Exploring Diverse Oral Pathologies among Various Breeds of Canines: A Review

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ABSTRACT

The paper summarizes the existing state of knowledge, which provides a resource for reviewing the oral pathologies in canines that may possibly be helpful in curative or analytical goals for human and veterinary medicine. It reviews the data of 462 cases that have been reported in 17 previously published articles. A search was conducted to identify appropriate papers from different databases (Google Scholar, PubMed, SCOPUS and Web of Science) and were analyzed for quality. In addition to this, outcome data were extracted in the form of graphs for summary. A high degree of heterogeneity was observed in the included studies regarding their inclusion and exclusion criteria, pathologies in different breeds, and the definition of survival. There is a need to standardize the reporting of diseases with appropriate treatment modalities. This present paper covers the various oral pathologies that may support the design of future studies.

Keywords: Canines, Oral pathologies

INTRODUCTION

Oral diseases are quite common in canines, with a variety of pathologies in the oral cavity. The oral diseases, which are most frequently encountered in canines, are gingivitis and periodontitis. It is important to diagnose various oral pathologies and conditions at the veterinary healthcare centres. It is difficult to understand the signs and symptoms of the diseases in canines because of the rare display of discomfort and almost normal behavior which can lead to serious complications in dogs. Though oral tumours are commonly seen in dogs as described in different epidemiological studies of pharyngeal and oral neoplasias, there is a lack of awareness about the prevalence of these disorders. Benign neoplasms have been found to quite common in canines. There is a dire need to spread the knowledge amongst the veterinary general practitioners and the pet owners about the signs and symptoms, course of disease, pathogenesis and treatment options. Due to disagreements in the available classifications, there is difficulty in firmly concluding about the prevalence of various oral pathologies in canines from the literature (Svendenius and Warfvinge, 2010). A variety of different pathologies emphasise the dire need to establish a diagnosis before initiating any treatment modalities. The animal models of different human diseases are a vital tool for biomedical research and also for studying the pathogenesis of various diseases, including benign and malignant disorders. Additionally, the development of treatment strategies for humans benefits the field of veterinary medicine.

SEARCH STRATEGY AND SELECTION CRITERIA

The details of this selected topic have been identified and chosen from an extensive search of databases (Google Scholar, PubMed, SCOPUS and Web of Science), along with the cross references to the published articles on the incidence of the various oral pathologies in different canine breeds for appropriate case reports or studies which have been published since 1994 to date. Keywords used included a combination of malignant neoplasms in dogs, oral pathologies in canines, head and neck lesions in different breeds of canines, and dental anomalies reported in canines. Canines

were organised and categorised into different categories of diseases. Moreover, supplementary citations that were acknowledged through lists of determined references and bibliographic linkages were also meshed in the review. We also explored journals parallel to subjects like oral pathology, oral medicine, oral surgery and veterinary science. Inclusion criteria for this systematic review comprise case reports and series on the contingency of oral pathologies in different breeds of canines and articles related to common generalised conditions like gingivitis and periodontitis in canines were excluded (Figure 1).

RESULTS

Developmental Disturbances

Regional Odontodysplasia: A 7-month-old male Beagle dog was found to have a swelling in the right maxillary region. Microscopically, an intermingling of disorganised dentin and cementum was observed, especially in the crown, with poorly mineralised enamel (Schamberger *et al.*, 2010).

Cleft Palate: A male (complete cleft; primary+secondary palates) and a female (complete cleft; secondary palate) old Spanish pointer was treated with a palatal prosthesis (Martínez-Sanz *et al*., 2011).

Amelogenesis imperfecta (AI): AI is a genetic developmental disorder of teeth affecting the structure. To date, only three cases have been reported in three standard poodle dogs in the literature (Svendenius and Warfvinge, 2010).

Inflammatory Lesions/ Reactive Lesions

Mandibular Periostitis Ossificans: In the literature, a total of 5 dogs with an age-range of 3 to 5-months have been reported for a jaw swelling. Two were Labrador retrievers, one was a Great Dane, one was a Dogue de Bordeaux, and one was a Great Pyrenees. Histopathological examination showed periosteal new bone formation with no signs of inflammation/malignancy (Blazejewski *et al.,* 2010) as mentioned in Table I.

