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CASE REPORT

Companion or pet animals

Multimodal pain management in a dog with oral fibrosarcoma

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Abstract

An 8-year-old lurcher presented at the Pain Clinic of the Queen Mother Hospital following a 7-month history of progressive right-sided facial pain that was poorly responsive to multimodal oral analgesia. Initial investigations had revealed dental changes. Despite appropriate treatment, the patient's clinical signs had deteriorated, resulting in the inability to chew, behavioural changes, and his owner's being unable to administer oral medication, all resulting in progressive weight loss. Computed tomography imaging revealed marked soft tissue thickening of the upper lip, extending along the infraorbital canal and periorbital inflammation. The biopsy confirmed fibrosarcoma. The patient received a multimodal analgesia approach, with systemic analgesia and electroacupuncture performed perioperatively. Neurolysis of the infraorbital nerve was also attempted using an alcohol solution. Following recovery from anaesthesia, the patient showed improved comfort and ate before leaving the hospital. Initial improvement was seen for a number of days at home; however, following this, the owners reported deterioration.

KEYWORDS
anaesthesia, analgesia, neoplasia, oncology, pain

BACKGROUND

A multimodal approach is vital in oncological pain management[1] and can contribute to the patient's quality of life. Due to the presence of nociceptive and neuropathic components, oncological pain is particularly challenging to manage either during chemotherapy or as palliative care.[2] The implementation of palliative care not only upholds patient comfort but also holds promise in prolonging survival durations without compromising patient welfare.[3]

In cases where pain is poorly controlled with oral analgesics, further routes and techniques can be considered. Local anaesthetic techniques can provide analgesia without systemic side effects.[4] When using local anaesthetic drugs, the duration of action is relatively short, unless continuous infusion can be achieved through a catheter. Continuous peripheral nerve block catheters have been used in human medicine for prolonged periods, with reported durations of up to 83 days in the at-home management of phantom limb pain.[5] Use of continuous nerve block catheters can result in various complications, including dislodgement of the catheter, accumulative toxicity and infection,[6] with risk of infection correlating with duration of infusion.[7] Chemical neurolysis, commonly performed with a phenol solution, provides much longer lasting effects through destruction of nerve fibres[7] and is frequently used in management of severe pain in human cancer patients.[8] Phenol (carbolic acid) causes denaturing of proteins when delivered locally.[9] This provides a prolonged but impermanent block of nerve conduction.[2]

Electroacupuncture is another alternative to oral medication that can be utilised in the management of various types of pain.[10] Electroacupuncture involves the passage of pulsed electrical current through the body tissues via one or more pairs of acupuncture needles. It is often considered to give a greater analgesic effect than traditional acupuncture methods, resulting in release of endogenous opioids and other neuropeptides.[10]

This case report describes a multimodal analgesia approach, including electroacupuncture, regional anaesthesia and neurolysis, to manage refractory pain associated with oral fibrosarcoma in a dog. This case highlights the role anaesthetists can play within a multidisciplinary team in treating chronic painful conditions. As referral pain clinics increase in number in the veterinary field, the availability of advanced multimodal treatment protocols for managing complex cases such as this increases.

CASE PRESENTATION

An 8-year-old, male, neutered lurcher was admitted at the Pain Clinic of the Queen Mother Hospital for Animals for further investigation following a 7-month history of progressive oral pain.

The patient had initially shown signs of discomfort in January 2022. The discomfort was particularly associated with eating. Initial investigation at the primary care practice had revealed periapical abscessation of the right maxillary

second and third premolar teeth, with osteolysis of the maxillary and alveolar bone extending along the right infraorbital canal. This was assumed to be related to the dental disease, and extractions of these teeth were performed. The patient was also treated with a course of antibiotic therapy (clindamycin). Cytology of the area was submitted and found to be consistent with lymphoplasmacytic inflammation. Following the procedure, the patient showed no improvement in comfort, and was trialed on several analgesic agents over the following 4 months. This included non-steroidal anti-inflammatory drugs, gabapentin, amantadine and a paracetamol and codeine combination, none of which provided adequate pain relief. The patient began to develop clear distortion of the right side of the muzzle, atrophy of the temporalis muscle and ocular changes. It became unable to eat at home, and was unable to vocalise. Additionally, it began showing aggressive behaviour towards its owner in anticipation of contact around its face. The patient was thus referred to the Pain Clinic for further investigation and management.

