



Diagnosis of canine gastric adenocarcinoma using squash preparation cytology

Fulvio Riondato ^{a,1,*}, Barbara Miniscalco ^a, Enrica Berio ^a, Elvio Lepri ^b, Silvia Rossi ^c, Enrico Bottero ^{d,1}

^a Department of Veterinary Sciences, University of Torino, Via L. Da Vinci 44, 11095 Grugliasco, Italy

^b Department of Veterinary Medicine, University of Perugia, Via S. Costanzo, 4, 06126 Perugia, Italy

^c San Francesco Veterinary Clinic, Via ciardi 5, 20148 Milano, Italy

^d Poliambulatorio Veterinario Argentina, Via Levà 58 Arma di Taggia, Imperia, Italy

ARTICLE INFO

Article history:

Accepted 29 April 2014

Keywords:

Canine
Gastric adenocarcinoma
Diagnosis
Squash cytology

ABSTRACT

Adenocarcinoma is the most common gastric tumour in dogs. Clinical signs and laboratory results are often non-specific, with histopathological examination of gastric biopsies being required to reach a definitive diagnosis. Use of cytology would potentially shorten the time to diagnosis and allow early interventional measures to be implemented. However, there are relatively few studies of the cytological features of gastric samples. The present study was designed to investigate whether cytology might be useful for diagnosis of canine gastric adenocarcinomas and to evaluate the performance of squash preparation cytology for this purpose. Squash preparations of gastric biopsies from 94 dogs were reviewed to determine the presence or absence of specific cytological features associated with adenocarcinomas and to compare findings with the results of histopathological examination of gastric biopsies. The presence of signet ring cells, microvacuolation, cellular pleomorphism and single cell distribution of epithelial cells were positively associated with a diagnosis of gastric adenocarcinoma. Combined evaluation (parallel testing) for the presence of signet ring cells and microvacuolation demonstrated excellent results for recognition of adenocarcinomas. Cytological examination of squash preparations from gastric biopsies and identification of signet ring cells and cytoplasmic vacuolation can allow rapid and reliable diagnosis of canine gastric adenocarcinomas.

© 2014 Elsevier Ltd. All rights reserved.

Introduction

Gastric tumours represent <1% of all canine neoplasms (Fonda et al., 1989; Gualtieri et al., 1999), with adenocarcinomas representing 70–80% of all gastric tumours (Withrow, 2012). Clinical signs, haematology and biochemistry results, are relatively non-specific (Gualtieri et al., 1999; Willard, 2012). Radiology and ultrasonography can indicate the presence of ulcers, masses or thickening of the gastric wall, which are suggestive of the presence of neoplasia (Kaser-Hotz et al., 1995; Rivers et al., 1997; Lamb and Grierson, 1999; Withrow, 2012). However, histopathological examination of tissue biopsies is the most reliable way of reaching a definitive diagnosis (Gualtieri et al., 1999; Willard, 2012).

In first-opinion veterinary practice, obtaining a histopathological diagnosis usually requires biopsies to be taken for submission

to a diagnostic laboratory, often with a delay of 3–5 working days before results are received. Therefore, a reliable technique for identifying adenocarcinomas using cytology would potentially shorten the time to diagnosis and allow treatment to be initiated more rapidly in affected animals.

The accuracy of cytology for diagnosing gastrointestinal diseases has not been investigated thoroughly in veterinary medicine. Ultrasound-guided fine needle aspiration (FNA) frequently yields non-diagnostic samples, often due to low cellularity (Crystal et al., 1993; Bonfanti et al., 2006). Impression smears from surgical and endoscopic biopsies, and brush techniques, are reliable and show good agreement with histopathology (Jergens et al., 1998; Bonfanti et al., 2006; Von Babo et al., 2012). Although limited in number, studies describing squash preparation cytology of endoscopic biopsies from human beings and companion animals have shown acceptable results. Batra et al. (2008) reported that squash preparation cytology of endoscopic biopsies correctly diagnosed 76% of human gastric adenocarcinomas, while other studies have reported a sensitivity (Se) >90% for diagnosis of gastric (Kochhar et al., 1990; Rout et al., 1993) and central nervous system malignancies (Shah et al., 1998; Mitra et al., 2010).

* Corresponding author. Tel.: +39 011 6709068.