Maxillary osteomyelitis with chronic ulcerative paradental stomatitis: A 10-year-old male Scottish terrier reported with discomfort and was on an almost continuous dosage of antibiotics and corticosteroids. There was bilateral mandibular lymph node enlargement. The other male dog, a 4-year-old Scottish terrier, presented with discomfort in the oral cavity for the past 10 months. The details are presented in Table II (Boutoille and Hennet, 2011).

Cryptococcal Maxillary Osteomyelitis & Osteonecrosis: An 18-month-old male mixed-breed dog had a history of a 2-week duration of halitosis and avoidance to chew on sticks/treats. An inflammatory lesion on the left mucogingival region was noted along with a missing 207. Low bone density and lytic areas extending from 105 to 107 and 205 to 208 were observed, which were consistent with the diagnosis of acute osteomyelitis. Histopathology revealed necrotising and pyogranulomatous osteomyelitis with intra-lesional yeast (Cryptococcus). Positive latex agglutination serum antigen titer (1:256) confirmed the diagnosis (Block and Battig, 2017).

Fibrous Hyperplasia / Calcifying fibroblastic granuloma/ Pyogenic granuloma

Out of 280 biopsies, 279 canines were included in the study. Out of which, 132 were females and 144 males. Seventy-seven different breeds were included. Sixty nine percent of the biopsies were epulides. The most common entity, being gingival fibrous hyperplasia [66 cases (24%)] consisted of 34% of epulides. Presented exclusively as epulides, the total number of calcifying fibroblastic granuloma (8%) cases was 22 and consisted 11% of epulides. Pyogenic granulomas (1%) were 3 and comprised 2% of epulides (Svendenius and Warfvinge, 2010).

Cystic Lesions

Bilateral Dentigerous Cysts: A 5-year-old

Boston terrier (neutered/male) had impacted 304, 305 and 404. On oral examination, a brown-colored fluid was oozing out from the 405-extraction site. Radiolucent areas were seen associated with 404 and 304. On histopathological examination, 2-4 cells thick squamous epithelial lining showing no nuclear atypia was seen. Extraction of 304 and 404, along with cystic lining removal, along with removal of 303, 305, 403 and 406 was planned. Demineralised freeze-dried bone graft was used with no complications (MacGee, 2012).

Benign Neoplasms

Oral osteoma: Total 6 dogs were reported with oral osteomas (3 in the maxilla, 2 in the mandible). All lesions showed bone proliferation with no bone lysis. Four of the masses were identified as central and 2 as peripheral osteomas. Rostral maxillectomy was performed for four masses, while the other 3 had an en bloc resection (Volker and Luskin, 2014).

Odontogenic Tumors

Mixed Odontogenic Tumors

Compound Odontome: There are two cases (male dogs) discussed in the present review. Compound odontomes are identified as numerous tiny tooth-like structures.

Ameloblastic fibroma and Ameloblastic fibro-odontoma: There were a total of three cases reported in the maxillary region and were showing cystic lesions radiographically. All were diagnosed as ameloblastic fibro-odontoma. (Huang *et al.,* 2019) The detailed clinical, radiographic and histopathological features are listed in Table III.

Epithelial and Mesenchymal Odontogenic Tumors

Ameloblastoma and Odontogenic Fibroma: As listed in Table IV, out of the 279 dogs (77 breeds), 58 (21%) were diagnosed with peripheral odontogenic fibroma (POF), 10 (4%) cases of acanthomatous ameloblastoma and 3 (1%) of inflammatory myofibroblastic tumor (Svendenius and Warfvinge, 2010).

Malignant Neoplasms

Multiple Sarcoma: An ulcerative mass was detected in a 5-month-old mixed-breed dog. Radiographic examination revealed multiple round radiopaque masses in the lungs. There were 7 tumors in the jaws along with 3-cm masses associated with the left mandibular region. The cells were positive for vimentin and were stained for tartrate-resistant acid phosphatase, indicating origin from dental follicular mononuclear cells (Dubielzig *et al*., 1994).

