

# Persistent socket pain in a dog after the enucleation of the eye and its clinical management

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## Abstract

Persistent socket pain is a condition described in humans after enucleation of the eye. This report aims at describing this condition in dogs.

A 10-year-old male-neutered crossbreed was presented to the referral veterinary surgeon for enucleation of the right ocular globe. Anaesthesia and surgery were uneventful although during the postoperative period the dog was reluctant to open the mouth and to be explored by the referral veterinary surgeon. Despite treatment with meloxicam, paracetamol and tramadol, no improvements were observed.

Ten weeks after surgery, the dog was referred to the Dick White referrals for further investigations. Ophthalmic examination was normal, though palpation of the wound triggered an avoidance response. Magnetic resonance imaging showed changes compatible with orbital cellulitis.

The area of interest was evaluated with the use of the mechanical Von Frey filaments. A response, characterised by sudden turning of the head and attempts to withdraw it, was evoked with filament 4.93 (8.0 g) during stimulation of the periorbital area.

After induction of anaesthesia, an ultrasound-guided injection containing levobupivacaine 0.5% and methylprednisolone was performed within the retrobulbar area.

Three hours after recovery from anaesthesia, no discomfort was observed during palpation of the area. Re-evaluation was performed with the Von Frey filaments; no response could be evoked during testing with all 20 filaments (from 2.36 to 6.65) applied on either side of the face.

The patient was discharged with a course of gabapentin and, 3 weeks after the intervention, the dog showed no clinical signs of pain.

Persistent socket pain is an unpleasant sensation at the level of the enucleated orbit, and it should be regarded as a challenging condition to diagnose and treat. The MRI findings appeared to be essential to select the most appropriate interventional treatment. The injection of local anaesthetic and steroid into the retrobulbar space was

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useful for both confirming the diagnosis and treating pain by reducing the peripheral signalling and decreasing the residual inflammation.

**KEYWORDS**

analgesia, dog, eye, persistent socket pain (PSP)

## 1 | INTRODUCTION

Ocular pain has become a topic of interest in both humans and animals with the continuous development of various analgesic techniques (Otero & Portela, 2019).

Patients with ocular pain are usually referred to the ophthalmologist for the investigation and treatment. In the event of a recent injury, infection or inflammation, the treatment of the underlying cause may improve symptoms leading to a resolution of the pain. With more complicated history and/or symptoms compatible with chronic or maladaptive pain, diagnosis and treatment may become challenging (Jacobs, 2017). Maladaptive ocular pain is difficult to assess due to lack of agreement upon the diagnostic criteria and variety of symptoms (Hogeboom et al., 2018). To date, the diagnosis of maladaptive eye pain is largely based on clinical findings and, in human patients, supported by specific clinical investigations such as the use of quantitative sensory testing (Rosenblatt, 2016). Regarding treatment, in human medicine persistent periorbital pain postenucleation is usually treated with local infiltration of corticoids and local anaesthetics (Asensio et al., 2003; Jacobs, 2017).

To the authors' knowledge, assessment and treatment options for ocular pain refractory to medical treatment have been poorly described in veterinary medicine. This case report aims describing this condition in veterinary patients and at encouraging research in this field.

## 2 | CASE DESCRIPTION

A 10-year-old male neutered Corgi cross, weighing 9.3 kg and with a body condition score of 6/9, was presented for therapeutic enucleation of the right ocular globe due to a painful corneal ulceration unresponsive to medical treatment. The dog's past medical history was incomplete due to a change in ownership, but included blindness following an unspecified ocular trauma. The surgical procedure was performed by the referring veterinary surgeon. Anaesthesia and surgery were described as uneventful, and the dog was discharged with a 5-day course of meloxicam (Metacam 1.5 mg/mL oral suspension; Boehringer Ingelheim, UK). In the immediate postoperative period, the dog showed reduced appetite, decreased willingness to interact with the owner and intermittent yelping while attempting to eat. During postoperative assessment performed by the veterinary surgeon 7 days after surgery, although the wound appeared healed without any obvious complication, the dog displayed avoidance behaviours

(reluctance and head withdrawal) on attempts to examine the surgical site.