On presentation, the patient was dull and quiet. It was sedated intramuscularly, with its owners present, before a full exam was performed due to increasing aggression at its primary care practice on examination. Examination under sedation revealed marked thickening of its right upper lip, marked atrophy of the right temporalis muscle and rostral and dorsal displacement of the right globe. Some discoloration was noted on the right side of the hard palate. There was right mandibular lymphadenopathy. The rest of the physical examination was otherwise normal.

INVESTIGATIONS

The patient was sedated intramuscularly with methadone (0.2 mg/kg; Synthadon, Animalcare) and medetomidine (0.01 mg/kg; Medetor, Virbac). Following this, an intravenous cannula was placed, and general anaesthesia was induced with propofol to effect (PropoFlo, Zoetis; 2.8 mg/kg). The patient was intubated and maintained on sevoflurane vaporised in oxygen.

Computed tomography (CT) imaging with contrast was performed of the head and thorax, and tissue biopsies were taken from the lip and oral cavity. Figure 1 shows a CT rendering of the patient's facial distortion, with tumour tissue indicated in blue. Figure 2 demonstrates the infraorbital foramen utilised in placement of the infraorbital nerve block in this patient.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for the patient's presenting complaint included progressive dental disease, inflammation and neoplasia.

TREATMENT

Following CT imaging, acupuncture was performed using the Governing Vessel 17, Yintag and Taiyang acupuncture points. Trigger points in the left and right temporalis muscles and epaxial muscles of the cranial cervical muscles, and along the left infraorbital canal were used to avoid needling the affected area. Electroacupuncture was applied to four pairs of needles, starting stimulation at 0.2 mA. This was increased at 2-minute intervals by 0.1 mAs, with a gradual increase to 1 mA over a 30-minute period.

During manipulation for surgical biopsy, the patient became reactive under anaesthesia, and thus a further 0.1 mg/kg methadone was administered. This showed limited improvement with the patient remaining reactive despite increased inhalant anaesthetic (end tidal sevoflurane 2.5%). A bolus of ketamine (0.5 mg/kg) was administered, which gave a reduction in nociception. In the period following completion of the electroacupuncture, during biopsy of the second site, the patient received medetomidine (0.001 mg/kg) that had only a moderate effect.

An infraorbital neurolytic nerve block was performed using an epidural catheter inserted into the infraorbital foramen. An epidural catheter was used to provide a viral filter for the injectate and increase the catheter rigidity. Palpation of the infraorbital foramen apical to the third maxillary premolar was used to identify the site for the infraorbital block.[11] The needle was advanced rostro-caudally a short distance into the infraorbital canal before drug administration. An ethanol/methanol solution (BP surgical alcohol, Covetrus)

LEARNING POINTS/TAKE-HOME MESSAGES

- A multimodal pain relief plan gives the best chance of managing both acute and chronic pain.
- Neurolysis can be an alternative for pain management in palliative care cases of localised poorly controlled pain.
- Electroacupuncture can be used as an adjuvant analgesic treatment.
- Neuritis-associated pain can provide a particular challenge to management.

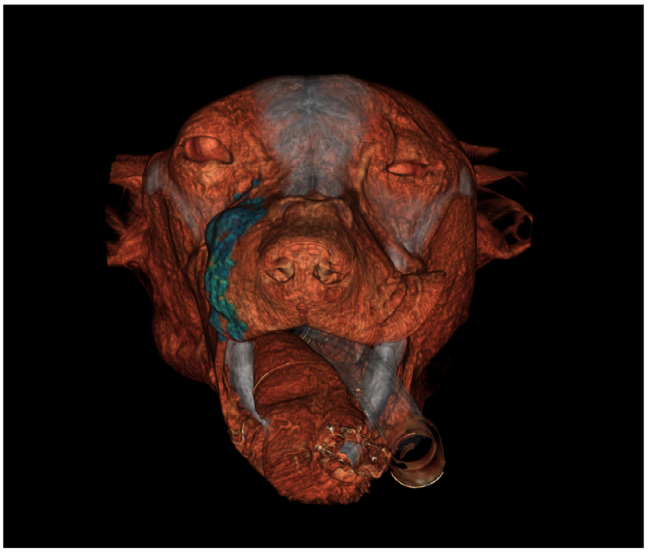

FIGURE 1 Computed tomography rendering of the patient's face, with abnormal tissue highlighted in blue.

FIGURE 2 Computed tomography image of the dorsal plane of the skull. The yellow star and red colouring marks the lesion on the right side of the skull. The green arrow highlights the opening of the infraorbital canal, utilised in the infraorbital nerve block performed in this patient.

was administered after filtration through a 0.2 μm filter, alongside 0.5 mL of bupivacaine (Marcain Polyamp Steripack 0.5% solution, AstraZeneca).

