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Diagnostic value of cytological analysis of tumours and tumour-like lesions of the oral cavity in dogs and cats: A prospective study on 114 cases

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ABSTRACT

Neoplastic or non-neoplastic masses are common findings in the oral cavity of cats and dogs. The aim of this prospective study was to compare the results of cytological examinations of lesions of the oral cavity following fine-needle aspiration (FNA), fine-needle insertion (FNI), and impression smear (IS) with histopathological results being considered as the diagnostic gold standard.

In total, 85 dogs and 29 cats were included in the study. Cases were included when histology and cytology (FNA, FNI, and/or IS) were available from the same lesion; κ-agreement and accuracy between cytological and histopathological results were calculated. Eighteen cytological specimens were excluded, with a retrieval rate of 84.2%. Of the 96 samples analysed, FNA, FNI, and IS were available from 80, 76, and 73 animals, respectively. Overall, 60/67 (89.6%) and 21/29 (72.4%) lesions were neoplastic in dogs and cats, respectively, with the remaining being non-neoplastic. For all lesions, κ-values obtained by FNA, FNI, and IS were in dogs 0.83 (95% confidence interval [CI]: 0.77–0.90), 0.87 (95% CI: 0.81–0.93) and 0.75 (95% CI: 0.67–0.84), respectively, and in cats 0.92 (95% CI: 0.87–0.96), 0.92 (95% CI: 0.88–0.97) and 0.86 (95% CI: 0.79–0.92), respectively. The diagnostic accuracies of FNA, FNI, and IS in dogs with neoplasia were 98.2%, 98.1%, and 91.8%, respectively, and in cats with neoplasia were 95.6%, 95.6% and 95.8%, respectively. In conclusion, the high agreement with histopathology suggests that cytological examinations by FNI, FNA, and IS are all appropriate methods to correctly diagnose lesions of the oral cavity in dogs and cats.

Introduction

Masses in the oral cavity are commonly observed in dogs and cats, with a large variety of diagnoses spanning from benign and malignant tumours to tumour-like conditions (Spodnick and Page, 1995; Goldschmidt and Hendrick, 2002). The most frequent oropharyngeal cancer in dogs is melanoma (Smith et al., 2002), and the majority of these are malignant (Bradley et al., 1984; Spodnick and Page, 1995), whereas the most common oral neoplasm in cats is squamous cell carcinoma (SCC) (Bradley et al., 1984; Spodnick and Page, 1995; Liptak and Withrow, 2006). SCCs account for 70% of feline and 25% of canine oral neoplasms and may arise from virtually any surface of the oral cavity (Bradley et al., 1984).

Cytological examination is a minimally invasive diagnostic tool that is routinely used in companion animal medicine. The results of cytology correlate well with histopathological findings for many tumours (Bonfanti et al., 2006; Ghisleni et al., 2006; Simon et al., 2009) including angiosarcoma, mammary tumours, and osteosarcoma in dogs (Allen et al., 1986; Bertazzolo et al., 2005; Reinhardt et al., 2005; Simeonov and Stoikov, 2006; Simon et al., 2009; Sontas et al., 2012), as well as thymoma, lymph node and splenic lesions, and abdominal, cutaneous or subcutaneous masses in dogs and cats (Ménard et al., 1986; Rae et al., 1989; Chalita et al., 2001; Bonfanti et al., 2004; Ghisleni et al., 2006; Ovejero Braun and Hauser, 2007). However, the diagnostic reliability of cytology in the evaluation of oral masses has not been previously investigated in dogs and cats.

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In humans, only a few reports have explored the diagnostic potential of fine-needle aspiration (FNA) for oral lesions and for lesions of the maxillofacial region. Nonetheless, the limited information available supports the clinical utility of cytological analysis, with a sensitivity ranging from approximately 75% to 96%, and a specificity and positive predictive value reaching almost 100% (Cramer et al., 1995; Singh et al., 2011).

The aim of this prospective study was to determine the diagnostic reliability compared to histopathology of cytology obtained by FNA, fine-needle insertion (FNI; non-aspiration technique), and impression smear (IS) from masses of the oral cavity of dogs and cats.

Materials and methods

Criteria for selection of cases

Dogs and cats with masses of the oral cavity examined at the authors' institutions (MG, GR and WB) between 2007 and 2010 were included. Most animals were from the northern part of Italy and were referred to large clinics in this region. Cases were included when cytological and histopathological specimens were available from the same lesion.

Procedures

From oral cavity lesions, cytological specimens were obtained by FNA and FNI using different gauge needles (21–25 G) and 2.5–5 mL syringes for aspiration. All samples were obtained by inserting the needle through the oral mucosa. The insertion path was placed in the anatomical region included in the planned excisional procedure of the mass. IS were obtained from surgically excised lesions and prepared after accurate blotting of the specimen with clean absorbent paper to remove excess blood and tissue fluid. When possible, FNA, FNI, and IS were performed on the same lesion.

