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Case Report

SURGICAL MANAGEMENT OF EXTRAMEDULLARY PLASMACYTOMA (EMP) IN THE EAR CANAL OF A DOG

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SUMMARY

Extramedullary plasmacytomas (EMPs) have been commonly reported to occur at solitary sites involving the skin of the digits, lips, and ears. An 8-year-old castrated local dog was presented for a mass obstructing the right ear canal. On physical examination, an ulcerated, pink, firm mass at the base of the pinna with active bleeding was observed. Radiography and computed tomography revealed stenosis of the right horizontal ear canal and soft tissue attenuation of the external auditory canal with thickening of the tympanic membrane respectively. Total ear canal ablation with lateral bulla osteotomy was performed. Histopathological examination confirmed the mass to be a plasmacytoma. The dog had an uneventful recovery.

Keywords: canine, ear, immunohistochemistry, plasmacytoma, TECA-LBO

INTRODUCTION

Ear canal tumours are uncommon, accounting for merely 1.5% to 6.0% of all canine tumours (Goldschmidt and Shofer, 1992; Morris and Dobson, 2001; Boostrom et al., 2017). Extramedullary plasmacytomas (EMPs) may arise from the skin or other soft tissues (Wellman and Kisseberth, 2020). Cutaneous EMPs have been identified in canine and feline mostly affecting middle-aged to elderly animals with an average age of 9 to 10 years (Rakich et al., 1989; Morris and Dobson, 2001; Gross et al., 2005; Henrich, 2016). However, their aetiology is unknown (Gross et al., 2005; Wellman and Kisseberth, 2020). Commonly reported cutaneous regions are the skin of the head (including ears) and limbs (Baer et al., 1989; Morris and Dobson, 2001; Quiroz-Rocha et al., 2017; Ehrensing and Craig, 2018). Predisposed breeds in literature include Cocker Spaniel, Terriers (West Highland White, Airedale, Kerry Blue, Scottish, Yorkshire), Poodle, Boxer, and German Shepherd (Rakich et al., 1989; Goldschmidt and Shofer, 1992; Stilwell and Rissi, 2018) with few studies reporting a male predominance (Platz et al.,1999; Cangul et al., 2002). A female predominance was reported by Mikiewicz et al., (2016) whereas Lucke (1987) and Miller et al., (2013) reported no sex predilection at all. Cutaneous EMPs are typically benign in canines cured by surgical excision (Rakich et al., 1989; Clark et al., 1992; Fukumoto et al., 2012; McHale et al., 2018). This case report describes the clinical manifestation, diagnostic imaging findings, treatment, histopathology, immunohistochemistry, and prognosis of a dog with cutaneous EMP.

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CASE REPORT

An 8-year-old, 18-kg castrated local dog was referred to the University Veterinary Hospital, Faculty of Veterinary Medicine, Universiti Putra Malaysia for the evaluation of a mass that was completely obstructing the right ear canal. The mass, progressively increasing in size, was noticed by the owner 2 months prior to the presentation. The dog was bright, alert, showed moderate pruritus, head shaking and responsive with a body condition score of 2/5. The general physical and neurological examination was unremarkable. Aural examination revealed an ulcerated, pink, firm mass at the base of the right ear pinna, obstructing the ear canal. The mass was approximately 3cm x 2cm with active bleeding (Figure 1). The left ear and bilateral regional lymph nodes were apparently normal. The differential diagnosis for the aural mass included inflammatory polyp, squamous cell carcinoma, adnexal neoplasm, plasmacytoma, mast cell tumour as well as basal cell tumour.

Figure 1. Gross physical examination findings: ulcerated, pink, firm mass at the base of the right pinna.