E-mail address: fulvio.riondato@unito.it (F. Riondato).

¹ These authors contributed equally to the work.

The use of the squash cytology technique in veterinary medicine has revealed a concordance of 90% with histopathology for nervous system lesions (De Lorenzi et al., 2006) and a Se of 94% for nasal cavity masses (De Lorenzi et al., 2008). This technique has potential for diagnosis of gastric adenocarcinomas, with the advantages that samples for both histopathology and cytology can be collected simultaneously, preparation of cytology specimens is technically easy and rapid, and examination of squash specimens allows evaluation of cellular components and tissue architecture.

Studies of the squash cytology technique for gastrointestinal lesions in companion animals are lacking, and few papers describe the cytological features of canine gastric adenocarcinomas (Gualtieri et al., 1999; Dell'Orco et al., 2005). The present study was designed to evaluate squash cytology as a method for identifying cytological features of canine gastric adenocarcinomas and to determine the accuracy of this diagnostic approach.

Materials and methods

Case selection

A database of canine gastrointestinal endoscopies, undertaken between January 2006 and December 2012, was screened to identify suitable cases presenting with chronic gastrointestinal signs, including anorexia, weight loss, vomiting, melaena, hematochezia and tenesmus, of more than 14 days duration. Cases were included if a biopsy, a concurrent squash preparation for cytology and a conclusive histopathology report were available. Dogs affected with gastric adenocarcinoma or non-epithelial tumours were preferentially recruited, then additional clinical cases were selected to include dogs with unremarkable findings ('normal stomach'), gastritis or benign epithelial neoplasia on histopathological examination.

Histopathology and cytology

Four to eight endoscopic biopsies from each dog had been collected under anaesthesia using PE2-OVAL-22-230-EIN forceps (Endo-Technik). The biopsies were fixed in 10% neutral buffered formalin and processed routinely for histopathology. A European College of Veterinary Pathology board-certified pathologist (E.L.) reviewed the histopathological diagnoses, based on examination of haematoxylin and eosin-stained sections, according to the World Health Organization histological classification of tumours of domestic animals (Head et al., 2003).

Gastric epithelial tumours were subdivided into adenomas, adenocarcinomas and undifferentiated carcinomas. Adenocarcinomas are typically composed of cuboidal cells, with intracytoplasmic vacuoles containing acid mucin, or large cells with eccentrically placed nuclei and distension of the cytoplasm with mucin (signet ring cells) (Head et al., 2002). Other cases were classified as normal gastric epithelium, gastritis, benign epithelial neoplasm or non-epithelial neoplasm.

Two to four additional biopsies per dog had been used to prepare squash preparations for cytological examination. Biopsies had been crushed between two slides, pulled apart without smearing, air-dried and stained with a rapid Romanowsky stain. Two cytopathologists, designated A (S.R.) and B (B.M.), reviewed all cytological preparations in an independent, blinded manner. A third cytopathologist, designated C

(F.R.), examined slides in which the diagnoses conflicted. Each of the cytopathologists was blinded to the histopathological diagnosis and the history, clinical findings and endoscopic observations. The presence or absence of the following cytological features were specifically recorded: signet ring cells (medium-sized to large cells, typically round, each with a large vacuole displacing the nucleus eccentrically), cytoplasmic microvacuolation (discrete clear cytoplasmic vacuoles primarily with a perinuclear distribution), infiltration by neutrophils or lymphocytes, necrosis, cellular pleomorphism, presence of increased extracellular matrix, atypical mitoses, tubular or acinar cell arrangement and the presence of epithelial cells as single intact cells. This last feature is particularly suggestive of epithelial neoplasia in squash preparations, where cells tend to retain their original organisation and many isolated nuclei are present.

Statistical analysis

Statistical analysis was performed using SPSS version 19 (IBM) using consensus results (two out of three observers in agreement). Contingency tables were prepared for each feature and Pearson's χ^2 with z test for column proportion comparisons and Bonferroni adjustment for multiple comparisons were calculated to test the relationship between the presence and absence of each feature with the histopathological diagnosis. The result was considered to be significant if $P < 0.05$.