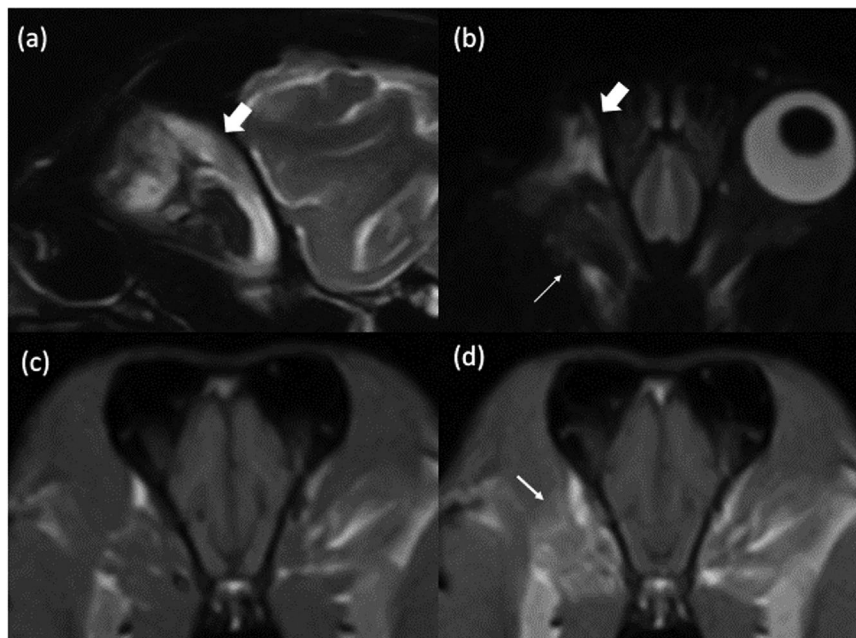
Oral paracetamol (Pardale, Dechra, UK) (125 mg, BID) and tramadol (Tralieve, Dechra, UK) (50 mg, BID) were added to the meloxicam for the following 3 weeks without any clinical improvement. A course of clindamycin hydrochloride (Antirobe, Zoetis, UK) (75 mg BID) was also initiated. Four weeks after surgery, no major improvements were observed. Both tramadol and meloxicam were discontinued due to mild gastrointestinal signs and were replaced with oral gabapentin (Gabapentin, Weldricks Pharmacy, UK) (100 mg BID). By 6 weeks after surgery, the avoidance behaviours were mostly resolved, but the dog remained reluctant to open the mouth fully when eating.

Full haematology and biochemistry panels, radiographic exam of the head and ultrasonographic exam of both the former retrobulbar region and the temporomandibular joints (conducted under general anaesthesia) did not reveal an underlying cause.

The dog was referred 10 weeks after surgery for further investigations. The ophthalmic examination did not reveal abnormalities in the left eye, and the right enucleation wound appeared well healed. Palpation of the area generated avoidance response as previously described. No obvious lesions were observed on the examination of the mouth. Magnetic resonance imaging of the head under general anaesthesia was performed on the following day. The dog was assigned an American Society of Anesthesiologists risk classification of 2. Methadone (Comfortan, Dechra, UK) (0.2 mg/kg) and dexmedetomidine (Dexdomitor, Orion, UK) (0.002 mg/kg) were administered intravenously (IV) through a preplaced cannula in the right cephalic vein. After preoxygenation using a flow-by technique, anaesthesia was induced with IV propofol (PropoFlo Plus, Zoetis, UK) (3 mg/kg). The trachea was intubated with a 5.5 mm internal diameter cuffed endotracheal tube. Anaesthesia was maintained with isoflurane (Isoflurane-Vet, Merial, UK) vapourised in 100% oxygen and delivered using a circle breathing system. Hartmann's solution (Aqupharm, Animalcare Ltd, UK) was started at 5 mL/kg/h. A multiparametric module (S5, Datex Omheda, UK) which consisted of capnography, gas analyser and oscillometric blood pressure and an oesophageal stethoscope were used to monitor the physiological parameters.

The anaesthetic procedure and patient recovery were uncomplicated. Magnetic resonance imaging of the head was performed using a 0.4 Tesla low field scanner (Hitachi Aperto Lucente, Berkshire, UK) and the following sequences were performed: sagittal T2-weight (T2W); dorsal Short Tau Inversion Recovery (STIR) dorsal; and transverse T2W, fluid-attenuated inversion recovery (FLAIR), T2 gradient echo (T2\*), T1-weighted (T1W) pre- and postadministration of 0.1 mmol/kg

**FIGURE 1** Sequences of the MRI of the head of a dog with suspected cellulitis and persistent postenucleation eye socket pain (a) STIR DOR MRI sequence; (b) T1 TRA subtraction MRI sequence; (c) T2 sagittal MRI sequence; (d) T1W transverse postcontrast of the retrobulbar space. There is a T2 and STIR hyperintensity encircling the residual right orbital cone (thick arrow) and mild irregular thickening, STIR hyperintensity and contrast enhancement of the residual right extraocular muscles (thin arrow).



gadobutrol. A moderate, relatively well defined, heterogeneous T2 and STIR hyperintensity was identified in the right orbit, encircling the residual part of the right orbital cone and extending along the medial orbital wall. Mild irregular thickening, STIR hyperintensity and contrast enhancement of the remaining right extraocular muscles were also appreciated. These changes were compatible with orbital cellulitis (Figure 1A–D).

