Gingival mass in a dog

Contributors

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Specimen
Fine needle aspirate cytology of an ulcerated mass at the mucogingival junction.

Signalment
7-year-old male neutered Labrador retriever dog

History
A dog was referred to the Royal (Dick) School of Veterinary Studies, University of Edinburgh, for investigation of right hind limb lameness.

Clinical findings

Clinical examination with the Dick Vet General Practice (DVGP) prior to orthopaedic referral revealed a 2 cm diameter, pink to purple, irregular, multilobulated oral mass arising from the mucogingival junction adjacent to the maxillary incisors. The mass appeared pedunculated and was mobile on palpation. There were no clinical signs of involvement of underlying structures such as bone or deeper soft tissue. As no images of the lesion in situ were available, the appearance of the mass after submission and fixation for histopathology is shown in Figure 4. Fine needle aspirates (FNA) of the gingival mass were submitted for cytologic examination.

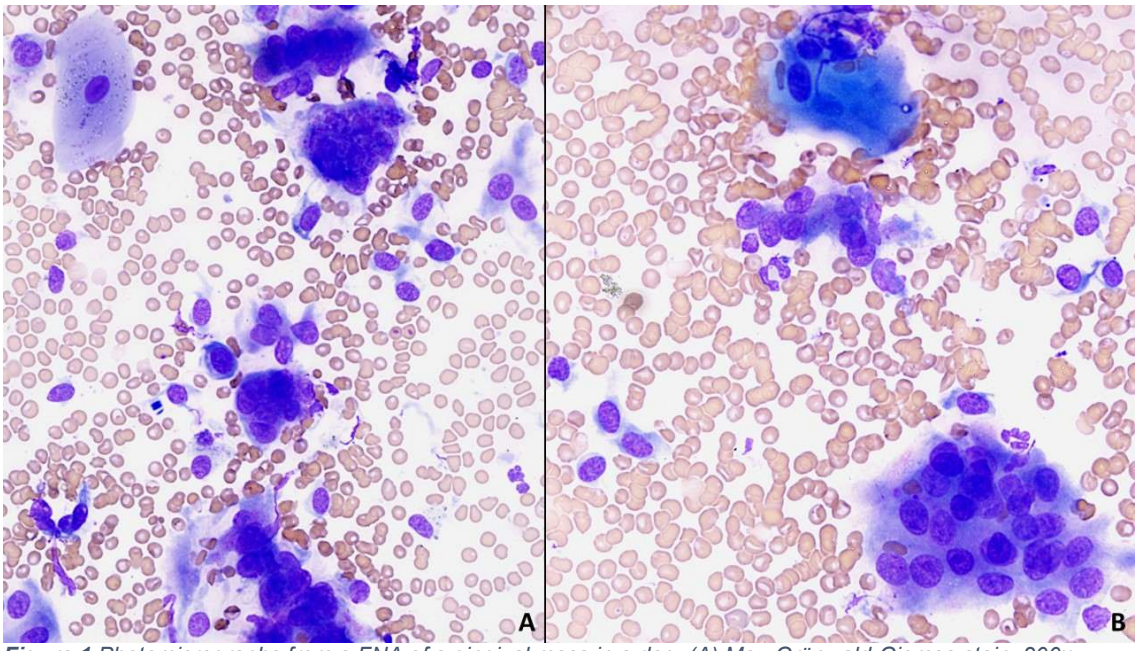

Figure 1 *Photomicrographs from a FNA of a gingival mass in a dog. (A) May-Grünwald-Giemsa stain, 200× magnification, (B) May-Grünwald-Giemsa stain, 400× magnification.*

