



Oral melanoma with pulmonary metastasis in a Nigerian local dog

IA Faramade^{1*}, RE Antia², TK Adebisi³ & OA Lawal⁴

1. *Diagnostic & Extension Division, National Veterinary Research Institute, Vom, Plateau state, Nigeria*
2. *Department of Veterinary Pathology, University of Ibadan, Ibadan, Nigeria*
3. *Veterinary Teaching Hospital, University of Ibadan, Ibadan, Nigeria*
4. *Oyo state Veterinary Hospital Complex, Mokola, Ibadan, Nigeria*

*Correspondence: Tel.: +2348028305284; E-mail: tendercarevet@yahoo.com

Abstract

Melanomas are the most commonly diagnosed neoplasm of the canine oral cavity accounting for about 7% of all malignant tumours in the dog. Less frequently, metastasis via regional lymph nodes and to the lungs and other organs may occur. A case report of oral melanoma with pulmonary metastasis in a Nigerian local dog is hereby presented. Grossly, irregularly shaped, markedly dark, soft mass was located beneath the premolar and molar teeth on the left mandible. The lungs were also covered with numerous raised, dark, glistening nodules of various sizes ranging from 0.2cm-0.5cm in diameter. Cytomorphological evaluation of the mass via impression smear stained with Giemsa revealed monomorphic round cells with deeply basophilic cytoplasm with grey to dark fine intracytoplasmic pigments. Histological section stained with Haematoxylin and Eosin revealed similar cells with fine grey to dark intracytoplasmic pigments.

Keywords: Melanoma, One Health, Oral cavity, Pulmonary Metastasis, Tumor

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Introduction

Melanomas are one of the most commonly diagnosed malignant neoplasms of the canine oral cavity (Dorn & Priester, 1976; Goldschmidt, 1985). It accounts for about 7% of all malignant tumours in dogs (Cotchin, 1955) and is the second most frequent sublingual neoplasm (Marino *et al.*, 1995). The tumor can be located in any part of the oral cavity but the gingiva is the most common site (Brodey, 1960; Delverdier *et al.*, 1991). Melanomas are usually aggressive in nature. They are characterized by focal infiltration but metastasis via regional lymph nodes to the lungs and other organs may occur less frequently (Withrow, 1996). Nearly all melanomas are considered malignant (Bostock, 1979). The diagnosis of oral melanoma may be difficult because variation exists in the degree of pigmentation; some tumors may be completely

unpigmented (Head, 1976). The diagnosis of melanoma in domestic animals usually carries a guarded prognosis. This is because melanomas are usually detected at a late stage when excision may not be curative. Histologically, melanomas may resemble carcinomas, sarcomas, lymphomas and osteogenic tumors. This is why immunohistochemistry is a vital diagnostic tool for the confirmation of a diagnosis of melanoma and to determine the prognosis and treatment plan (Smith *et al.*, 2002).

Melanoma accounts for less than 1% of the tumors of feline oral cavity, (Miller *et al.*, 1993). It consists of 15% of all skin tumors in equine (Johnson, 1998), in which it is capable of widespread metastasis (Valentine 1995). Melanocytic tumors can also occur in domestic animals such as cattle, sheep, pigs and

alpaca (Reddy *et al.*, 1998) and laboratory animals, (Andre *et al.*, 1993). In addition, a case of poorly pigmented cutaneous melanocytoma has been reported in the ferret (Tunney & Well, 2002). In humans, according to Desmond & Soong, (2003), there is a substantial variation in the incidence of melanoma. The highest incidence in the world is found in Auckland, New Zealand while the lowest incidence is reported in China, Japan, and Singapore. About 20% of worldwide incidence is reported to affect black Africans and Asians. Melanoma represents a significant health challenge with more than 76,000 cases diagnosed and almost 10,000 mortality annually in the United States of America alone (Howlader *et al.*, 2013).