It was decided to perform an ultrasound (US)-guided injection of 0.5 mg/kg of levobupivacaine 0.5% (Chirocaine, Abbvie, UK) and 0.5 mg/kg of methylprednisolone (Depomedrol, Pfizer, UK) into the former retrobulbar space. The procedure was scheduled for the following day, under general anaesthesia. Prior to premedication and after 10 min of acclimatisation in the room, the area of interest was evaluated in the conscious dog with the use of the mechanical Von Frey filaments (Von Frey filaments, Bioseb, France).

A series of 20 filaments, from filament 1.65 (0.008 g) to filament 6.65 (300 g), were subsequently applied with a 30-s interval elapsing between applications. The filaments were applied perpendicular to the skin until either the filament bent or an avoidance behavioural response (turning the head to the opposite site, attempting to escape, or aggression) was observed. On each side, the filaments were applied in the periorbital, periauricular and perioral regions. The left side was tested first and produced no response to any filament. On the right side an avoidance response, characterised by sudden turning of the head and attempts to withdraw it, was evoked with filament 4.93 (8.0 g) during the stimulation of the periorbital area. The measurements were repeated 5 min later, and a similar reaction was observed. After completion of sensory testing, 0.2 mg/kg of butorphanol (Torbugesic, Zoetis, UK) and 0.001 mg/kg of dexmedetomidine (Dexdomitor, Orion, UK) were given IV as premedication. Anaesthesia was induced with 3 mg/kg of IV propofol (PropoFlo Plus, Zoetis, UK) and maintained with

sevoflurane (Sevotek, Animalcare, UK) vapourised in oxygen, delivered with a circle breathing system connected with a 5.5 mm internal diameter cuffed endotracheal tube. The region of interest was scanned with a linear US transducer (6–18 MHz; Esaote Netherlands), positioned so that the US beam was parallel to the former medial and lateral canthus of the eye. The needle was then inserted percutaneously, with an out-of-plane technique, immediately below the anterior border of the frontal bone. Thereafter, the needle was tilted by 45° and advanced into the former orbital cavity until it reached the former intraconal space (Otero & Portela, 2019). The area next to the retrobulbar vascular plexus was considered to be the main injection point as it was the main anatomical landmark after the enucleation of the eye globe and nerve structures, such as oculomotor and ophthalmic nerve, were not possible to be identified with the US. After a negative aspiration test, the solution was injected over 1 min.

During the injection, the dog developed bradycardia (HR: 40) followed by second-degree AV blocks, which was treated with 0.01 mg/kg of IV glycopyrrolate (Glycopyrronium Bromide, Martindale Pharmaceuticals, UK). Heart rate increased to 90 bpm, and the rhythm normalised within 5 min of glycopyrrolate administration. The dog was allowed to recover from anaesthesia and was offered some food as soon as he was fully conscious, approximately 1 h after the end of the anaesthetic. The dog immediately showed good appetite, and no discomfort was observed during palpation of the area. Reassessment with the Von Frey filaments was performed 3 h after recovery, as previously described; no response was evoked on either side of the face during testing.

The patient was discharged with a course of oral gabapentin (100 mg BID) until further assessment. Telephone updates with the owner, 1 and 3 weeks after the interventional treatment, revealed that appetite, eating behaviour and level of activity of the dog had remarkably improved.

The dog was reportedly able to open and close the mouth with no obvious clinical signs of pain and had returned to play as was normal prior to his medical problems.

### 3 | DISCUSSION

To the authors' knowledge, this is the first report of persistent socket pain (PSP) and its treatment after enucleation in a dog.

PSP is defined as an unpleasant sensation at the level of the enucleated orbit (Hogeboom et al., 2018). It appears to have a great impact on human patients' life with an overall incidence of 0.7% (Rasmussen et al., 2011; Shams et al., 2015). It may be considered a specific type of persistent postoperative pain as it matches the following criteria: (1) it develops after surgery, (2) pain lasts at least 3–6 months, (3) other causes of pain can be excluded, (4) pain of neuropathic origin, (5) pain occurs spontaneously in the absence of clear nociceptor activation (Galor et al., 2015; Richebe et al. 2018). Another similar emerging phenomenon in human medicine is the 'phantom eye syndrome'. Phantom eye syndrome is classified as either painless or painful sensations referred to the amputated eye and associated with phantom vision (Andreotti et al., 2014). While the lack of verbal feedback makes it impossible to evaluate if visual hallucinations are experienced, the occurrence of this syndrome in animals cannot be completely ruled out.