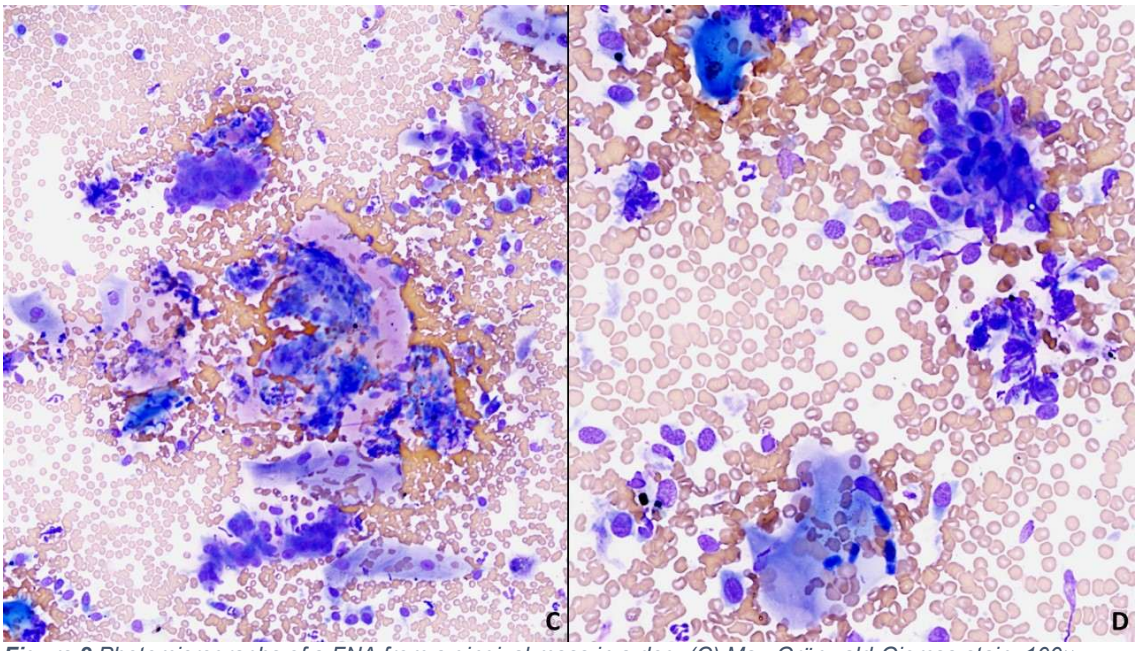

Figure 2 *Photomicrographs of a FNA from a gingival mass in a dog. (C) May-Grünwald-Giemsa stain, 100× magnification, (D) May-Grünwald-Giemsa stain, 200x magnification.*