Sunlight, pre-existing naevus, some genetically determined diseases such as xeroderma pigmentosa and Von Recklinghausens disease (McGovern, 1970) may predispose to the disease. Predilection sites of melanoma in dogs include mouth, lips, skin, eyes and digits while it is more prevalent in the trunk (Desmond & Soong, 2003) in men and in the extremities in women. The foot is the commonest site, with 80% of the cases in Nigeria located there (Yakubu & Mabogunje, 1995). The aim of this report is to document the occurrence of oral melanoma with pulmonary metastasis in a Nigerian local dog as this is rarely found in existing literature. The report is also intended to raise awareness of dog owners on the need to seek veterinary intervention as soon as

they observe any growth on their pets in order to increase their chance of survival.

Case Report

History

A nine year-old Nigerian local dog was presented at the Veterinary Hospital, Mokola, Ibadan with clinical signs of salivation, halitosis, dysphagia and dyspnoea. The animal was slightly emaciated. The temperature was 38.6°C and the PCV was 28%. The MCV and MCH were 62fl and 20pg respectively (moderate normochromic normocytic anaemia). The total white blood cell count was within the reference interval. Upon clinical examination, there was an irregularly shaped, very dark, soft mass located beneath the base of the premolar and molar teeth (gingival area) on the left mandible Plate I.

Cytomorphological evaluation

An impression smear of the oral mass was made and stained with Giemsa. The smear had a purple background and was moderately cellular, though the cells were clearly discrete. The cells were round and monomorphic, and showed anisocytosis. Their cytoplasm was deeply basophilic and contained numerous grey to dark pigments. Their nuclear: cytoplasmic ratio was high. They contained darkly stained nuclei with single prominent nucleoli; there was anisokaryosis and anisonucleolosis. The nuclear chromatin pattern was coarse to granular (Plate II).

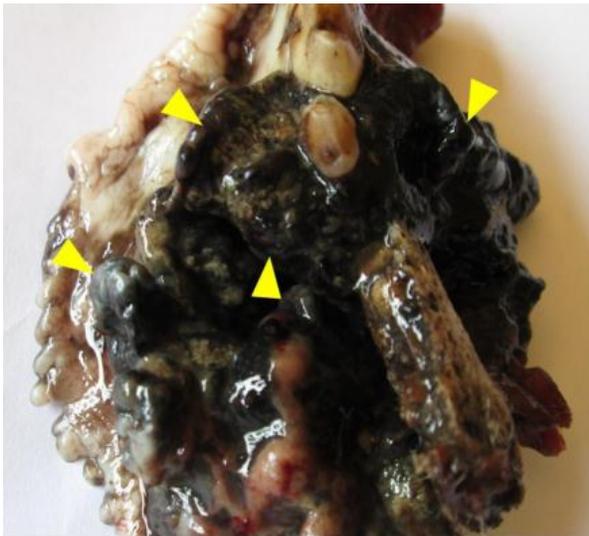


Plate I: Gross appearance of mass showing Irregularly shaped, very dark tumor located beneath the base of the premolar and molar teeth (yellow arrow heads)

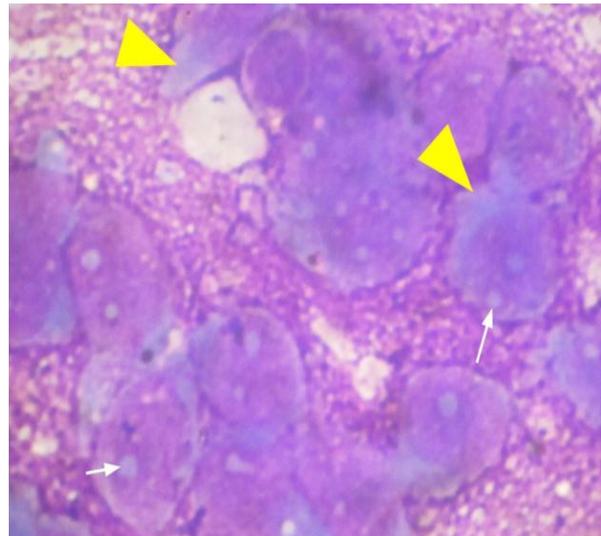


Plate II: Cytomorphological examination of mass showing numerous large, round cells with single large round hyperchromatic nuclei with prominent multiple nucleoli (white arrows) and intracytoplasmic pigments (yellow arrow heads). Giemsa stain X1000



Plate III: Gross post mortem appearance of the lungs showing multiple foci of numerous dark, raised, glistening nodules scattered on all the lobes of both lungs (yellow arrow heads)

The animal died before any treatment could be administered.