All cytological smears were stained with May-Grünwald-Giemsa. For each case, one to five slides from each sampling technique were reviewed by two European College of Veterinary Clinical Pathologists (ECVCP) Board-certified clinical pathologists (UB, WB) who were unaware of the histopathological diagnosis. Histopathological specimens were fixed in 10% neutral buffered formalin and bisected along their longer axis with a scalpel blade. Tissues were embedded in paraffin and stained with haematoxylin and eosin. All samples were reviewed by a single European College of Veterinary Pathologists (ECVP) Board-certified pathologist (PR) who was not aware of the cytological diagnosis.

The classification by Head et al. (2003a, 2003b) was used to categorise the neoplasms. When necessary, immunohistochemical staining was performed to allow for a definitive histopathological diagnosis.

Data analysis

For all cases, each cytological diagnosis made by FNA, FNI, or IS was compared with its paired histopathological diagnosis, with the latter set as the gold standard. Agreements between cytological methods and histopathology were assessed using Cohen's kappa coefficient (κ) and were calculated for all lesions and tumours in dogs and cats.

The extent of concordance between cytological and histopathological diagnosis was classified as complete agreement, no agreement, or undetermined. Complete agreement was defined as concordance for both cell lineage (i.e. epithelial, mesenchymal, haematopoietic or melanocytic) and cell type (e.g. squamous epithelium, odontogenic epithelium, fibroblastic cells). No agreement was defined as the lack of concordance for cell lineage (e.g. mesenchymal instead of epithelial) or cell type in case of neoplasia (e.g. acanthomatous ameloblastoma instead of squamous cell carcinoma), or if a cytological diagnosis of any non-neoplastic lesion (e.g. inflammation) was obtained instead of diagnosis of neoplastic lesion and vice versa. Agreement was classified as undetermined if the cytological specimen was unsatisfactory because of hypocellularity, haemodilution, or necrosis. A value of $\kappa < 0$ indicated no agreement, $\kappa = 0$–0.20 indicated slight agreement, $\kappa = 0.21$–0.40 indicated fair agreement, $\kappa = 0.41$–0.60 indicated moderate agreement, $\kappa = 0.61$–0.80 indicated substantial agreement, $\kappa = 0.81$–0.99 indicated almost perfect agreement, and $\kappa = 1$ indicated perfect agreement (Landis and Koch, 1977).

In addition, the diagnostic reliability of each of the three cytological methods to identify neoplastic and non-neoplastic lesions was further tested in dogs and cats separately by calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. Sensitivity, specificity, PPV, NPV, and accuracy were arbitrarily considered low if <70%, moderate if ≥70% and <80%, high if ≥80 and <90, and very high if ≥90%.

The clinical utility of the three cytological methods was also calculated for the most represented tumours collected in this series. For this purpose, κ-agreement as well as sensitivity, specificity, PPV, NPV, and accuracy were calculated if >10 cases were available for each cytological method in both species. For each analysis, histopathology was considered the gold standard. Statistical analysis was conducted using Microsoft Office Excel 2007.

Results

Animals and samples

A total of 114 animals were initially recruited for the study, including 85 dogs and 29 cats. The dogs consisted of 39 intact males, 25 intact females, 12 spayed females, and 9 neutered males. The median age of dogs was 9 years (range, 1–17) (Table 1). The cats included were 13 spayed females, 10 neutered males, 3 intact males, and 3 intact females. The median age of cats was 11 years (range, 1–17 years) (Table 2).

Oral lesions

Of the 114 animals, 110 (96.5%) had a single oral lesion and 4 (3.5%) had multiple lesions (Table 3). Sixteen (14.0%) cases from dogs were excluded because cytological results were unsatisfactory with all methods (i.e. FNA, FNI, and IS) and so no cytological specimen was available for review (Table 4). Two additional cases were ex-

Table 1
Canine breeds included in the study.

Breed	*n* (%)
Mongrels	30 (35.3)
Labrador Retrievers	8 (9.4)
Boxers	6 (7.1)
Yorkshire Terriers	4 (4.7)
Rottweilers	3 (3.5)
American Cocker Spaniel	2 (2.4)
Bernese Mountain dogs	2 (2.4)
Dachshund	2 (2.4)
English Setter	2 (2.4)
Fox Terrier	2 (2.4)
German Shepherd	2 (2.4)
Pinscher	2 (2.4)
Poodle	2 (2.4)
Shih-Tzu	2 (2.4)
Alaskan Malamute	1 (1.2)
American Staffordshire Terrier	1 (1.2)
Andes Shepherd	1 (1.2)
Bobtail	1 (1.2)
Chihuahua	1 (1.2)
Doberman	1 (1.2)
Dogue de Bordeaux	1 (1.2)
English Cocker Spaniel	1 (1.2)
Golden Retriever	1 (1.2)
Italian Bloodhound	1 (1.2)
Maltese	1 (1.2)
Maremma Sheepdog	1 (1.2)
Newfoundland	1 (1.2)
Rhodesian Ridgeback	1 (1.2)
Schipperke	1 (1.2)
Schnauzer	1 (1.2)
Total	85 (100)

Table 2
Feline breeds included in the study.

Breed	*n* (%)
Domestic shorthaired	30 (65.5)
Persian	8 (13.8)
Exotic shorthaired	6 (6.9)
Siamese	1 (3.4)
Scottish Fold	1 (3.4)
Norwegian Forest	1 (3.4)
Sphynx	1 (3.4)
Total	48 (100)