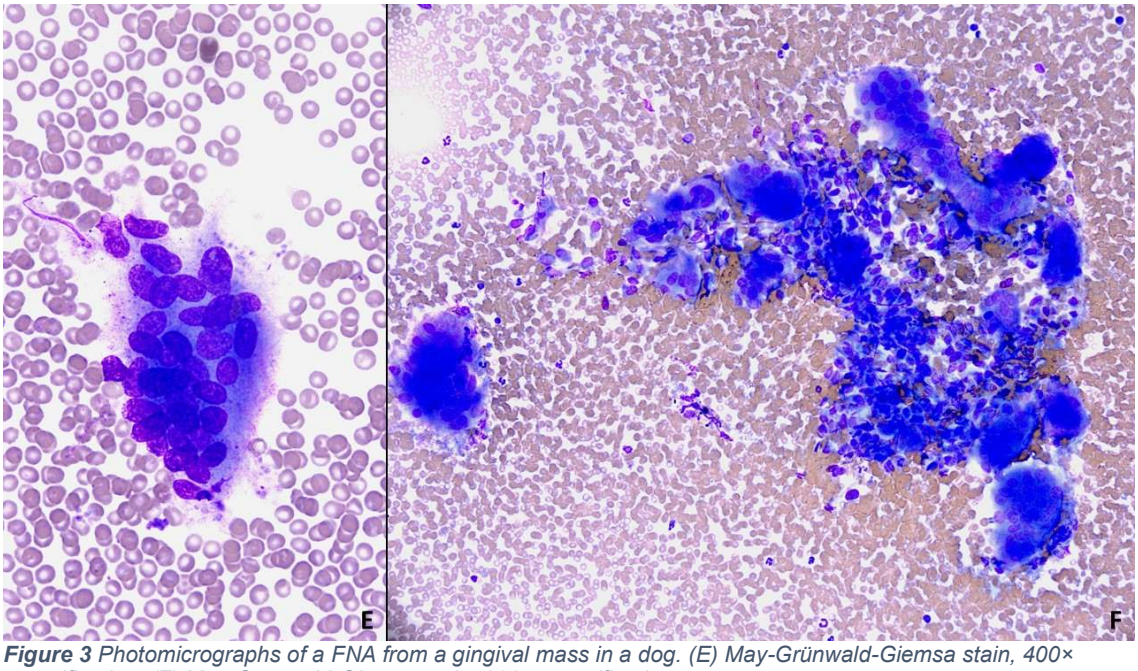

Figure 3 *Photomicrographs of a FNA from a gingival mass in a dog. (E) May-Grünwald-Giemsa stain, 400× magnification, (F) May-Grünwald-Giemsa stain, 200× magnification.*

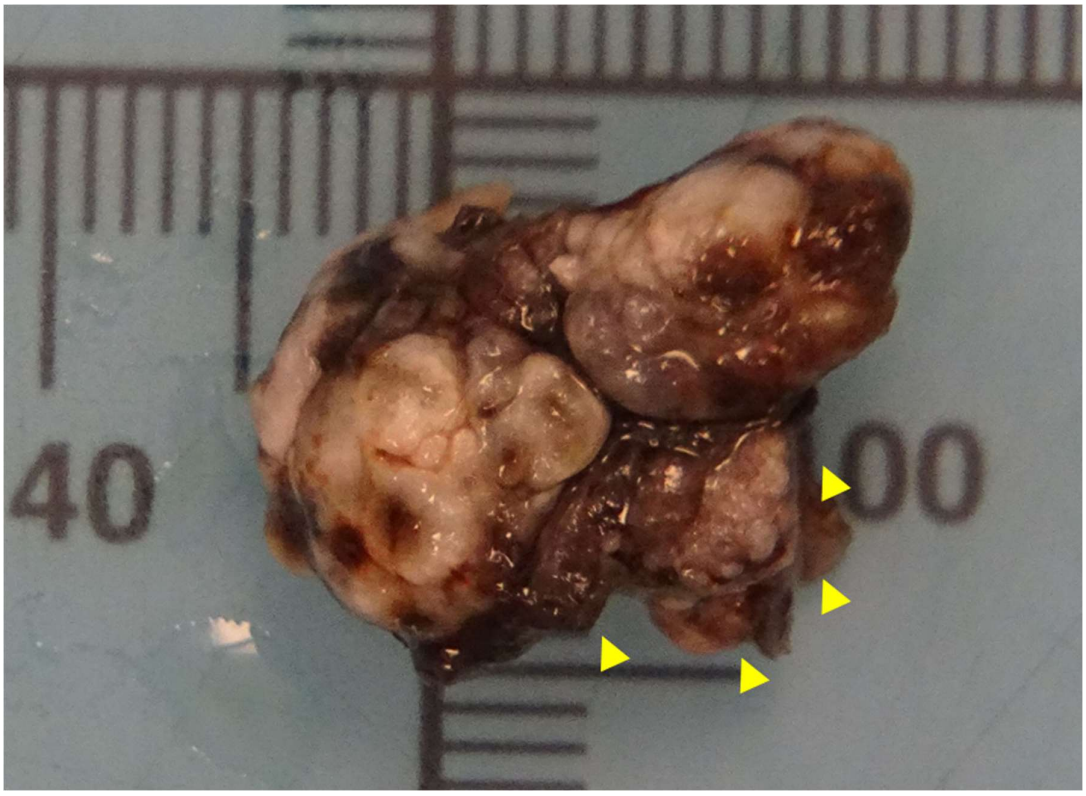

Figure 4 *Gross photograph of the lesion, post formalin fixation. A raised, multilobular mass of multifocally tan to dark brown tissue measuring approximately 1.5cm x 1.5cm x 1.5cm was removed surgically from the mucogingival junction adjacent to the maxillary incisors. The deep surgical margin is indicated by the yellow arrowheads.*