Post mortem pathology

At necropsy, the lung was diffusely covered with numerous raised, dark, glistening nodules of various sizes ranging from 0.2cm to 0.5cm in diameter (Plate III). Giemsa stained smears of the crushed nodules revealed similar cells as described for the oral mass. Samples of the pulmonary nodules were fixed in 10% formalin, processed routinely and stained with Haematoxylin and Eosin.

Histopathological examination

There were multifocal, dense alveolar aggregates of homogenous polygonal epitheloid cells (Plate IV). There was marked anisocytosis. The cytoplasm was moderate and contained fine grey to black pigments. The nuclei were moderately hyperchromatic and showed anisokaryosis. There was moderate thickening of the interalveolar septae. There was widespread hemorrhage in the interstitium.

Based on the clinical presentation, cytopathology, and histopathological features, a diagnosis of oral melanoma with pulmonary metastasis was made.

Discussion

According to Goldschmidt & Hendrick (2002), melanocytic neoplasm of dogs can be classified as benign or malignant. On the basis of differentiation, cytological and histopathological evaluation, the

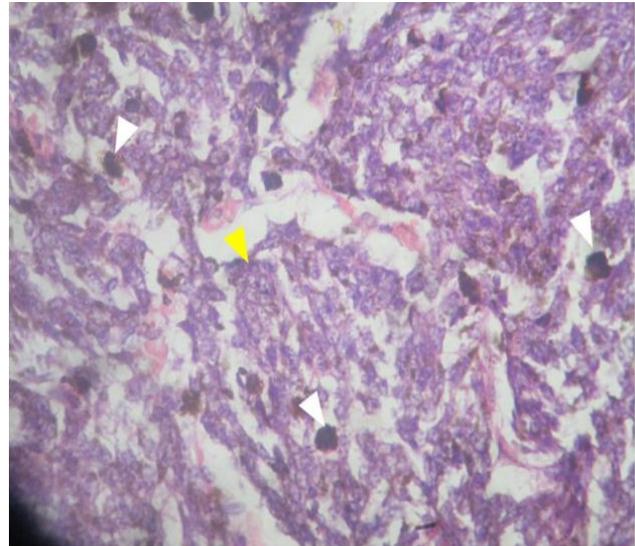


Plate IV: Discrete large round cells with dark brown (melanin) pigments (white arrow heads) and numerous foci of epithelioid syncytial giant cells (yellow arrow). H&E X400)

diagnosis of malignant oral melanoma with pulmonary metastasis was made. Although, the age range for occurrence of oral melanoma, according to Head *et al.* (2002) is between 10.5 and 12 years, with an average of 11.4 years, the age of the dog in this case was 9 years which is not significantly different. On the basis of the World Health Organization's template for staging of tumors in dogs (Owen, 1980), this case may be classified as stage IV oral melanoma. Oral melanoma may be found in any part of the oral cavity, but according to McEntee (2012) the gingival mucosa is the commonest site. The current case agrees with this previous finding. If the case was presented earlier, it could have afforded the clinician opportunity to explore various treatment plans which could have increased its chance of survival.

Naturally occurring canine melanoma is very significant to solving the human melanoma disease due to the following reasons: (a) Many novel anticancer agents that are effective in mice fail in humans, probably because mouse models used in cancer drug development lacked the manifestation of critical characteristics such as long latency period, tumor cell heterogeneity, recurrence and metastasis which are determinants of patient outcome (Couzin-Frankel, 2013) (b) Naturally occurring neoplasms in small animals, especially in dogs share clinical and biological similarities to human cancers which may be difficult to replicate in other models, for example,