Se and specificity (Sp) for the detection of adenocarcinoma were calculated for each feature (Stockham and Scott, 2008). The agreement between observers A and B was calculated using the Cohen κ coefficient and used to identify operator-dependent features. Concordance was described as poor ($\kappa < 0.2$), fair ($\kappa = 0.21-0.40$), moderate ($\kappa = 0.41-0.60$), good ($\kappa = 0.61-0.80$) or excellent ($\kappa = 0.81-1.0$) (Landis and Koch, 1977). Two features were selected from the results of the tests (Pearson's χ^2 , Se, Sp and κ agreement). The performance of the combined assessment of selected features in parallel testing was evaluated in terms of accuracy, κ , Se, Sp, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-) and diagnostic odds ratio (DO) (Fletcher and Fletcher, 2012).

Results

A total of 94 dogs were included in the study, with histopathological diagnoses of adenocarcinoma ($n = 32$), gastritis ($n = 38$), benign epithelial neoplasia ($n = 7$), non-epithelial neoplasia ($n = 7$; two leiomyosarcomas, two gastrointestinal stromal tumours and three lymphomas) and 'normal stomach' ($n = 12$).

A comparison of cytological features and histopathological diagnosis is shown in Table 1. In cytological preparations, the presence of signet ring cells (Fig. 1), cytoplasmic microvacuolation (Fig. 2), cellular pleomorphism and single cell distribution of epithelial cells were typically seen in samples from dogs with adenocarcinomas (Table 1). Cytological features not significantly associated with a diagnosis of adenocarcinoma included the presence of lymphocytic infiltration, necrosis and increased amounts of extracellular matrix.

There was a significant association between the presence of atypical mitotic figures and a histological diagnosis of adenocarcinoma (atypical mitotic figures more likely to be present) when compared

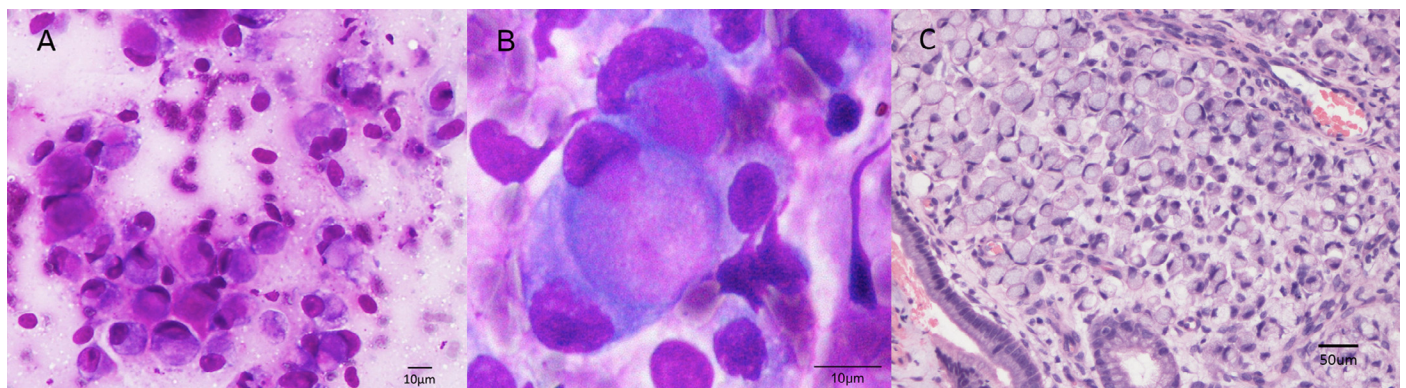


Fig. 1. A and B. Squash preparation of a gastric biopsy from a dog with gastric adenocarcinoma showing signet ring cell morphology. Loosely cohesive medium-sized to large epithelial cells with a large cytoplasmic vacuole that contains pink amorphous material, displacing the nucleus eccentrically. Romanowsky stain. Original magnifications 400 \times (A) and 1000 \times (B). C. Histopathological section of a gastric biopsy from a dog with adenocarcinoma. Signet ring cells are the large cells with clear cytoplasm that displaces the nucleus to the periphery of the cell. Haematoxylin and eosin. Original magnification 200 \times .

Download English Version:

<https://daneshyari.com/en/article/5797991>

Download Persian Version:

<https://daneshyari.com/article/5797991>

[Daneshyari.com](https://daneshyari.com)