Questions

1. What is the main differential diagnosis based on the cytologic findings and lesion location?

2. Which of the following best describes biological behaviour of this growth?
    a. Malignant and locally invasive
    b. Reactive and benign
    c. Metastatic potential with bony destruction
    d. Indolent neoplasm with high reoccurrence rate

Cytological Interpretation/Diagnosis
A diagnosis of “most consistent with peripheral giant cell granuloma” was made based on cytological findings characterized by a mixed population of multinucleated giant cells and stromal cells, along with the lesion’s gingival location as indicated in the submitted history.

1. **What is the main differential diagnosis based on the cytologic findings and lesion location?**

   The main differential diagnosis based on the cytologic findings of multinucleated giant cells and spindle cells within a maxillary gingival mass is a peripheral giant cell granuloma (PGCG). Other differentials to be considered could include granulomatous inflammation (e.g., foreign body reaction, Mycobacteriosis etc), and bone lesions such as giant cell tumour of bone, giant cell-rich osteosarcoma and central giant cell granuloma.

2. **Which of the following best describes biological behaviour of the lesion in question?**

   Correct answer: b. Reactive and benign. Surgical excision is the treatment of choice for PGCG in dogs, and recurrence is rare — with a reported rate of 2 in 16 cases — supporting its classification as a reactive, benign and non-invasive lesion that typically arises in response to local irritation.

Additional information
Cytological examination revealed moderate to high cellularity and good cell preservation on a pale eosinophilic background with a large amount of blood. Numerous spindle to oval cells exfoliated individually or in tight aggregates. They had moderately distinct cytoplasmic borders, a small amount of pale, basophilic, wispy cytoplasm, and a centrally positioned oval nucleus with ropy chromatin and 1-2 small, distinct nucleoli. Moderate to occasionally marked anisocytosis, anisokaryosis and infrequent binucleation were present. Several, large, multinucleated cells with up to 20 uniform nuclei and abundant, basophilic cytoplasm with some eosinophilic dusting were seen. Spindle and multinucleated cells were occasionally associated with a small amount of eosinophilic, extracellular matrix. Rare individualized squamous epithelial cells occasionally containing melanin and rarely associated with bacteria with Simonsiella-like morphology, were also present (oropharyngeal contamination).

The mass was removed via an elliptical incision and submitted for histopathological examination (excisional biopsy). This mass was firm, brown, multi-lobular and measured 2 cm x 1 cm x 1 cm. Histopathological examination revealed an unencapsulated, infiltrative, multilobular to coalescing proliferation within the submucosa. The cellular proliferation was composed of two distinct cell populations; a major population of spindleoid cells and a smaller population of large, multinucleate giant cells, both of which were embedded within a dense collagenous stroma. Spindle cells were arranged in haphazard streams and had a moderate amount of eosinophilic cytoplasm. Cell nuclei were oval, nuclear chromatin was finely stippled and there was an occasionally prominent single nucleolus. There was moderate anisocytosis and anisokaryosis. Six mitotic figures were seen in 10 high power fields (2.37 mm^2). Spindle cells surrounded lower numbers of large, multinucleate cells. These cells had up to 20 nuclei per cell with marked anisocytosis and anisokaryosis but no mitotic figures in 10 high power fields (2.37 mm^2).

Histological Interpretation/Diagnosis
Histopathological findings confirmed the cytological diagnosis of peripheral giant cell granuloma, whilst the multifocal extension to both the deep and horizontal tissue margins indicated an incomplete local excision.

