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How to Use Bioabsorbable Cisplatin Beads to Treat Cutaneous Neoplasia

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1. Introduction

The skin is the most common site for equine neoplasia.¹ The most common cutaneous equine neoplasias are equine sarcoid, squamous cell carcinoma, melanoma, fibrosarcoma, and cutaneous lymphosarcoma, respectively.¹⁻⁴ A variety of treatments has been used to treat cutaneous neoplasia, including surgical excision, cryotherapy, laser surgery, radiofrequency, hyperthermia, brachytherapy, chemotherapy, and combinations.^{1,5-9} Excisional surgery alone is often unsuccessful because of residual tumor cells remaining at the margins with fronds of neoplastic cells extending into normal tissue.⁷ Adjunctive intralesional chemotherapy is beneficial peri-operatively because incomplete excisions may facilitate accelerated growth of remaining neoplastic cells.⁷

Cisplatin (*cis*-diamminedichloroplatinum) is commonly used as an intralesional chemotherapeutic agent for equine cutaneous tumors and has been found to be effective against a variety of solid tumors.^{5-7,9,10} To minimize the systemic effects and increase exposure of the tumor to the chemotherapeutic drug, intralesional injections and slow release biodegradable polymer delivery systems have been developed.^{5,6,10-13} For injection of cisplatin solution, the drug is mixed with sterile sesame oil and injected in a cross-hatch pattern throughout the tu-

mor site.⁷ Another form of local therapy is the slow release biodegradable polymer delivery systems, which are placed at the tumor site for local diffusion of chemotherapeutic medication. Cisplatin-containing biodegradable beads have been successfully used to treat cutaneous neoplasias in the horse.¹⁴ This paper will describe the procedure to implant cisplatin-containing biodegradable beads.

2. Materials and Methods

The cisplatin-containing biodegradable beads are manufactured commercially and available ready to use for the veterinarian. The beads are made from a commercially available matrix material^a (calcium sulfate and dextran sulfate) to which cisplatin^b is added to a final concentration of 7%. Beads are 3 mm in diameter and contain ~1.6 mg of cisplatin/bead.^c Beads are sterilized by means of gamma irradiation and stored in the dark at room temperature until use.

For use of cisplatin beads, tumors are divided by size to determine the method of treatment. Small accessible masses (<1.5 cm) can be treated in a standing sedated horse, whereas large masses >1.5 cm should be surgically debulked before implantation of the cisplatin beads.

All horses should receive an antibiotic, such as procaine penicillin G (22,000 U/kg [10,000 U/lb], IM,

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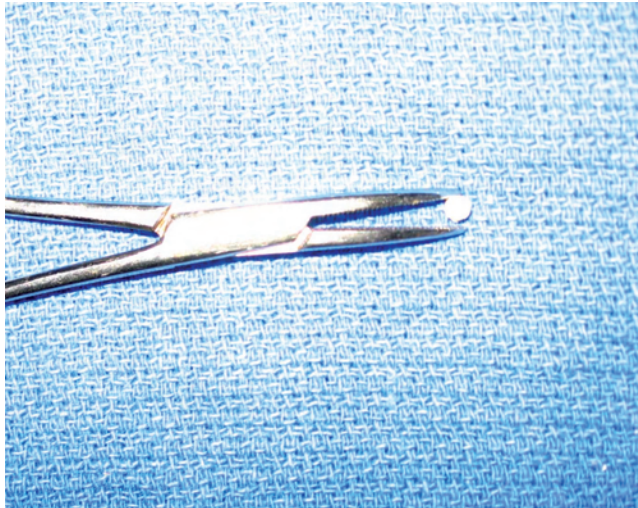


Fig. 1. The cisplatin bead is held at the tips of mosquito forceps for implantation into a stab incision.

once) and phenylbutazone (2 g, IV, once) or flunixin meglumine (1.1 mg/kg [0.5 mg/lb], IV, once), before bead implantation. Anti-inflammatory therapy should continue after implantation for 3 d to minimize swelling. Antibiotic therapy should continue if a large area is treated.