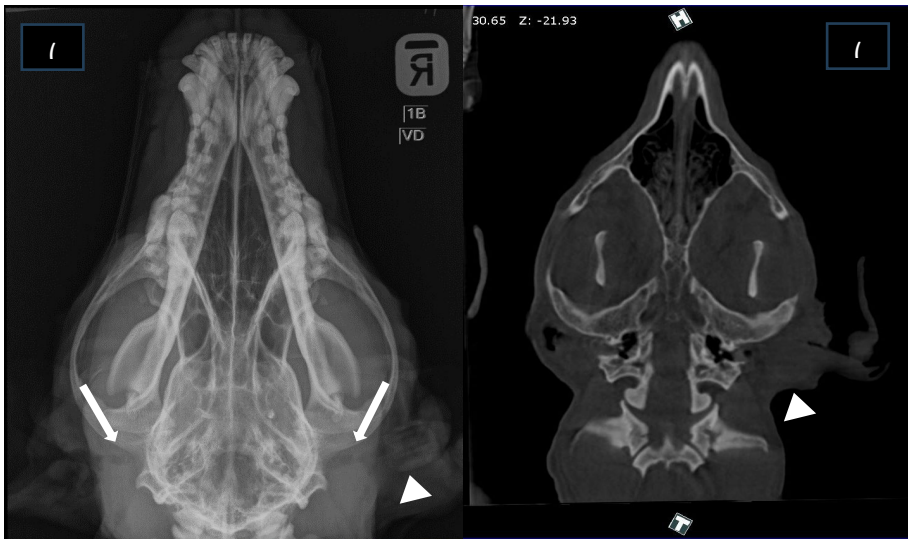

Figure 2. Diagnostic imaging findings: (a) Ventrodorsally radiographic view of the skull. Narrowing of bilateral ear canals (arrows). Increased soft tissue opacity indicating the presence of a mass involving the right ear canal (arrowhead). (b) Cross-sectional computed tomography image of the head. Arrowhead indicates presence of a dense mass measuring 3.1cm x 2.2cm x 2.6cm.

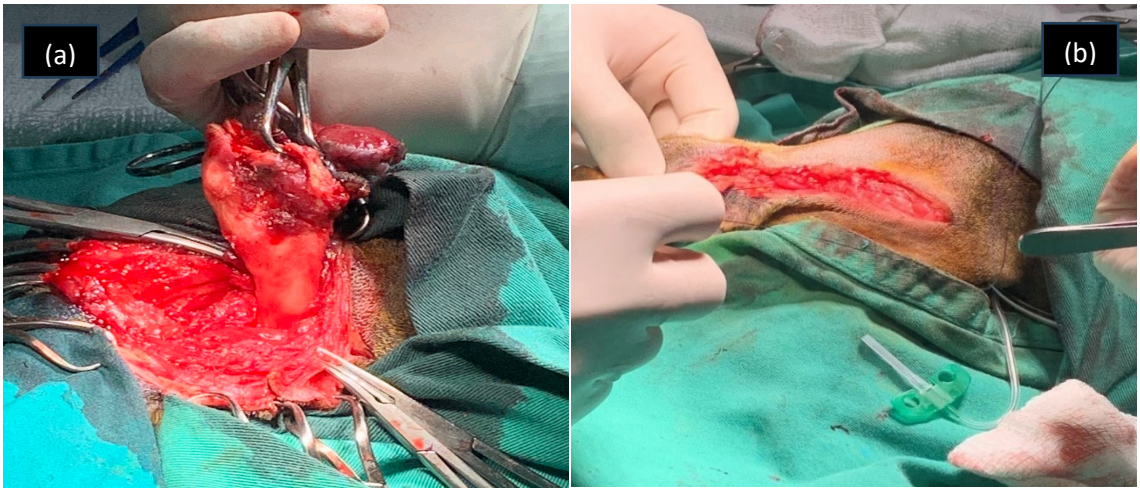

Figure 3. (a) Dissection around the proximal and medial aspects of the vertical canal. (b) Active drainage placement with butterfly catheter size 21G.