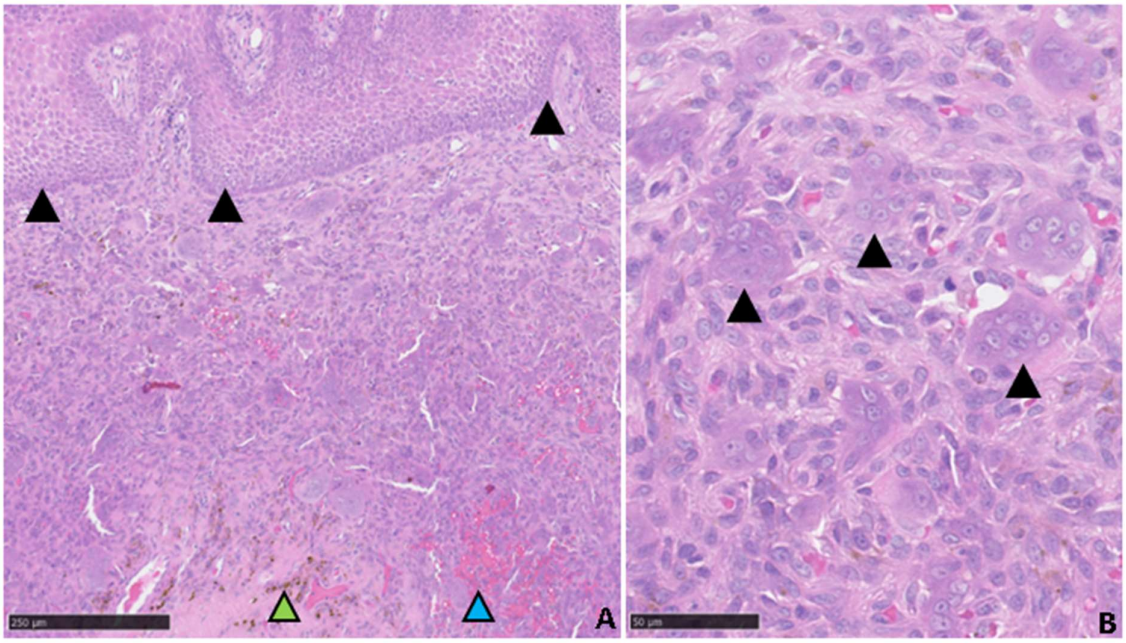

Figure 5 *Photomicrographs of the histopathology of this gingival mass. (A) Low power image demonstrating the proliferation of a mixture of large multinucleated giant cells amongst a background of spindle cells. This proliferation is within the submucosa below a hyperplastic oral mucosa (indicated by the black arrowheads). There are also multifocal aggregates of haemorrhage (indicated by the blue arrowhead) and clusters of haemosiderophages (indicated by the green arrowhead). Haematoxylin and Eosin, 100x magnification, scale bar 250µm. (B) High power image of this proliferation demonstrating multiple giant cells with multiple nuclei (indicated by the black arrowheads), interspersed by a proliferation of relatively bland spindle cells. Haematoxylin and Eosin, 400x magnification, scale bar 50µm.*

Follow up and clinical outcome

The dog recovered well after both surgical removal of the gingival mass and also, following orthopaedic referral, tibial-plateau-levelling osteotomy (TPLO) surgery. At the last follow up, one month after the oral surgery, there was no evidence of oral mass recurrence, and recovery after TPLO surgery was uneventful.