Multicentric Oral Plasmacytoma: A 10-year-old Bichon Frise dog reported with two epuli. On histopathology, the diagnosis of plasmacytoma, a malignant plasma cell neoplasm, was made (Smithson *et al*., 2012).

DISCUSSION

In the dental field, developmental anomalies of the teeth in humans are more commonly reported than in the general veterinary practice. There are a few reviews on dental anomalies in dogs available in the literature (Fulton *et al*., 2014). Regional odontodysplasia, often referred to as odontogenic dysplasia, is a localised condition that affects one or more teeth in humans, the cause of which is not known. Despite not being inherited, no single element has been proven to be the direct cause. Localised trauma, localised ischemia, viral infections, irradiation, medications, metabolic or nutritional abnormalities, somatic mutation and impediment to neural crest cell migration are some of the suspected causes. In the case of the 7-month-old male beagle, no history of any facial trauma or endodontic disease was present. Also, animals with congenital cleft palate are extremely prevalent (Ferguson, 1981). Some dog breeds rapidly develop a cleft palate, making them suitable animal models for studies on novel surgical techniques. A good illustration of this is the

old Spanish pointer dog, as 15 to 20 per cent of its offspring have a cleft palate. Inflammatory lesions commonly seen in the oral cavity of dogs are PO, osteomyelitis, osteonecrosis, chronic ulcerative paradental stomatitis, and pyogenic granuloma. The mandible's distinct developmental characteristics in dogs make it more susceptible to periosteal disease. Even though the cause of bone inflammation was unknown in 11.8 percent of the cases, it was indicated that PO is merely an osteomyelitis variant (Nortjé *et al*., 1988). A total of 55 mandibular osteomyelitis cases in a survey of 200 human patients were later determined to be PO. Extraction of mandibular third molar with pericoronitis, neighbouring tooth follicle infection and periapical infections were a few possible causes of PO. This was due to the direct extension of inflammation into the subperiosteum, leading to periosteal new bone formation (Kawai *et al.,* 1996).

The veterinary and human dentistry literature provides detailed descriptions of maxillary osteonecrosis. The four etiologies of osteonecrosis of the jaws are radiation-induced, traumatic, nontraumatic, and bisphosphonate-related (Manfra-Marretta and Lommer, 2012). Soft tissues, teeth, and alveolar bones can all become devitalized as a result of oral trauma. Non-traumatic and idiopathic factors of osteonecrosis can be complex and result from localised endothelial cell dysfunction. Cocker Spaniels are overrepresented in documented cases of idiopathic mandibular osteonecrosis and bone sequestra, which may be related to underlying osteomyelitis and vascular impairment (Manfra-Marretta *et al*., 1997). Oral bacterial and fungal infections can occur in osteonecrosis, both traumatic and nontraumatic. The literature describes maxillofacial bone lysis and mucogingivitis that are compatible with blastomycosis. (Manfra-Marretta and Lommer, 2012), but no case of maxillary osteonecrosis caused by primary oral cavity inoculation or secondary to nasal infection with Cryptococcus sub-species has been documented in canines.

Fluid accumulation between the reduced enamel epithelium and crown of an impacted tooth is the major causative factor for dentigerous cysts (Niemiec, 2010 and Soukup *et al*., 2009). Neoplasms are commonly reported in dogs. Different neoplasms occurring in the oral cavity of dogs are osteomas, odontomas, ameloblastic odontoma, peripheral ossifying fibroma, ameloblastomas, oral cancer, melanomas, etc. Carcinomatous changes in canines can be compared with human cancers because both live in the same environment. Despite having a shorter lifespan, dogs develop neoplasias, which enables quicker research into the role of environmental factors in the disease's aetiology. In dogs, osteoma is a rare benign primary bone tumour. There is no recognised cause for osteoma. The origin of the lesion, whether reactive or neoplastic, has been in dispute (Ogbureke *et al.*, 2007).