Preoperative haematology and serum biochemistry revealed borderline anaemia (haematocrit, 35%; reference range: 35-55%; haemoglobin, 117 g/L; reference range: 120-180 g/L, lymphopenia, 0.33 X 10^9/L; reference range: 1.5-1.8 X 10^9/L), and hyperproteinaemia (plasma protein, 98 g/L; reference range: 60-80 g/L). Skull radiography revealed stenosis of the right horizontal ear canal, by the presence of a soft tissue mass within the ear canal (Figure 2a). On computed tomography an ill-defined, soft tissue attenuation of the right external auditory canal without clear margins, thickening of the tympanic membrane without extension of the mass (3.1cm x 2.2cm x 2.6cm in size) into the tympanic cavity was observed (Figure 2b). Based on clinical examination and diagnostic imaging, surgical excision was performed.

The dog was premedicated with tramadol (5 mg/kg SQ), induced with propofol (5mg/kg, IV), intubated, and maintained on isoflurane vaporised in oxygen (2-3%), positioned and stabilised on left lateral recumbency. Physiological parameters (respiration and heart rate, blood pressure and oxygen saturation, SpO2) were monitored periodically during the surgery.

Total ear canal ablation with lateral bulla osteotomy (TECA-LBO) was performed on the affected right ear. A T-shaped incision was made with the horizontal component parallel and just below the upper edge of the tragus. From the midpoint of the horizontal incision, a vertical incision that extended just past the level of the horizontal canal was made. The skin flaps were retracted, loose connective tissue was reflected, and the lateral aspect of the vertical canal was exposed. The horizontal incision was continued around the opening of the vertical ear canal. Region around the proximal and medial aspects of the vertical canal was dissected and the dissection was continued to the level of the external acoustic meatus (Figure 3a). The horizontal canal attachment to the external acoustic meatus was excised along with lateral bulla osteotomy. Lateral and ventral aspects of the bulla were conquered until the caudal aspect of the middle ear canal was exposed. Interior of the bulla was examined for inflammatory debris, neoplastic tissue or foreign bodies, and samples were taken for bacteriological culture, sensitivity, and histopathological examination. Using a 3-0 nylon, active drainage (butterfly catheter size 21) was sewed in place with Chinese finger trap suture pattern (Figure 3b). Muscle layer was sutured with Cruciate mattress suture pattern using 3-0 polydioxanone (PDS); subcutaneous tissue was sutured with modified Cushing suture pattern using 2-0 PDS and skin was sutured with simple interrupted suture pattern using 3-0 nylon.

Immediate post-surgical analgesia was achieved with pethidine (2mg/kg SQ). The dog had an uneventful initial

post-surgical period. Post-operative wound management and progression of the dog were recorded. Neurological examination was unremarkable 24 hours after surgery. Elizabethan collar was always used, the surgical site was cleaned with povidone-iodine, and chloramphenicol ointment was applied q12h topically.

Multimodal analgesia was achieved using a combination of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids (meloxicam 0.1mg/kg/SQ q24h for 7 days; pethidine 2mg/kg/SQ q12h for 7 days and tramadol 3mg/kg orally q12h for 19 days). Bupivacaine topically q12h for 5 days was instilled when the dog displayed heightened anxiety and discomfort through signs of vigorous head shaking, and vocalisation during wound cleaning. When ample analgesia was not attained, gabapentin 10mg/kg orally q12h was administered.

Post-operative antibiotic treatment involved amoxicillin-clavulanic acid, 17mg/kg orally q12h for 14 days. Additionally, oral administration of, serratiopeptidase (5mg total dose q12h for 10 days); papain (150,000 USP q12h for 6 days) and cetirizine (10mg total dose q12h for 15 days) were given.

Two days post TECA-LBO, the dog developed a seroma at the base of the right ear, serosanguineous discharge at the surgical site with minimal suture breakdown, and severe head shaking. Complete suture breakdown was observed five days later, and the dog was scheduled for revision surgery. The wound was debrided followed by re-suturing of the surgical site. The dog was discharged 20 days after TECA-LBO.

