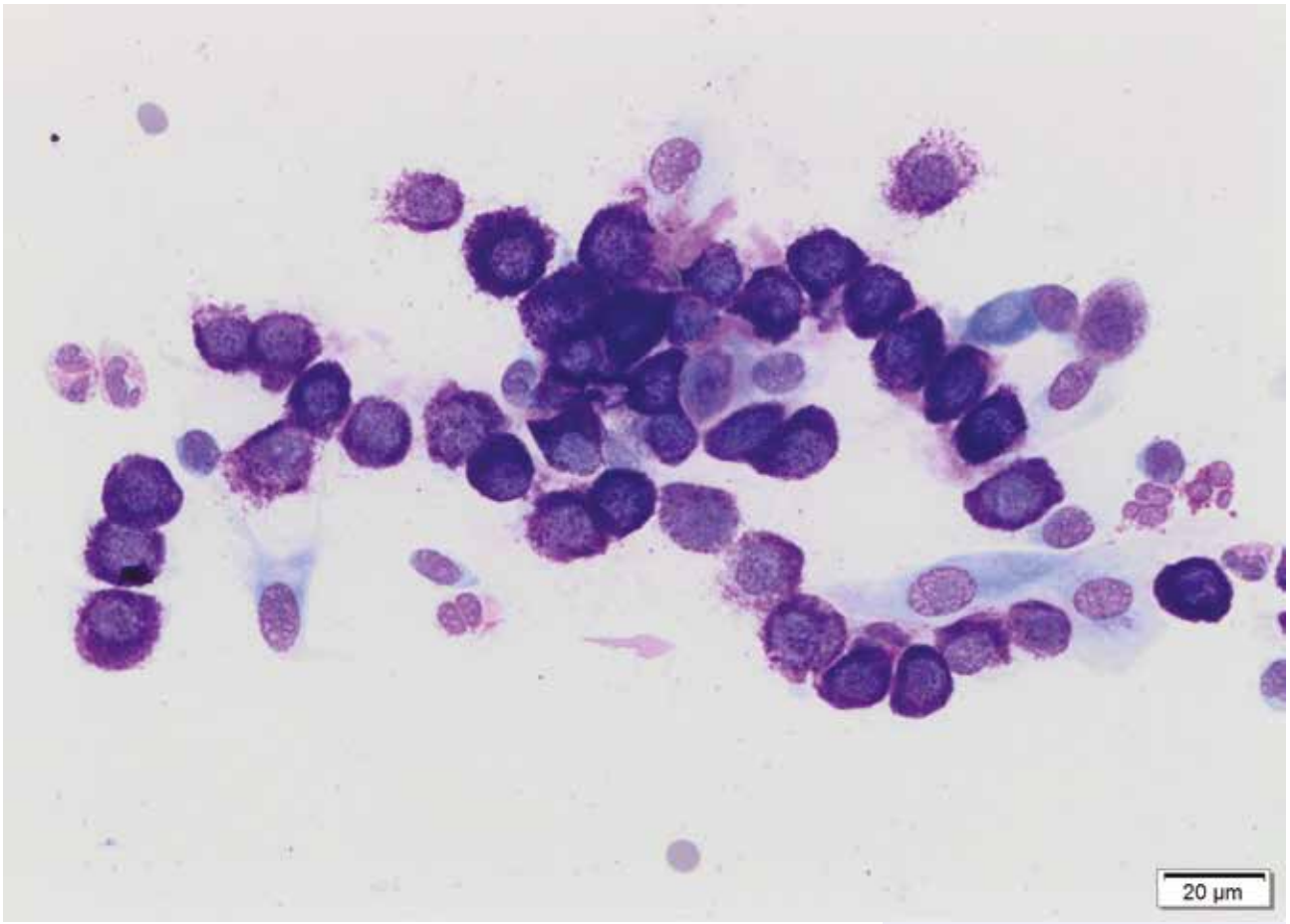


FIGURE 1: Image from a highly granulated cutaneous mast cell tumour. The mast cells pictured have abundant fine, bright purple granules. Nuclear detail is somewhat obscured, but the size of the nuclei is appreciated. Nuclei are of uniform size and shape. Also present in this image are eosinophils and fibroblasts, as well as a small amount of pink proteinaceous material suggestive of collagen. These are frequent findings in mast cell tumour cytology.

Can cytology provide prognostic information in canine cutaneous mast cell tumours?

Amy Weeden of Gribbles Veterinary, Auckland, investigates the predictive value of cytology.