Discussion

Peripheral giant cell granuloma (PGCG), formerly referred to as "giant cell epulis",[1] is an uncommon oral lesion in dogs. It is generally regarded as a benign, reactive lesion rather than a true neoplasm,[2,3] as it originates from the connective tissue of the periosteum or from the periodontal membrane, in response to local irritation or chronic trauma (e.g. calculus, bacterial plaque, periodontitis).[4] A PGCG prevalence of 0.99% among 2,609 canine epulides was reported in a large retrospective study.[5] PGCG typically presents as a solitary exophytic mass on the gingiva, with a predilection for the maxilla over the mandible.[1,2,5-7] However, multiple lesions have also been documented.[8]

The terminology used to describe gingival masses has evolved to better reflect their histopathological features and clinical behaviour. In veterinary medicine, the term 'epulis' is now considered outdated when referring to an exophytic gingival proliferation, as it encompasses a heterogeneous group of both reactive and neoplastic lesions. The World Health Organization classification[9] recommends reserving the term 'epulis' for fibromatous epulis of periodontal ligament origin (previously referred to as fibromatous and ossifying epulis), which is now more commonly termed peripheral odontogenic fibroma in the literature.[2] Other forms of epulids which have been re-named include acanthomatous epulis, which is now termed acanthomatous ameloblastoma, and giant cell epulis which is now referred to as PGCG.[2,5,6]

In the present case, the mass had clinical features consistent with PGCG, including its gingival location and gross appearance of a multilobulated mass. Cytologic evaluation revealed a cellular population composed predominantly of multinucleated giant cells (MNGCs) and spindle-shaped stromal cells, consistent with what would be expected in a PGCG. A few squamous epithelial cells

were also present, some containing melanin granules and admixed with oropharyngeal bacteria. These cells were interpreted as sampling contaminants from superficial oropharyngeal mucosa.

Differential diagnoses based on cytological findings include granulomatous inflammation due to a foreign body reaction or atypical bacterial infections such as *Mycobacterium spp.* as well as bony lesions such as giant cell-rich osteosarcoma, giant cell tumour of bone (GCTB) and central giant cell granuloma (CGCG). Foreign body reactions are a common cause of inflammatory oral lesions and may include multinucleated giant cells, reactive fibroblasts and chronic inflammatory cells such as lymphocytes, plasma cells and macrophages.[12] The three bone lesions mentioned — giant cell-rich osteosarcoma, GCTB and CGCG — have similar cytological and histological features to PGCG, which makes them important differential diagnoses despite their rarity. All are characterised by abundant osteoclast-like multinucleated giant cells in a background of spindle-shaped to ovoid mononuclear stromal cells, but their clinical presentation and biological behaviour differ.
Giant cell-rich osteosarcoma contains numerous osteoclast-like giant cells, but differs in the presence of malignant osteoblasts, which are often obscured by the giant cell component. Diagnosis depends on the presence of cytological atypia, high mitotic activity and other features of malignancy in the mononuclear population that distinguish it from benign giant cell lesions.[2] To date, this variant has not been described in the canine maxilla therefore the location of presentation in this case makes it a less likely differential diagnosis.
GCTB is defined cytologically by a high proportion of evenly distributed osteoclast-like giant cells between spindle to ovoid mononuclear stromal cells, which represent the neoplastic component.[2] This tumour is rare in dogs and has only been reported in long bones, also making it an unlikely differential diagnosis in this case due to the location, although maxillary involvement has been described in humans.[17]
CGCG is a non-neoplastic, expansile intraosseous lesion composed of multinucleated giant cells in a fibroblastic stroma and is often associated with previous trauma or intraosseous haemorrhage. Although CGCG can also occur in the maxilla, reports in dogs are rare and describe an intraosseous rather than gingival presentation.[11,16]

Histopathology is required for a definitive diagnosis of PGCG, with only few reports of cytological descriptions found in the literature.[12] In this case, histopathologic sections revealed features consistent with the “classic” histologic subtype of PGCG.[5] These included numerous MNGCs interspersed in a background of spindle-shaped stromal cells within a dense collagenous matrix. Additional histologic features included regions of hemorrhage, hemosiderin deposition, and a predominantly lymphoplasmacytic inflammatory infiltrate, with localized neutrophilic inflammation in areas of ulceration.
Two histologic subtypes of canine PGCG have been described by Desoutter et al. (2012)[5]: a “classic” subtype with the aforementioned features, and a “collision” subtype, which contains regions resembling a peripheral odontogenic fibroma with stellate mesenchymal cells, fibrous stroma, and regularly spaced vessels. The collision type may represent either a histologic variant or true concurrent lesions.