Bead Implantation Alone for Small Masses

1. The horse is restrained and sedated as needed for the procedure.
2. The area around the mass is clipped with a no. 40 blade and aseptically prepared.
3. Mepivacaine hydrochloride is placed subcutaneously to the mass and in the adjacent surrounding tissues.
4. A 1-cm stab incision is created with a no. 15 blade.
5. Mosquito forceps are placed in the stab incision. The jaws are opened to expand the stab incision and ensure that adequate space is available for the bead.
6. Mosquito forceps are used to grasp the cisplatin bead (Fig. 1) and place it into the stab incision to place the bead(s) at the deep margin of the mass.
7. Beads are placed at 1.5-cm intervals if more than one bead is necessary, one at either edge of a 1.5-cm mass.
8. The incision is closed with a cruciate pattern with 2-0 polyglactin 910 suture to hold the bead in place.
9. The suture is absorbable and is not removed.
10. If the small mass is removed and a bead is placed at the site of removal, beads can be placed at 2-cm intervals.

Surgical Debulking

This is used for tumors >1.5 cm in size.

1. The horse is placed under general anesthesia for the procedure.
2. The area around the mass is clipped with a no. 40 blade and aseptically prepared.
3. The mass is resected or debulked with a scalpel or a CO₂ laser.
4. Beads are placed in the closure along the resected margins at 2-cm intervals.
 - a. The cisplatin beads are grasped with mosquito forceps and placed through a stab incision created with a no. 15 blade at the edges of the incision and deep tissue. The incision over the bead is closed with a cruciate pattern with 2-0 polyglactin 910 suture, beneath the subcutaneous suture line.
 - b. If implanted beads would be unstable or free in dead space, they are folded into an absorbable hemostatic sponge^d to secure them into the deeper tissue. The deeper and subcutaneous tissues are apposed with 0 or 2-0 polyglactin 910 sutures.
5. The skin is closed routinely.
6. For very large tumors that cannot be completely resected, debulking the tumor is preferable to treatment with beads alone. As much of the tumor should be removed as possible. (Steps 4 and 5 should be followed to place beads in the surgical wound. If the wound cannot be closed, see step 7a.)
7. For flat tumors or tumors where primary closure would not be possible, vaporization should be performed with a CO₂ laser. The wound should be left open to heal after vaporization, but cisplatin beads should be placed.
 - a. For the open wound, the beads are placed circumferentially along the skin margin at 2-cm intervals, followed by parallel concentric patterns allowing a 2-cm distance between the edges of the beads in the remaining tissue at the tumor site after vaporization. The cisplatin beads are grasped with mosquito forceps and placed through a stab incision created with a no. 15 blade. The incision over each bead was closed with a cruciate pattern with 2-0 polyglactin 910 sutures.

Surgical Tips

1. The beads should be handled with mosquito or kelly forceps to minimize exposure of the surgeon to the cisplatin in the beads.
2. The beads should be grasped gently with the forceps to prevent crushing of the bead. The beads lose strength once they become moist-

ened with blood or fluid and should be handled very carefully.

3. It is important to place mosquito forceps in the stab incision and open the jaws before placement of the bead. This ensures that adequate space is available for the bead and prevents crushing or loss of the bead in an inadequate incision.
4. Neoplasia around the eye should be treated carefully, especially around the dorsal orbital rim. Beads should be placed at 3-cm intervals to minimize complications, such as corneal ulceration.

Aftercare

The area of bead placement and tumor removal should be bandaged if possible. Owners should not clean the wound because cisplatin could be present in the wound drainage. If the wound needs to be cleaned, chemotherapy gloves should be worn. The gloves and material used to clean the wound should be disposed of in a biohazard container.

If non-absorbable sutures are used, they should be removed by a veterinarian wearing gloves to prevent exposure to cisplatin. Absorbable sutures should be left in place to dissolve.

The surgical wound should be monitored for regrowth of the mass, swelling, discharge, character of discharge, erythema, or alopecia. Horses should be re-examined by the veterinarian at 30 d after treatment to determine whether there is regrowth of the tumor or the tumor is unchanged or increased in size. If the tumor is regrowing or still present, implantation of cisplatin beads under sedation and local anesthesia is recommended. The area should be monitored and treated every 30 d until the tumor does not regrow. Squamous cell carcinoma and other refractory tumors, such as fibrosarcoma around the eye, should have three treatments at 30-day intervals for improved results.