Follow-up treatment at home consisted of tramadol 3 mg/kg orally q12h for 7 days; cetirizine 10mg total dose orally q12h for 7 days, and papain 150,000 USP orally q12h for 7 days. Additionally, the owner was instructed to dab the surgical site with povidone-iodine-impregnated gauze followed by topical application of chloramphenicol ointment q6h for 14 days. On revisit (2 weeks post-discharge), there was adequate wound healing with epithelisation. The owner was advised to continue E-collar usage till complete wound healing.

Proteus mirabilis, sensitive to amoxicillin-clavulanic acid, enrofloxacin, and resistant to cephalexin, doxycycline, and azithromycin was isolated from a swab of the bulla during the surgery. The amoxicillin-clavulanic acid, prescribed on the day of surgery as empirical therapy for this dog was deemed suitable and aided in the dog's recovery.

The excised tissue sample, measuring 4cm x 7.5cm (Figure 4) was fixed in 10% neutral buffered formalin, trimmed, and processed according to the standard protocol (Ramos-Vara et al., 2007).

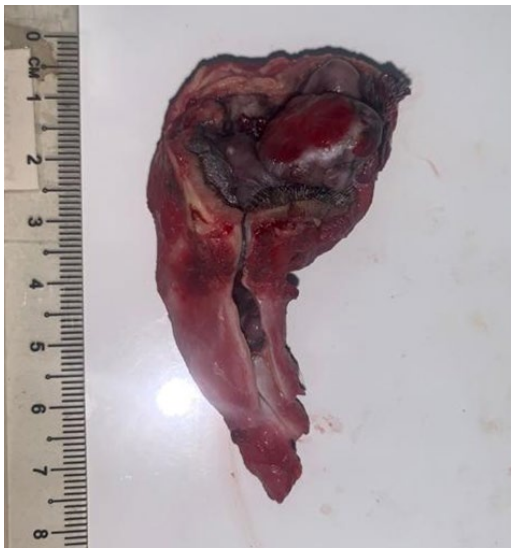

Figure 4. Excised tumour of the ear canal.