CANINE CUTANEOUS MAST cell tumours (MCTs) are commonly encountered in practice. These tumours are readily recognised on cytology by their characteristic bright purple granules (Figure 1). This is generally the straightforward part of the diagnostic process (when there is a straightforward

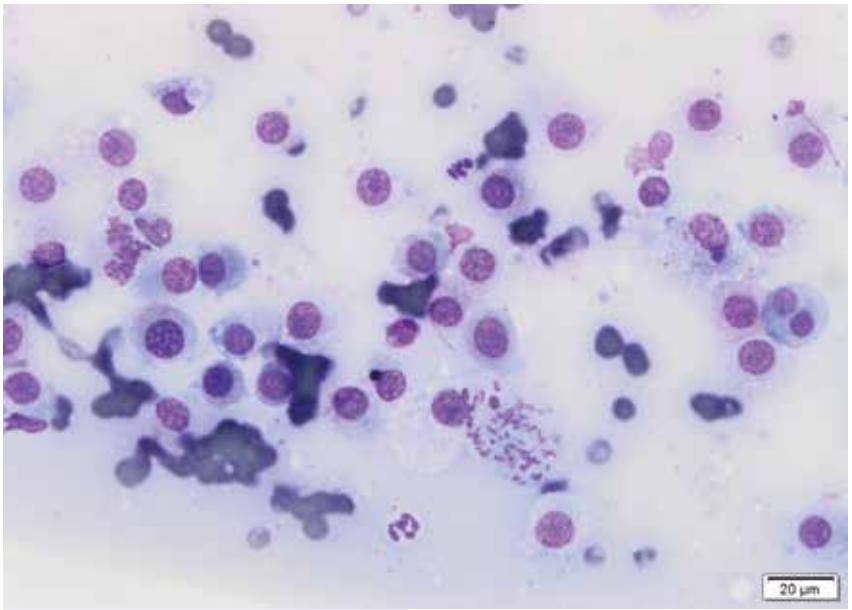


FIGURE 2: Two mitotic figures and a bi-nucleated mast cell are present in this 50x magnification field. Note the eosinophil at the centre.

FIGURES 2-3: Images from a poorly granulated cutaneous MCT in a dog with lymph node metastasis. The mast cell population is more pleomorphic in this lesion, and the round cells contain very low numbers of pink to purple granules.

MCT HISTOLOGIC GRADING IS CONSIDERED THE **"MOST IMPORTANT SINGLE PROGNOSTIC FACTOR FOR MCT".**

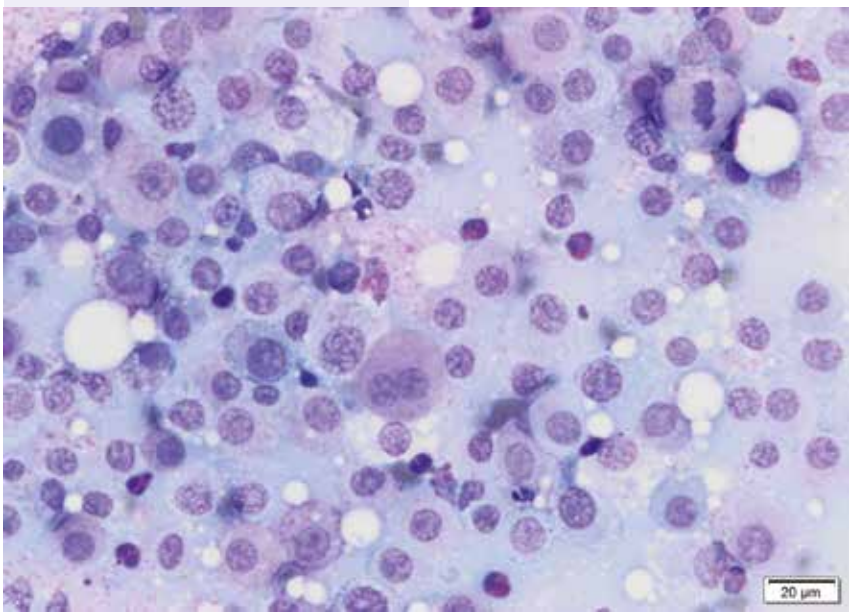
part). The more challenging component of MCT diagnosis and management is being able to predict biologic behaviour and provide prognostic information.

There are two main histologic grading systems in common use for the evaluation of canine cutaneous MCTs. The Patnaik grading system was introduced in the 1980s and has three grades (Patnaik et al., 1984). This scheme utilises cellularity, cell morphology, mitotic index, tissue involvement and stromal reaction to help predict biologic behaviour (Patnaik et al., 1984; Camus et al., 2016). Grade I MCTs are expected to have the most benign behaviour; grade III MCTs are expected to have aggressive behaviour, and grade II MCTs are difficult to predict. The main criticism of this grading system is that many MCTs fall into grade II, which limits the overall usefulness of this scheme.

Kiupel's two-tiered grading scheme for canine cutaneous MCTs was proposed in this decade (Kiupel et al., 2011). This scheme eliminates the difficult-to-predict grade II category and relies heavily on cell morphology. The criteria for separating low- and high-grade MCTs include the number of mitotic figures, multinucleated cells, bizarre nuclear features and karyomegaly. There is less variability in interpretation between pathologists with this system (Camus et al., 2016; Kiupel et al., 2011).