Ameloblastic fibroma (AF) and ameloblastic fibro-odontoma (AFO) are examples of mixed odontogenic tumors that are composed of both epithelial and mesenchymal components. AFO has been reported in both the mandible and maxilla in dogs up to 1 year of age (Nold *et al*., 1984 and Poulet *et al*., 1992). AF has only been reported in one 4-year-old dog (Miles *et al*., 2011). Given the scarcity of identified instances, the exact pathophysiology of these tumors has not been well investigated in either humans or animals. According to Poulet *et al*. (1992), neoplastic odontogenic epithelium emits signalling molecules that cause the underlying ectomesenchymal tissue to proliferate widely and non-cancerously (dental pulp). A layered dental matrix is formed as a result of odontoblast differentiation and/or ameloblast stimulation (AFO). Physical interference (trauma) with a developing tooth might be a significant risk factor for AF as well as AFO.

Odontogenic lesions are frequently the cause of neoplastic tumours in puppies. Rare odontogenic tumours called odontomas have been observed in a range of animal species (Wiggs and Lobprise, 1997). Odontomas have an unknown etiopathogenesis in both human and nonhuman species. Odontomas have been linked to dentigerous cyst formation in the human literature, although this has never been proven in veterinary research (Head *et al*., 2002). The prognosis for typical canine acanthomatous ameloblastomas is good with complete excision. They are locally invasive odontogenic epithelial tumours. Canine acanthomatous ameloblastomas (CAA) and human ameloblastomas (AM) have clinicopathologic and molecular characteristics, making spontaneous CAA an effective translational model of illness. However, knowledge of the molecular underpinnings of CAA and how it differs from AM is lacking. Recent findings point to mutations that, when they are mutually exclusive, activate the RAS-RAF-MAPK pathway and indicate shared molecular pathways in AM and CAA (Peralta *et al*., 2019). The most typical origin of destructive tumours of the jaw in young canines is dental epithelial. According to studies, mononuclear cells, which are probably derived from monocytes (Wise *et al.,* 1985) start to build up in the dental follicle of developing teeth right before eruption. Osteoclasts, which appear shortly after these cells and are in charge of resorption of bone tissue and deciduous dental tissue visible during tooth eruption, are thought to be precursors for these cells. The findings suggest that dogs' malignancies originate from dental follicular mononuclear cells. Follicles without tumours frequently exhibited aberrant cell proliferations with a distribution that matched that of follicular monocytes. These cells resembled the tumour.

Squamous cell carcinoma (SCC) is the 2nd most common oral malignant tumor in dogs (Hoyt and Withrow, 1984). Similar to humans, male dogs have a 2.4 times higher risk of developing oropharyngeal malignancy compared to female dogs. The tumours are staged similarly to those in humans, but only 17-25% of the carcinomas are of the squamous cell type. The role of human papillomavirus in certain groups of head and neck SCC is being widely investigated (Thomas and Primeaux, 2012). Though some canine papilloma viruses can stimulate SCC formation, their role has not been addressed properly (Teifke *et al*., 1998) and therefore warrants further investigation. Analysing the expression of HMGA gene in canine and human neoplasias revealed similar results in both species. While HMGA2 was discovered to be significantly elevated in both the primary samples and the examined cell lines, its sister gene, HMGA1, displayed variation in expression between two and threefold. In this case, HMGA2 expression displays possible marker traits in both species, whereas HMGA1 lacks the necessary traits (Sterenczak *et al*., 2014).

Dogs frequently develop malignant melanoma. One of the most widespread tumours in dogs, canine oral melanoma has a poor prognosis and a high rate of metastasis. Melanomas represent ~7% of all malignant tumors in dogs (Gillard *et al*., 2014). Canine melanomas have been extensively studied for the expression of metalloproteinases, COX-2, KIT, SOX, EGFR and proteins involved in epithelium-mesenchymal transition (Veloso *et al*., 2020). The relevance of NRAS gene, ERK1/2 and PTEN KIT is yet unknown (Prouteau and André, 2019). Certain autoimmune diseases affect dogs. One such disease is myasthenia gravis, wherein an autoantibody is directed against acetylcholine nicotinic receptors (AChR) in the neuromuscular junctions of skeletal muscles (Dewey *et al.*, 2000). Canine histiocytic proliferative disorders, a distinct group that comprises a range of disorders i.e. from reactive to neoplastic. The group includes various disorders such as cutaneous