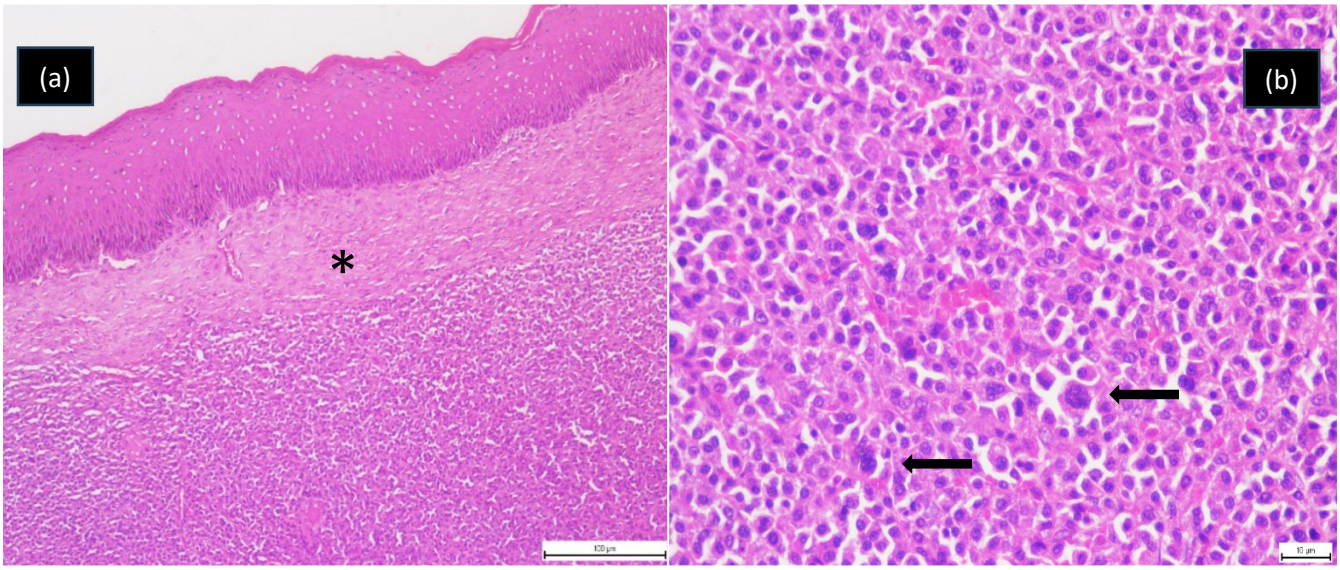

Figure 5. Tumour histopathology. (a) The neoplasm was separated from the epidermis by a dermal band (Grenz zone) (*) (HE, scale bar: 100 µm). Neoplastic cells had distinct cell borders, moderate amounts of eosinophilic cytoplasm with central to eccentrically located nuclei. They contained clock-face chromatin, occasional karyomegalic cells as well as bi- and multinucleated cells (arrow) (HE, scale bar: 10 µm).

Table 1: Primary antibodies used with their immunohistochemical details.

Primary Antibody	Antibody Type	Source	Dilution	Antigen Retrieval
CD20	pAb (PA5-16701)	Invitrogen, USA	1:300	HIER* Citrate buffer pH 6.0
COX-2	mAb (SP21)	Invitrogen, United Kingdom	1:100	HIER* Citrate buffer pH 6.0

*HIER= Heat Induced Epitope Retrieval

The tissue was sectioned at 4 µm thickness and was stained with haematoxylin and eosin. Microscopically, the dermis was expanded by a fairly well-delineated, nonencapsulated neoplasm composed of round cells arranged in sheets supported by a pre-existing fibrovascular stroma. Neoplastic cells had distinct cell borders and moderate amounts of eosinophilic cytoplasm. Nuclei were central to eccentrically located and contained clock-face chromatin. Karyomegalic cells and scattered bi- and multinucleate cells were occasionally observed. The neoplasm was separated from the epidermis by a dermal band (Grenz zone) (Figures 5a, 5b). Additionally, immunohistochemistry against COX-2 and CD20 was performed to demonstrate the expression of a common anti-inflammatory COX-2 gene, which was not reported for plasmacytomas in current literature, whereas CD20 was included as plasmacytomas have been reported to express this cell marker (Ramos-Vara et al., 2007; Vail et al., 2020).

The tissue sections were mounted on frosted glass sides, deparaffinised in xylene, and rehydrated in decreasing concentrations of alcohol. Antigen retrieval was achieved using heat-induced epitope retrieval (HIER) with citrate buffer (pH 6.0) at 121°C for 30 minutes. To block nonspecific reactions, the sections were submerged in 3% hydrogen peroxide in methanol at room temperature for 5 min and incubated in 8% skimmed milk at 37°C for 30 min. Subsequently, the sections were incubated overnight with the primary antibodies (Table 1) at 4°C, followed by three washes with Tris-buffered saline (TBS). Sections were then incubated with horseradish peroxidase (HRP)-labelled anti-rabbit secondary antibodies (Abcam, Waltham) at 37°C for 40 min. After three washes with TBS, sections underwent chromogen treatment with 3,3′-diaminobenzidine and counterstained with Mayer's haematoxylin. Neoplastic cells were negative for CD20 and COX-2 but few scattered CD20-positive B-cells were observed within the stroma.

DISCUSSION

Cutaneous plasmacytomas account for 1.5% of all canine skin tumours (Goldschmidt and Shofer, 1992). Extramedullary plasmacytoma (EMP) and solitary osseous plasmacytoma (SOP) are solitary collections of monoclonal plasmacytic tumours originating from soft tissues or bone, respectively (Clark et al., 1993; North and Banks, 2009; Perlmann et al., 2009; Vail et al., 2020). According to Mikiewicz et al., (2016) local dogs (14/19 dogs) accounted for much of the examined canine EMPs. Predisposed locations in dogs include the skin of the digits, ears, and oral cavity (Cangul et al., 2002; Quiroz-Rocha et al., 2017). Although tumours as large as 10cm have been documented, majority of cutaneous EMPs are solitary, smooth, firm, stationary, elevated, pink to red typically 1 to 2 cm in diameter (Vail et al., 2020).