histological appearance, biological behavior and biological targets (Paoloni & Khanna, 2008). (c) The prevalence of cancer in companion animals, rapid progression and delayed metastasis (when compared with rodents) allows rapid completion of clinical trials. (d). Because of ethical constraints, novel agents are not readily deployed in human cancer treatment trials. However, novel agents can often be studied in companion animals because, in most cases, treatment protocols have not been standardized (Paoloni & Khanna, 2008) and (e) The relatively large body size of dogs, coupled with the fact that spontaneous tumour bearing animals are immunocompetent, offers better possibilities for surgical procedures and imaging (radiography and ultrasonography) as well as immunological studies. If concurrent clinical trials of drugs for the treatment of canine and human patients were approved, additional insight into drug activity, toxicity, regimen and schedule, biomarkers, and possible combination therapies would be gained (Paoloni & Khanna, 2008). Canine patients are also relatively outbred unlike the laboratory animals such as the mice.

In order to get tumor bearing animals for clinical trials In Nigeria, dog owners should be encouraged to seek prompt veterinary attention for their sick animals, especially, when unusual growths are observed in any part of the body. This will greatly improve our epidemiological documentations.

The breakthrough already achieved in melanoma treatment and control in the dog through the development of melanoma vaccine i.e. Oncept^R Merial (Grosenbaugh *et al.*, 2011), approved for use by the United States Department of Agriculture

References

- Andre JP, Delvendier M, Cabanic P & Bartel G (1993). Malignant melanoma in an African gray parrot (*Psittacus erithacus erithacus*). *Journal of the Association of Avian Veterinarians*, **7**(2): 83 – 85.
- Bergman PJ & Wolchok JD (2008). Of mice and men (and dogs); development of a xenogeneic DNA vaccine for canine oral malignant melanoma. *Canine Therapy*, **6**: 817-826.
- Bostock DE (1979). Prognosis after surgical excision of canine melanomas. *Veterinary Pathology*, **16**(1):32-40.
- Brodey RS (1960). A clinical and pathologic study of 130 neoplasms of the mouth and pharynx in the dog. *American Journal of Veterinary Research*, **21**(84):787-812.

(USDA) in 2010 is an encouragement for the advocates of the concept of “One World, One Health, One Medicine”. This is because the vaccine is the first therapeutic vaccine in man and animals licensed by the USDA. (Bergman & Wolchok, 2008). This is an example of possible breakthrough inherent in professional partnership between human and veterinary practitioners. As of now in Nigeria, collaboration between physicians and veterinarians, including medical and veterinary researchers is at its lowest ebb. This may not augur well for the achievement of the ideals of “One Health Concept” as envisioned by the World Organization of Animal Health (OIE), World Health Organization (WHO) and the Food and Agricultural Organization of the United Nations (FAO). This professional synergy was also suggested for the purpose of maximal utilization of the potentials of both professions by Bergman & Wolchok (2008).

In conclusion, Nigerian veterinarians and physicians should do more to close ranks to maximize opportunities obtainable in the adoption and practice of “One health” approach to solving myriad health problems plaguing man and animals, especially, in Nigeria. This should not be limited to the area of zoonoses or emerging and re-emerging diseases, but should also encompass neoplastic and metabolic diseases and disorders.

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- Cotchin E (1955). Melanotic tumours of dogs. *Journal of Comparative Pathology and Therapeutics*, **65**:116-129.
- Couzin – Frankel J (2013). When mice mislead. *Science*, **342**(6161): 922-925.
- Dorn CR & Priester WA (1976). Epidemiologic analysis of oral and pharyngeal cancer in dogs, cats, horses and cattle. *Journal of the American Veterinary Medical Association*, **169**(11):1202-1206.
- Desmond RA & Soong S (2003). Epidemiology of malignant melanoma. *Surgical Clinics of North America*, **83**(1): 247-267.
- Delverdier M, Guire E & Van Haverbeke G (1991). Les tumeurs de la cavite buccale du chien: Etude anatomoclinique a partir de 117