histiocytoma, cutaneous and systemic reactive histiocytosis, malignant histiocytosis and localised histiocytic sarcoma. Reactive histiocytosis originates from dermal dendritic cells. In the present review, a neural disorder of the trigeminal nerve resulting in salivation abnormality in dogs is observed. It can be speculated that trigeminal nerve neoplasms in dogs may involve invasion or compression of parasympathetic axons associated with the nerve or the branches of the nerve. This may lead to loss of parasympathetic innervation.

CONCLUSION

The present review comprises various cases and case-series describing various parameters like clinical, radiographic and histopathological features of different oral pathologies in canines. It was observed that malignant neoplasms like melanoma, SCC, and sarcomas were the most common ones in malignant lesions. A dentigerous cyst, which is commonly associated with an impacted permanent tooth, has been observed with deciduous teeth. Local bone destruction and tooth loss resulting from pathologies like cysts and neoplasms associated with unerupted teeth were also observed. Partial anodontia associated with unerupted teeth is the most common clinical finding in canines. Prognosis was found to be good in cases of odontomas. Crytococcus infection was documented to be associated with canine maxillary osteonecrosis. Mixed odontogenic neoplasms have also been reported, but rarely. Thus, it was a new challenge in the veterinary dentistry field in terms of diagnosis and therapeutics of various oral pathologies because of their vast array and rare occurrence in canines.

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Figure 1: PRISMA flow diagram