Cutaneous extramedullary plasmacytomas in dogs have a benign course of disease with a good prognosis and are often cured with complete surgical excision (Meuten, 2017; Vail et al., 2020). Conservative surgical resection is regarded as a negative prognosticator for extensive aural tumours (Morris and Dobson, 2001) hence aggressive surgical resection via TECA-LBO was preferred and considered the best approach in this case due to extension of mass to the horizontal canal with thickening of the tympanic membrane. This might also prevent recurrence. TECA-LBOs also provide satisfactory surgical margins with better prognosis (Henry and Higginbotham, 2010).

The TECA-LBO is regarded as an extremely invasive and painful surgical procedure therefore, effective post-operative multimodal analgesia is imperative (Stathopoulou et al., 2018). Administration of oral analgesics (NSAID/opiate combinations) is recommended post-surgery (Tranquilli et al., 2004). Local anaesthetic solutions like bupivacaine is an excellent substitute or adjunct to opioid analgesics and non-steroidal anti-inflammatories (NSAIDs) due to their negligible systemic absorption and comparatively low cost (Wolfe et al., 2006; Layne & de Miguel Garcia, 2019).

While fine needle aspiration cytology (FNAC) is frequently used for diagnosing cutaneous plasma cell tumours, histopathology confirmation is recommended (Boostrom et al., 2017; Miller et al., 2020). Most cases of cutaneous extramedullary plasmacytomas can be confirmed based on histopathology examination (Vail et al., 2020). However, immunohistochemistry for MUM-1 is recommended to differentiate poorly differentiated plasmacytomas from other round-cell tumours (Meuten, 2017; Vail et al., 2020; Wellman and Kisseberth, 2020). MUM-1 was not performed in this study due to the unavailability of a MUM-1 antibody that could cross-react with canine tissues in our laboratory. The present case displayed several distinct features of plasmacytomas, including neoplastic cells with eccentrically located nuclei, occasional bi- and multinucleation, and separation of neoplastic cells from the epidermis by a distinct zone of dermal collagen (Grenz zone), allowing for the diagnosis of plasmacytoma based on histologic evaluation alone.

In this case, *Proteus* spp. was isolated as a single type of organism where the isolates were sensitive to amoxicillin-clavulanic acid, the antibiotic of choice. De Martino et al., (2016) ranked Proteus spp. as the third most frequent contributor to canine otitis externa. Other common bacterial genera isolated from canine otitis cases include Gram-positive *Staphylococcus* spp., *Streptococcus* spp., *Corynebacterium* spp., and Gram-negative

Pseudomonas spp. and *E. coli* (Gotthelf, 2005). Kwon et al., (2019) reported Proteus spp. as one of the major causative agents of canine otitis externa with most isolates being resistant to cefazolin (75%), trimethoprim–sulfamethoxazole (72%), chloramphenicol (72%), ampicillin (59%) and amoxicillin–clavulanate (63%).

Canine EMPs is behaviourally benign and can be cured by complete surgical excision (Cangul et al., 2002; Henrich, 2016; Vail et al., 2020). However, some dogs can be presented with multiple plasmacytomas. Canine EMPs is not typically associated with multiple myelomas (Cangul et al., 2002; Henry and Higginbotham, 2010; Meuten, 2017; Vail et al., 2020).

CONCLUSION

This was a case of canine extramedullary plasmacytoma involving the skin of the ear canal, which was surgically managed. Diagnostic imaging techniques like radiography and computed tomography were important tools in the diagnosis of aural neoplasm to assess tumour invasiveness into the middle ear and surrounding tissues, to determine the best surgical approach for the case. Given the complete resection of the tumour and the benign behaviour of plasmacytomas, the patient's prognosis is good following TECA-LBO.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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