- cases. *Revue de Medecine Veterinaire*, **142**: 811 – 816.
- Goldschmidt MH (1985). Benign and malignant melanocytic neoplasms of domestic animals. *American Journal of dermatopathology*, **7**(Suppl.): 203-212.
- Goldschmidt MH & Hendrick MH (2002). Tumors of the Skin and Soft Tissues. In: Tumors of Domestic Animals (DJ Meuten, editor), fourth edition, Iowa state Press. Ames, IA, USA. Pp 78-82.
- Grosenbaugh DA, Leard AT, Bergman PJ, Klein MK, Meleo K, Susaneck S, Hess PR, Jankowski MK, Jones PD, Leibman NF, Johnson MH, Kurzman ID & Wolchok JD (2011). Safety and efficacy of a xenogeneic DNA vaccine encoding for human tyrosinase as adjunctive treatment for oral malignant melanoma in dogs following surgical excision of the primary tumor. *American Journal of Veterinary Research*, **72**(12): 1631-1638.
- Head KW (1976). Tumors of the upper alimentary tract. *Bulletin of the World Health Organization*, **53**(2-3): 145-166.
- Head KW, Else RW & Dubielzig RR (2002). Tumors of the Alimentary Tract. In: Tumors in Domestic Animals, fourth edition (DJ Meuten, editor), Iowa State Press, Ames, Iowa, USA. Pp 401-481.
- Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ & Cronin KA (2013). SEER Cancer Statistics Review 1975 – 2010 Bethesda MD National Cancer Institute. https://seer.cancer.gov/csr/1975_2013/, retrieved 20-07-2016.
- Johnson PJ (1998). Dermatologic tumors (excluding sarcoids). *Veterinary Clinics of North America: Equine Practice*, **14**(3): 625 – 658.
- Marino DJ, Matthiesen DT, Stetanacci JD & Moroff SD (1995). Evaluation of dogs with digit masses: 117 cases (1981 – 1991). *Journal of the American Veterinary Medical Association*, **207**(6): 726-728.
- McEntee MC (2012). Clinical Behavior of Nonodontogenic Tumors. In: *Oral and Maxillofacial Surgery in Dogs and Cats* (Verstraete FJM, Lommer MJ, editors) Elsevier Saunders: Pennsylvania, PA, USA. Pp 387-402.
- McGovern VS (1970). The classification of melanoma and its relationship with prognosis. *Pathology*, **2**(2): 85-98.
- Miller WH, Scott DW & Anderson WI (1993). Feline cutaneous melanocytic neoplasms: A retrospective analysis of 43 Cases (1979 – 1991). *Veterinary Dermatology*, **4**(1): 19-26.
- Owen LN (1980). TNM Classification of Tumors in Domestic Animals. World Health Organization. Veterinary Public Health Unit WHO Collaborating Center for Comparative Oncology, Geneva. Pp 53.
- Paoloni M & Khanna C (2008). Translation of new cancer treatments from pet dogs to humans. *Nature Reviews Cancer*, **8**(2): 147-156.
- Reddy KP, Ramakrishna A & Reddy GCN (1998). Malignant melanoma in a dark skinned bull. *Indian Veterinary Journal*, **75**(5): 453 – 454.
- Simpson RM, Bastian BC, Michael HT, Webster JD, Prasad ML, Conway CM, Prieto VM, Gary JM, Goldschmidt MH, Esplin DG & Smedley RC (2013). Sporadic naturally occurring melanoma in dogs as a preclinical model for human melanoma. *Pigment Cell and Melanoma Research*, **27**(1): 37-47.
- Smith SH, Goldschmidt MH & McManus PM (2002). A comparative review of melanocytic neoplasms *Veterinary Pathology*, **39**(1): 651-678.
- Tunney SS & Well MG (2002). Cutaneous melanoma in a Ferret (*Mustela Putorius Furo*). *Veterinary Pathology Online*, **39**(1):141 – 143.
- Valentine BA (1995). Equine melanocytic tumors: A retrospective study of 53 horses (1988 to 1991). *Journal of Veterinary Internal Medicine*, **9**:291 – 297.
- Withrow SJ (1996). Tumors of the Gastro-Intestinal Tract. A Cancer of the Oral Cavity. In: Small Animal Oncology, (SJ Withrow, EG MacEwen, editors) second edition, WB Saunders, Philadelphia, PA. Pp 227 – 240.
- Yakubu A & Mabogunje OA (1995). Skin cancer in Zaria, Nigeria. *Tropical Doctor*, **25** (1): 63-67.