OUTCOME AND FOLLOW-UP

CT imaging revealed right maxillary bone lysis with marked soft tissue thickening of the upper lip and abnormal tissue within the infraorbital canal, and enhancement and swelling of the right orbital tissues. This was suggestive of osteomyelitis of the right maxillary bone, and severe myositis/cellulitis of the orbital tissues. The proximity of the infraorbital canal changes to the infraorbital nerve identified a risk of neuritis. There was also marked right temporal and digastricus muscle atrophy. Tissue biopsies from the lip and oral cavity revealed fibrosarcoma alongside lymphocytes and plasma cells.

On recovery from anaesthetic, the patient was bright and vocal. It ate soft food before leaving the hospital and showed no reaction to gentle contact with the affected side of its face. Pain scoring was not performed due to the patient's temperament. The patient was discharged, and its owners were advised to continue the previously prescribed oral medication and monitor the results.

Following discharge, the patient's owners reported an improvement in clinical signs lasting 5 days. Unfortunately, following this, the patient appeared to deteriorate again. Discussion with the Oncology and Surgery services showed limited options for its treatment, and due to its marked discomfort and lack of surgical option, its owners opted to trial oral prednisolone therapy following a wash out from the non-steroidal anti-inflammatory drugs to see if this provided relief. Due to the patient's stress in the veterinary environment, electroacupuncture was not repeated in this case as heavy sedation and/or general anaesthesia would be required to perform this procedure.

Sadly, the patient showed limited improvement on oral prednisolone, and its owners opted for euthanasia due to its continued discomfort 2 weeks following treatment.

DISCUSSION

This case report describes a multimodal analgesic approach, including use of systemic analgesics, neurolysis and electroacupuncture, to manage severe refractory pain due to fibrosarcoma and secondary inflammation in a dog. This patient's multifactorial oncological pain presented a challenge in pain management. Multiple analgesic drugs and techniques resulted in a significant but short clinical improvement. Identification of the contribution of each technique to this overall result is difficult.

The patient was administered a variety of systemic analgesics during its procedure. It is possible that the use of an *N*-methyl-D-aspartate (NMDA) receptor antagonist such as ketamine could be associated with prolonged analgesia due to management of wind-up pain and hyperalgesia in this patient.[12] Lasting analgesic effects have been reported in humans following prolonged or repeated ketamine infusions[13–15] and even following a single postoperative dose[16]; however, evidence of similar effects in companion animals is lacking. The reported elimination half-life of ketamine is approximately 60 minutes in dogs.[17] While a longer duration of effect has been suggested in dogs with prenociceptive administration,[18] this is not applicable in a case of chronic pain such as the patient in question. Additionally, the patient showed a poor response to long-term use of amantadine, another NMDA-receptor antagonist, and although the mechanism of action varies slightly between amantadine and ketamine,[19] the overall action is similar. Other analgesics administered to this patient perioperatively (alpha-2 adrenergic receptor agonists and opioids) would not be expected to persist, with a terminal half-life of 2–4 hours and a half-life of up to 1.6 hours, respectively.[20,21] This suggests that administration of systemic analgesic drugs was unlikely to be the cause of prolonged comfort as seen in this patient.

The successful placement of the infraorbital block was supported by the palpation of anatomical landmarks to guide needle placement and the increased patient comfort postoperatively. As both the neurolytic solution and the local anaesthetic were administered through the same needle, placed by an experienced anaesthetist, and a significant improvement in comfort was seen immediately postoperatively, error in administration is unlikely to be the cause of the shorter duration of comfort in this patient. Involvement of the maxillary nerve in this block cannot fully be excluded in the absence of repeat imaging using contrast; however, this was considered unlikely with the landmarks utilised. The short-lasting benefits in this case could be attributed to multiple causes. The trigeminal nerve compression identified on CT imaging could be an additional source of nerve pain, which would not have been alleviated by the infraorbital neurolysis and thus would have contributed to the ongoing

discomfort. The marked anatomical distortion present in this patient could have resulted in reduced contact between the nerve and the injectate, and reduction of the analgesic effect.