3. Results

A retrospective study was performed at the Marion DuPont Scott Equine Medical Center on the use of the cisplatin beads for treatment of cutaneous neoplasias.¹⁴ In this study, 40 of 48 (83%) of horses for which long-term follow-up information was available were relapse-free 2 yr after treatment.¹⁴

Spindle Cell Tumors

Spindle cell tumors in the study were histologically classified as sarcoids, fibromas, fibrosarcomas, fibrosarcomas with myxomatous degeneration, or peripheral nerve sheath tumors. Ninety-one percent (20/22) of horses with 2-yr follow-up after treatment had resolution of the tumor.¹⁴ Three horses with regrowth of the tumor at 1, 2, and 3 yr had successful resolution of the tumor after one additional treatment with cisplatin beads.¹⁴

Squamous Cell Carcinoma

Sixty percent (6/10) of horses with squamous cell carcinomas had resolution of the tumor 2 yr after treatment.¹⁴

Melanoma

Ninety-three percent (13/14) of horses with melanomas had resolution of the tumors.¹⁴ The one treatment failure was a non-pigmented malignant melanoma on a bay horse.¹⁴ All gray horses had complete resolution of the tumor after treatment.

Complications recorded with the use of cisplatin beads were swelling and erythema in the region, drainage from the wound, and subtle scars at the previous tumor site.¹⁴ One horse developed a severe corneal ulcer, which required enucleation, after treatment of a peripheral nerve sheath tumor involving the upper eyelid.¹⁴ Recurrence was more common with squamous cell carcinoma than other tumor types.

4. Discussion

The authors of the paper found the cisplatin beads easy to use, with similar treatment success to cisplatin injections in our hospital. Implantation of cisplatin beads is more convenient and precise than intralesional injection of a cisplatin-sesame oil emulsion in the authors' experience.¹⁴ Additionally, the pattern of bead insertion can be modified as necessary, depending on the size and texture of the tumor being treated. If a large area requires treatment for which injection of a cisplatin-sesame oil emulsion would be impractical, the area can be efficiently treated with cisplatin beads. Most horses received two treatments, which is in contrast with the four treatments recommended with use of the cisplatin-sesame oil emulsion.^{8,14}

Surgical debridement of the tumor is recommended to maximize the effect of the chemotherapy.^{5,7} Cisplatin has been reported to be most effective during the period when tumor burden is low and tumor cell activity is high, which occurs after surgical debulking.^{5,7} Chemotherapy is also recommended after debulking with the CO₂ laser. The CO₂ laser only vaporizes superficial cells because the energy is absorbed by water and should not be relied on to kill tumor cells beyond the visible surface.¹⁵

When using chemotherapy, the veterinarian should be cognizant of the toxicity of the cisplatin. Although there is no radioactive isotope in the cisplatin beads, chemotherapy gloves or two pairs of latex gloves should be worn to limit skin irritation. Materials that contact drainage from wounds treated with the cisplatin beads should be disposed of in biohazard containers. Areas with drainage should be bandaged if possible. The drainage from wounds should be cleaned by the veterinarian wearing double gloves and not by owners.

A very high success rate was found with spindle cell tumors and melanoma, which is similar to treat-

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ment with cisplatin injection. The lower success rate of treatment with squamous cell carcinoma was attributed to treating cases of a longer duration and the likelihood of metastasis of this tumor type. Because of the ease of implantation and lack of reconstitution, cisplatin beads are a favorable alternative to treatment of cutaneous neoplasia for the field practitioner. The potential need for fewer treatments and greater safety for the operator are additional benefits of the cisplatin beads.

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^aMatrix III, US Patent 6391336, Royer Biomedical, Frederick, MD 21703.

^bCisplatin, Sigma, St. Louis, MO 63103.

^cInvestigational New Animal Drug 10–829, Royer Biomedical, Frederick, MD 21703.

^dGelfoam, Pharmacia & Upjohn Company, Kalamazoo, MI 49001.