experienced, and increase patient QOL (Shigeyama et al. 2005; Kakimoto et al. 2010; Uno et al. 2010; Tsukada et al. 2012; Komine et al. 2014; Nakai et al. 2015). Similarly, its efficacy has been demonstrated in this study through significant decreases in tumor size and the number of dressing changes required. In particular, two cases (Cases 2 and 6) with open skin wounds occurred due to the presence of mammary gland tumors experienced the closure of their wounds with MPT. The same result has been reported in humans (Tsukada et al. 2012). A decrease in pressure from the tumor mass to the skin surface may allow re-epithelialization. MPT is indicated as an option to decrease the signs and alleviate the symptoms experienced by patients with malignant wounds.

In veterinary medicine, only two case reports have described MPT as a viable option for suspected mammary gland tumor (Hara 2012; Yamada 2011). These reports showed that the Mohs paste decreased the amount of bleeding, exudate, and degree of malodor from malignant wounds. However, the animals died within one month after the onset of treatment. In this study, we employed MPT not only on mammary gland tumors but also on soft tissue sarcoma, SCCs, and osteosarcoma in dogs and cats. All the seven animals survived at least two months after the start of the MPT, and especially one dog (Case 3) survived for 633 days using MPT as a cytoreductive agent prior to its surgical procedure. MPT has been shown to be an effective treatment option in the long-term management of cutaneous open malignant wounds in dogs and cats.

There are no existing guidelines for the contact time or frequency of MPT. In this study, the application time of the Mohs paste on tumor masses was set at one hour. Fixation time in Mohs chemosurgery is reported to last from a few minutes to 24 hours or more (Mohs 1970). Mohs (1989) described ‘the fixation process stopped abruptly after about 18 hours without damaging the tissue just beyond.’ Shigeyama et al. (2005) reported that 5 mm and 10 mm deep tumor tissues were fixed by Mohs paste of a 1-mm thickness after 48 and 72 hours, respectively. CT findings in Case 5 showed that 10 mm depth of the tumor surface was fixed in 24 hours by one hour treatment of the modified Mohs paste. In veterinary medicine, there is the possibility that animals may accidentally ingest the paste, requiring the animals to be monitored under controlled conditions for MPT. The hemostatic effect for active bleeding has also been obtained by contact of the paste for 10 min (Kakimoto et al. 2010). One hour is considered an optimum duration for MPT. In this study, the treatment period and repetition of treatment depended on factors such as the cooperation of the animals’ owners, and tumor characteristics, such as the size and frequency and duration of bleeding. Although the frequency of the MPT was different in each case (4–30 days, with a median of 7 days), once in a week appears to be effective. The limitations of this case series are the low number of cases (seven cases), pilot nature, and lack of randomized controlled trials. Further research is needed to establish the appropriate procedures for MPT in different types of superficial/accessible tumors, such as cutaneous tumors of SCC or non-cutaneous tumors of mammary gland and assorted sarcomas.

Localized pain in the healthy skin surrounding the malignant wounds where Mohs paste was applied was observed in Case 5. In human medicine, pain control in MPT was achieved by the administration of analgesics, the topical use of petroleum jelly to the surrounding healthy skin to protect it from the paste, and a reduction in the contact time of the Mohs paste to the skin (Shigeyama et al. 2005; Kakimoto et al. 2010; Tsukada et al. 2012). With subsequent pain monitoring, prescription analgesics may be used for management and control of ongoing pain at the wound site.

In conclusion, the Mohs paste was found to be effective for the reduction of tumor progression and the amount of exudate associated with malignant wounds. Benefits of MPT include controlling the amount of bleeding at the site of the wounds, reduction in degree of malodor, infection, and closure of malignancy-related wounds. MPT has been shown to be an effective treatment option to palliate the signs and symptoms of malignant skin wounds for veterinary patients in which health contraindications and/or financial difficulties of the animals’ owners exclude other treatment options.

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Disclosure statement

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