Additionally, sourcing phenol for neurolysis in this case was not possible. For this reason, surgical spirit (ethanol/methanol solution) was used (BP surgical alcohol, Covetrus). The efficacy of this has not been determined in the veterinary literature, and thus the effectiveness of this treatment may be limited. Phenol has been shown to cause considerable nerve fibre destruction in even weak solutions (1%)[22] in previous studies; however, limited reports exist on alternative neurolytic solutions. A retrospective comparison of alcohol and phenol solutions for neurolysis in humans found no significant difference in pain scores 1 month following the procedure with either solution.[8] To the authors' knowledge, use of surgical spirit as a neurolytic agent has not been described previously. An alternative treatment could have been placement of a continuous peripheral nerve block catheter for repeated administration of local anaesthetic.[5] However, while this could have provided consistent results, this was not considered suitable in this patient due to its temperament and the potential complications of dislodgement, infection and local anaesthetic agent toxicity.[6]

Electroacupuncture was utilised in this patient as an adjuvant analgesic technique. Electroacupuncture has been shown to increase the concentrations of endogenous opioids in the tissue and cerebrospinal fluid,[10] with plasma beta-endorphin levels shown to be increased at 1 and 3 hours after surgery in dogs treated with electroacupuncture perioperatively.[23] Electroacupuncture has been suggested to have a minimum alveolar concentration and drug-sparing effect during anaesthesia and surgical procedures,[10,23] making it a potentially beneficial addition in this case. The duration of analgesic effect is hard to predict, with a study[23] suggesting improved analgesia for 24 hours following perioperative electroacupuncture in dogs. When utilised for management of trigeminal mediated headshaking in horses, a single treatment gave a mean remission time of 5.5 days (range 0–13 days), with much greater effects with repeated treatments.[24] Trigeminal nerve-mediated headshaking is suspected to result from trigeminal neuropathic pain, which means these findings may be similar in the patient in question. Due to the large variation in duration of action seen both within and between species in the literature, predicting the duration of effect of electroacupuncture in this patient is difficult. While a course of electroacupuncture may have provided optimal effects in this patient, it was not recommended because of its demeanour, as it would need to be sedated for each session. Electroacupuncture was used as an adjuvant analgesic technique intraoperatively during manipulation and biopsy of the affected area; however, the main aim of electroacupuncture in this patient was to address the chronic pain during the postoperative period through desensitisation of peripheral sensory nerves and antihyperalgesia.[25] The intraoperative effects of electroacupuncture in this patient may have been limited, due to the requirement for additional analgesia while performing biopsies.

In human medicine, refractory pain is defined as pain that does not respond to 'standard' treatments, and is suggested to occur in 10%–30% of cancer patients.[26] 'Standard' treatments include the use of strong opioids in human cancer patients,[27] with techniques such as neurolysis being employed when standard treatments fail.[26] The use of strong opioids in dogs is limited by both the pharmacokinetics of administering these drugs orally in dogs and the legal controls around storage and use of controlled drugs within the United Kingdom,[28] thus other treatments must be considered as alternatives. In companion animal palliative care, maintaining the patient's quality of life must remain the priority, and is often the main concern of owners of these patients.[4] Prolonged hospitalisation for palliative care offers a poor quality of life for these patients, and thus alternative treatments to provide analgesia without requiring hospitalisation are optimal. Neurodestructive procedures, most commonly using phenol or other neurolytic chemicals, are commonly used in human cancer patients to provide palliative relief,[26] but similar reports in companion animal species are limited.

While multiple analgesics were administered during the patient's anaesthetic, effects lasting multiple days would not be expected, and the effects of both electroacupuncture and the neurolysis likely contributed to this temporary improvement. As the availability of referral pain clinics increases within the United Kingdom, complex multimodal protocols will become more available in companion animal veterinary care. Continuing to seek novel and effective interventional treatments to manage refractory pain in our companion animal patients may bring significant changes in the life expectancy and quality of life in these animals.

AUTHOR CONTRIBUTIONS

Lydia Hjalmarsson, Thaleia-Rengina Stathopoulou and Cristina Bianchi were involved in the clinical case management and manuscript writing and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

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ETHICS STATEMENT

The case presented shows management of a client-owned dog. No specific ethical approval was required as this is a case report containing no research data. The clients gave consent for publication of this case report.

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MULTIPLE-CHOICE QUESTION

Which of the following options is a common difficulty in the management of long-term peripheral nerve catheters in dogs?

POSSIBLE ANSWERS TO MULTIPLE-CHOICE QUESTION

A. Opioid-induced hyperalgesia
B. Catheter dislodgement
C. Catheter-induced thrombosis
D. Rapid catheter degradation
E. Anaphylactic reactions

CORRECT ANSWER

B. Catheter dislodgement

Maintaining a long-term peripheral nerve catheter in a canine patient is often limited by patient tolerance and interference, implying prolonged usage can be difficult.