**CASE REPORT**

Nasal melanosis in three dogs

Cytologically and histologically confirmed nasal melanosis was detected by rostrocaudal rhinoscopic evaluation of three dogs with unilateral nasal discharge caused by a chronic and severe odontopathic rhinitis. The extraction of affected teeth and prolonged antibiotic therapy led to a complete resolution of nasal disease. The nasal melanosis could be considered a partial metaplastic transformation of mucosal respiratory cells with accumulation of intracytoplasmic melanin.

**INTRODUCTION**

Nasal mucosal melanosis is a rare but well described pathological entity in human beings and has been associated with nasal melanoma (Cove 1979, Matias and others 1988, Hofbauer and others 2002). While some studies have been conducted relating to pigmentary inclusions in the normal olfactory mucosa of mammals (Ardouin and others 1968), to the authors’ knowledge, nasal mucosal melanosis has not previously been described in dogs in association with chronic inflammation.

This study describes clinical features, results of diagnostic tests, endoscopic findings and final outcome in three dogs with benign nasal mucosal melanosis likely related to chronic nasal inflammation.

**CASE HISTORIES**

The three dogs in this study had chronic, unilateral nasal discharge, routine haematological and serum biochemistry profile, and normal nasal and frontal sinuses radiographs or computed tomography (CT) scan (Lightspeed 16; GE Medical Systems) under inhalatory general anaesthesia, rostrocaudal rhinoscopy with a rigid endoscope (diameter 2.7 mm, length 18 cm, forward oblique 30°) and nasopharyngoscopy with a flexible bronchoscope (diameter 5.2 mm, length 85 cm) during the same anaesthetic episode.

From each dog, six to 10 samples were taken both for cytopathological and histopathological evaluation, under endoscopic guidance, from both nasal cavities. All cytopathological samples were air dried, then stained with May-Gruenwald Giemsa stain in automatic slide stainer (7100 Aerospray Slide Stainer; Wescor). All histopathological specimens obtained by endoscopic guidance were fixed in 10 per cent neutral buffered formalin and routinely processed; sections of 4 μm were stained with haematoxylin and eosin stain, periodic acid-Schiff stain, Fontana-Masson stain and Prussian blue stain.

**CASE 1**

A 12-year-old, entire male bichon, weighing 7 kg, was presented with a chronic, progressive, unilateral left nasal discharge of four-months duration. On physical examination, teeth mobility on left upper carnassial tooth and left upper canine tooth were seen.

Head CT scan (Fig 1) revealed severe alveolar bone loss both around the left upper carnassial tooth and left upper canine tooth, with the presence of an oronasal fistula between alveolar cavities and nasal cavity. Rostrocaudal left rhinoscopy showed mucoid exudate covering the left ethmoid nasal turbinates that appeared hypotrophic, dry and diffusely light brown in colour. Five biopsies were taken from different parts of the left nasal turbinates. During rhinoscopy of the contralateral nasal cavity, no abnormalities were found; three biopsies were taken from the right nasal turbinates.

On the basis of physical examination, CT scan and endoscopic examinations, a diagnosis of odontopathic rhinitis was made; both the left upper canine tooth and left upper carnassial tooth were extracted, and the dog was discharged with a 15 day course of 20 mg/kg oral amoxicillin-clavulanic acid (Symulox; Pfizer) twice a day.

The dog recovered uneventfully, and clinical re-examination after two months showed resolution of nasal discharge and sneezing.

Both cytopathology and histopathology on the submitted specimens from the left nasal mucosa were consistent with diffuse melanosis of nasal mucosa associated with mild to severe dysplasia and neutrophilic inflammation. Biopsies collected from the contralateral nasal cavity were all normal.

**Case 2**

An eight-year-old, neutered female cross-breed dog, weighing 15 kg, was presented...
with a history of sneezing and chronic nasal unilateral mucopurulent discharge of five-months duration. On clinical examination, an apical crown fracture with pulpar exposure of the fourth upper right premolar tooth was noted. A radiograph showed both horizontal and vertical alveolar bone loss, associated root involvement and periapical radiolucency due to endodontic disease of the fourth upper right premolar tooth.

Rostrocaudal rhinoscopy showed mucopurulent exudate mainly localised around the right nasal turbinates that appeared hypotrophic and locally ochreous. From this area, four biopsies were taken under endoscopic guidance. The contralateral endoscopic nasal inspection did not reveal any abnormality, and three biopsies were taken from different areas of nasal turbinates.

Following physical examination, radiographic and endoscopic results, a diagnosis of odontopathic rhinitis was made. The extraction of the right carnassial tooth and a two-week course of 20 mg/kg oral amoxicillin-clavulanic acid twice a day led to complete resolution of rhinitis and associated symptoms.

Diffuse melanosis and dysplasia of the right nasal mucosa associated with neutrophilic inflammation were described both in the cytopathological and histopathological reports. No abnormalities were found in the biopsies collected from the contralateral nasal cavity.

Case 3
An 11-year-old, entire male crossbreed dog, weighing 20 kg, was presented with a nine-month history of sneezing and occasional mucopurulent left nasal discharge. On clinical examination, the left carnassial tooth was mobile and periodontal pockets were noted.

An open-mouth radiograph showed increased radiolucency at the level of left nasal cavity with conserved turbinates structure, while in the oblique projections, periapical radiolucency and signs of root resorption were evident.

During rostrocaudal rhinoscopy, the mucosa of the left nasal cavity was completely covered with dense mucopurulent material and, once removed, locally light brown pigmentation was noted mainly at the ethmoturbinates level. Five biopsies were taken from different areas of left nasal turbinates, and four biopsies were taken from the right nasal mucosa that appeared endoscopically normal.