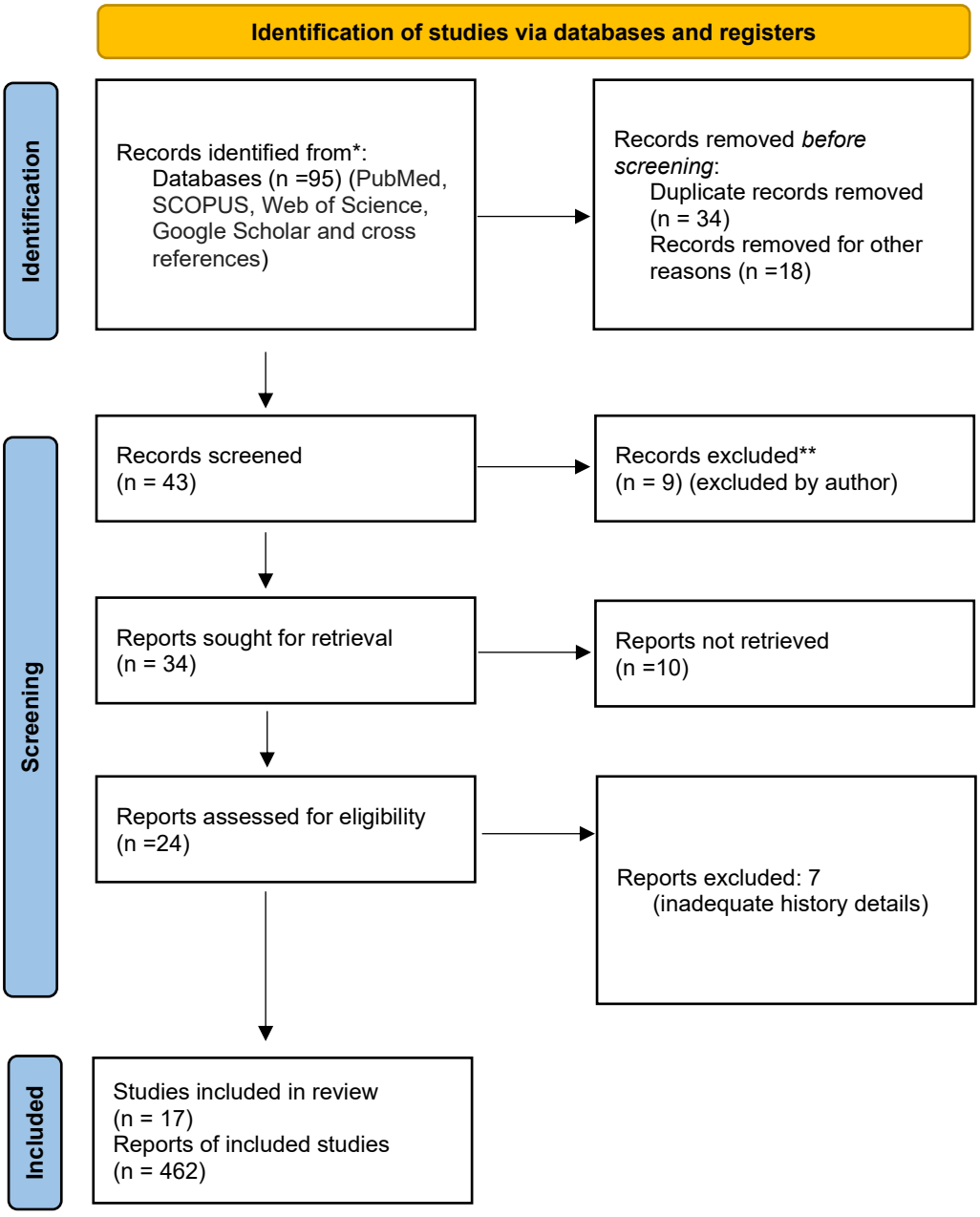

Table I: Clinical findings and investigations of the cases of mandibular periostitis ossificans

Case	Breed/Gender	Clinical findings	Biopsy findings
1	Labrador Retriever, Male	Left mandibular swelling (708-309)	Serosanguinous fluid, Periosteal new bone formation, Acute inflammation, Bone necrosis, Granulation of tissue with angiogenesis
2	Great Dane, Male	Grey firm mass (30mm x 80mm from 708 to ramus)	Periosteal new bone formation, No inflammation
3	Dogue de Bordeaux, Male	Hard swelling on the right mandible (3cm associated with I molar)	Sterile fluid, Periosteal new bone formation
4	Labrador Retriever, Male	Swelling with 309	-
5	Great Pyrenees, Male	Swelling with 309	Periosteal new bone formation, No inflammation, Well-differentiated lamellar bone

Table II: Clinical findings, histopathologic evaluation, treatment and follow-up

Case	Clinical features	Duration	Treatment	Histopathology	Follow up
1	Halitosis with generalized necrotizing ulcerative periodontitis and ulcerative labial mucositis, Missing 102,103,202,203	2 years	Antibiotics and corticosteroids	Lympho-plasmacytic infiltration in epithelium and lamina propria and chronic ulcerative paradental stomatitis (CUPS)	Post 8 months - no lesions
2	Oral discomfort	10 months	108,208,309,409 extracted and biopsy of ulcer done	Lymphoplasmacytic infiltration in epithelium and lamina propria and CUPS	Ulcers on labial mucosa

Table III: Clinical features, investigations and treatment of the case of Ameloblastic fibro-odontoma

Case	Canine breed	Age / Gender	Clinical features	Histopathology
1	Labrador Retriever	4 months, Female	Swelling around left maxillary canine tooth	**Epithelium:** Neoplastic odontogenic, plexiform and follicular pattern **Stroma:** Ectomesenchymal, loosely arranged, Tubular dentin formation, Anisocytosis, Anisokaryosis
2	Beagle cross	8 months, Female	Swelling around missing left maxillary molar region	
3	Mixed breed	9 months, Female	Gingival swelling related to extracted right maxillary premolar region	

Table IV: Distribution of 279 cases according to their diagnoses

Total dogs	Females	Males
279 (77 breeds)	133	144
Oral Pathology	**No. of Cases**	**Epulis (%)**
POF	58 (21%)	30
Acanthomatous ameloblastoma	10 (4%)	5
Inflammatory myofibroblastic tumor	3 (1%)	5