A notable and defining feature of PGCG is the presence of MNGCs. Two morphological subtypes of MNGCs have been described in the literature[5,7]: Type I cells are considered metabolically active, containing larger nuclei and more basophilic cytoplasm, while Type II cells are degenerative, with eosinophilic cytoplasm and condensed, smaller nuclei. In our case, the MNGCs observed were considered to fit the description of type I cells.
The cellular origin of the MNGCs is believed to be of osteoclastic lineage, arising from monocyte/macrophage precursors that differentiate under the influence of local stromal signalling. Stromal fibroblasts likely secrete cytokines and growth factors that recruit monocytes and promote their fusion into multinucleated osteoclast-like cells.[10,13]

Immunohistochemical characterization of MNGCs and stromal cells in PGCG supports osteoclastic differentiation to some extent. In dogs, MNGCs in PGCG are variably positive for tartrate-resistant acid phosphatase (TRAP), a marker of osteoclasts[5] while in cats they exhibit strong positivity.[13] Some spindle cells may also show TRAP positivity. One study in dogs investigated the expression of alkaline phosphatase (ALKP), cytokeratin 7 (CK7) and CD68 in MNGCs, which showed nonspecific binding of ALKP, weak positivity of CK7 and no specific CD68 immunolabelling.[6] In feline PGCG, vimentin positivity and RANK (Receptor Activator of Nuclear Factor κB) expression have been demonstrated, suggesting similarities in osteoclastogenic pathways.[2,13] Despite these findings, the

routine use of immunohistochemistry or special stains is not generally required for definitive diagnosis, as the distinctive histologic features of PGCG are sufficient for differentiation. Furthermore, TRAP or RANK IHC is not readily available as a routine diagnostic marker in most veterinary anatomic pathology laboratories.

Surgical excision is the recommended treatment for PGCG in dogs. It is generally curative, as PGCGs behave in a biologically benign and non-invasive manner. In a retrospective study by Desoutter et al. (2012)[5], recurrence was reported in only 2 of 16 cases with available follow-up data. Both recurrent cases experienced recurrence within 2 months post-surgery. Recurrence is generally attributed to incomplete excision or ongoing local irritation, such as concurrent dental disease. Interestingly, none of the “collision” type PGCGs recurred in that study, however, the small sample size limits the strength of this conclusion. Histologic features such as mitotic index, degree of cellularity, or MNGC count have not been shown to correlate with risk of local recurrence. No distant spread has been reported.

In this case, histopathologic evaluation revealed incomplete surgical margins with multifocal extension of the proliferation to the horizontal and deep tissue margins, yet no recurrence was noted at 1 month post-operatively. However, this is a limited observation period, and further clinical monitoring is warranted to assess for delayed recurrence. A nurse-led dental assessment has been recommended, but at the time of writing, this has yet to be undertaken. This indolent clinical course contrasts with feline PGCG, which tends to exhibit more aggressive behaviour, faster growth, and a higher recurrence rate.[13]

In summary, this case illustrates the key cytological and histopathological features of an uncommon gingival lesion in dogs. Canine PGCG is a rare, reactive lesion characterized by multinucleated osteoclast-like giant cells within a spindle cell stroma. Cytologic evaluation may support a diagnosis when classic features are present along with lesion morphology and localization. Histopathology remains the gold standard for definitive diagnosis and surgical margin assessment. PGCGs in dogs are typically cured by complete surgical excision, although complete deep surgical excision may be difficult to achieve due to location. Although recurrence is uncommon, continued monitoring is important, especially in cases with incomplete excision. Further remedial dental work may aid with reducing the rate of local recurrence by removing an inciting insult.

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