Following clinical evaluation, radiographic and endoscopic results, a diagnosis of odontopathic rhinitis was obtained.

The right fourth upper premolar tooth was extracted, and the dog was discharged with a 15 day course of 20 mg/kg oral amoxicillin-clavulanic acid twice a day. The sneezing disappeared soon after the dental extraction, but a moderate, occasional nasal discharge with nasal sounds was still present four months after the end of antibiotic therapy.

Cytopathology and histopathology from the right nasal cavity were consistent with diffuse melanosis of the nasal mucosa associated with dysplasia and neutrophilic inflammation. Biopsies collected from the contralateral nasal cavity were all normal.

**DISCUSSION**

Melanin is an endogenous, brown-black and finely granular pigment produced when the enzyme tyrosinase catalyses the oxidation of tyrosine to dihydroxyphenylalanine in melanocytes (Cotran and others 1999). In dogs and cats, apart from the usual occurrence in skin and eyes, moderate numbers of pigmented cells have been noted in other normal tissues such as the intestine, the kidney, the leptomeninges (Slauson 2002) and the pineal gland (Calvo and others 1992).

The presence of non-neoplastic melanin-containing cells in tissues or organs that usually produce a much smaller amount of melanin or none at all is termed melanosis or melanocytosis (Klein-Szanto and others 1991).

This uncommon finding is attributable to any or all of the following (Klein-Szanto and others 1991): an increase in numbers of some normally pigmented cells of neural crest origin; elicitation of melanin synthesis in some cells that normally have little melanin or none at all; unusual intracellular transfer of pigment granules from melanocytes into certain normally unpigmented epithelia and endothelia and profusion of melanine-phagocytosing cells.
As stated by Klein-Szanto and others (1991), the melanin synthesis in cells that normally do not produce this pigment can possibly follow a metaplastic process. In fact, certain epithelia and endothelia, particularly neuroectodermal derivatives like some components of the olfactory mucosa, may have an intrinsic developmental plasticity and dormant capacity for melanogenesis and, in addition, melanosis in tissues such as mucous membranes may signify metaplastic conversion.

Metaplasia, especially within epithelia, is usually a response to chronic irritation. Under these conditions, a mature, differentiated cell is replaced by a different type that is not normal to that tissue or organ.

In the three cases described here, the pathogenesis of nasal disease was identified as chronic and severe odontopathic rhinitis. The endoscopic evaluation of these areas showed smaller turbinates in the nasal cavity affected by chronic irritation and a light brown and “dry” aspect of the covering nasal mucosa. This particular endoscopic aspect was diffusely observed in two cases, while it was only localised in few areas of turbinates in case 3. In all three cases, the nasal mucosa of the corresponding controlateral areas was of normal size and colour.

The cytological features of the biopsy samples from affected areas showed analogous findings (Fig 2). All the samples had good cellularity and a prevalence of moderately dysplastic epithelial cells in cohesive groups with increased N:C ratio and moderate anisocytosis. All the cells retained their general structure but had a variable number of intracytoplasmic black granules, sometimes mixed with droplets of purple mucin.

The histological samples showed similar features. With haematoxylin and eosin stain, the cytoplasm of mucosal cells had a brown, finely granular appearance (Fig 3). The Fontana-Masson stain was used to confirm the melanic nature of the granules, and all the histological samples from affected areas stained positively (Fig 4), clearly showing the melanic origin of intracytoplasmic granules.

As ferritin stains black-blue with May-Grünwald Giemsa stain and yellow-brown with haematoxylin and eosin stain, it could be difficult to differentiate between iron-containing pigments and melanin (Fournel-Fleury and others 1994). Prussian blue reaction, specific for iron-containing pigments, was constantly negative in all the samples and therefore excluding the possibility of intracellular iron storage, while the periodic acid-Schiff reaction was positive in many respiratory cells that also stained positively with Fontana-Masson stain.

Since all the dogs suffered from chronic (four to nine month’s duration) nasal inflammation, a partial metaplastic transformation of mucosal respiratory cells with elicitation of melanin synthesis can be postulated in these cases, but to confirm this hypothesis, tyrosinase activity within these cells should be demonstrated.

Conclusions
The association between nasal melanosis and nasal melanoma is a rare but well described event in human medicine (Cove 1979, Guiral and others 1994, Hofbauer and others 2002), even if the function of melanocytes in mucosa is not clear.

In physiological states, the melanocytes in mucous membranes do not produce melanin and contain only non-melanised melanosomes in their cytoplasm. However, they produce substantial amounts of melanin under pathological conditions such as chronic irritation. Axell and Hedin (1982) demonstrated that chemical and physical irritation caused hyperproduction of the melanocytes in the human oral epithelium, resulting in oral pigmented lesions.

As it is accepted that malignant melanomas of skin commonly arise from pre-existing pigmented lesions, thus a pre-existing, dormant, non-functional variant of the melanocyte in normal nasal mucosa may get activated under certain conditions (such as chronic irritation) to neoplasia.

None of the three dogs developed further nasal diseases during the period that followed the extractions of affected teeth. Nevertheless, according to what has been described in human medicine, the possibility of a malignant transformation of pigmented nasal mucosa should be considered.

References

FIG 2. Cytology of the nasal mucosa of case 3. All the cells retain their general structure but show a variable number of intracytoplasmic black granules. May-Grünwald Giemsa. x>1000

FIG 3. Histology of the nasal mucosa of case 3. The cytoplasm of mucosal cells shows a brown, finely granular appearance. H&E. x>650

FIG 4. Histology of the nasal mucosa of case 3. Strong positive reaction with Fontana-Masson stain confirms the melanic origin of the intracellular pigments. x>650
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