MCT histologic grading is considered the "most important single prognostic factor for MCT" (Blackwood et al., 2012). Both MCT histologic grading systems provide useful prognostic information. However, a comparison of the two schemes revealed that a number of MCTs classified as grade I or low-grade metastasised (Stefanello et al., 2015). No grading system is perfect, prompting

FIGURE 3: Poorly granulated mast cells, including a mitotic figure (top right) and a bi-nucleated cell (centre) are pictured. Eosinophils are scattered throughout this field.



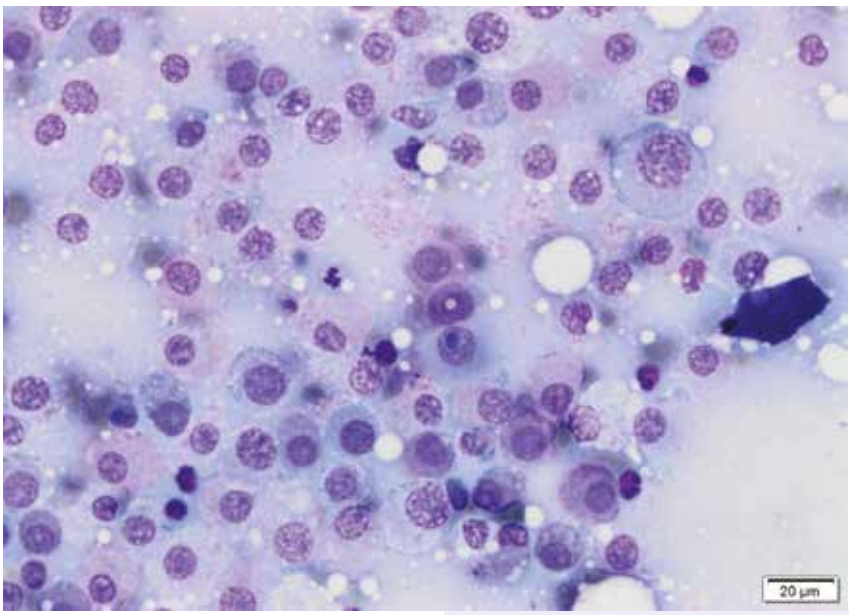


FIGURE 4: This image illustrates anisokaryosis, or marked variation in nuclear size. The mast cell toward the top right has a much larger nucleus than most of the other poorly granulated mast cells in this field. Eosinophils are increased in number.

studies and use of additional variables (cellular proliferation, genetic mutation and protein expression analysis) to better predict MCTs.

Most MCTs contain mast cells with minimal cytologically atypical features (Figure 1). These cells tend to be highly granulated and similar in cell and nuclear size.

Some MCTs appear atypical cytologically, and mast cells from these lesions have decreased cytoplasmic granulation and exhibit features of malignancy (eg variation in nuclear size, multi-nucleation, nuclear pleomorphism and mitotic figures).

Examples of atypical features are shown in photomicrographs from a dog with multiple cutaneous MCTs with lymph node metastasis (Figures 2-4).

A couple of recent studies have explored the predictive value of cytology in canine cutaneous MCTs (Camus et al., 2016; Scarpa et al., 2016). As both histologic grading systems include cell morphology in their classifications, and the Kiupel system relies heavily on morphologic features, it seems reasonable that information gained in cytologic evaluation would approximate that of histology. These two studies support that cytologic findings are predictive of histologic grade (Scarpa et al., 2016) as well as biologic behaviour (Camus et al., 2016).

Cytologic criteria used in these studies included poor granulation, mitotic figures, bi- or multi-nucleation, nuclear pleomorphism and anisokaryosis (Camus et al., 2016; Scarpa et al., 2016).

The findings from these studies have long been suspected by many clinical pathologists as being based on anecdotal information.

Cytologic evaluation of mast cells in MCTs from patients with metastatic disease frequently reveals a poorly granulated mast cell population with atypical nuclear features. These characteristics also make the cytologic diagnosis more challenging.

The cytologic grading schemes overall performed well for prediction of histologic grade and patient outcome, which suggests that cytology can be an early and minimally invasive prognostic tool. However, the studies did reveal the potential for both false negative and false positive results when attempting to predict high-grade disease, and cytologic evaluation of MCT is better used as an adjunct rather than a replacement for histopathology.

The information gained from atypical cytologic features can be used to alert the clinician to the likelihood of an aggressive MCT. This information can assist with proper surgical planning.

Additionally, preoperative staging may be employed (eg regional lymph node cytology, abdominal imaging +/- hepatic and splenic cytology) to better prepare the owner and clinician for overall case management.

In conclusion, cytology can provide prognostic information in canine cutaneous MCTs and can be an effective tool for treatment planning in the contexts of histologic grade, staging and other clinical information. VS

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