There is no unique technique for diagnosing PSP in human medicine, as Hogeboom et al. (2018) emphasise in their systematic review. Indeed, different authors utilised diverse diagnostic methods and approaches such as clinical examination, questionnaire, use of advanced diagnostic imaging, histology, cultures or retrobulbar injection of methylprednisolone and local anaesthetic.

The anophtalmic cavity is anatomically and physiologically dysfunctional, and pain that originates from there may be the consequence of various conditions, including dry socket, compression of the trigeminal nerve, inflammation, infection, neuromas or surgery-related complications (Andreotti et al., 2014; Hogeboom et al., 2018).

In the case reported here, the unresponsiveness to analgesic drugs such as meloxicam, tramadol and paracetamol, together with the improvement observed with the use of gabapentin, as well as the lower mechanical thresholds in the right periocular area compared to left side of the face, may suggest that the pain experienced by the dog had a maladaptive component. Currently, there is already a body of scientific literature describing the clinical use of mechanical thresholds and quantitative sensory testing (QST) in veterinary medicine (Adami & Spadavecchia, 2020; Manchin et al., 2020). In the case presented here, the application of mechanical thresholds appeared to be useful to evaluate the subject's response to the trials with different systemic medications or interventional procedures. Ideally, pain assessment with the assessment with QST should have been performed prior to the use of gabapentin and any other analgesic drugs to minimise the bias represented by potential confounding factors.

The use of MRI appeared to be an essential part of the investigation. Indeed, even if it is not always possible to strictly rule out the

presence of active infectious process, it may help to identify other possible causes of PSP (Shams et al., 2015). In the case described in this report, MRI findings were more consistent with inflammatory causes rather than infection and this rationale guided your clinical decisions. This was considered of crucial importance because, in the event of an infectious process, the interventional retrobulbar injection would have been contraindicated, and histology and culture of the area of interest would have been performed (Shams et al., 2015).

We opted to intervene for the diagnosis and treatment with an injection of local anaesthetic and steroid into the retrobulbar space with the aim of reducing the peripheral signalling and to decrease the residual inflammation. Interventional treatments for PSP or phantom eye pain syndrome have been reported in the literature (Asensio et al., 2003; Jaichandran & Bhaskar, 2017). The immediate clinical improvement after the block showed that the peripheral component of nociceptive pathways still played a key role in the manifestation of pain. When ongoing peripheral processes are believed to contribute to the pain syndrome, reducing the signal from the altered peripheral receptors is essential to reduce the risk of central sensitisation as well as the development or worsening of maladaptive pain. The electrical hyperexcitability of peripheral sensory neurons observed during inflammatory states is primarily due to an upregulation of the Na<sup>+</sup> channels in the damaged nerve endings (Devor, 2006). Once the ascending signalling from the altered peripheral nociceptors transmitted by branches of the trigeminal nerve is decreased through blockade of sodium channels, also the central sensitisation caused by over-signalling to the trigeminal nucleus, which is similar to the dorsal horn of the spinal cord, will most likely be reduced (Rosenthal et al., 2016). This would explain the immediate clinical improvement noticed after having performed the block, which lasted beyond the duration of action of the local anaesthetic.

Levobupivacaine was the local anaesthetic of choice in this case for its favourable pharmacological profile, long duration of action, and decreased toxicity (Taylor & McLeod, 2020). Corticosteroid injections are commonly used to manage many chronic pain conditions; however, whether the steroids have any direct effect on pain generation and transmission is not clear (Shanthanna et al., 2016). The injection of steroids may have helped in this case by decreasing the degree of inflammation of the peripheral nerve ending which, in turn, could have resulted in decreased signalling in the long term.

This case highlights that satisfactory pain management may not be achievable with the use of standard pharmacological therapy in cases where the presence of a maladaptive pain is suspected. The collaboration between different specialists and the compliance of the owner were essential aspects of the successful management of the case presented here. The owner needs to be made aware that treatment of maladaptive pain can potentially be long, frustrating, and expensive and that the use of interventional techniques is not necessarily supported by substantial body of scientific literature. In this perspective, open and direct communication with the animal's owner, as well as frequent consultation appointments scheduled at regular intervals, seem to be of primary importance for a successful management of complicated cases (Jacobs, 2017).

## AUTHOR CONTRIBUTIONS

Andrea Gomez Molins: writing – original draft preparation. Paolo Monticelli: conceptualisation – writing, review and editing. Hannah Shing: writing, review and editing. Chiara Adami: writing, review and editing.

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The author declares no conflict of interest

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## 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. No ethical approval was required as this is a case report with no original research data.

## DATA AVAILABILITY STATEMENT

No.

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## PEER REVIEW

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