

Canine nasal neuroendocrine carcinoma: case report with a brief review of the literature

A. Oryan¹ · A. A. Sarchahi² · A. Khodakaram Tafti¹ · F. Namazi¹ ·
G. Farjani Kish³ · M. Babazadeh⁴

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Abstract A mass of approximately 5×5×5 cm was located on the bridge of the nose, nasal septum, turbinates, and soft and hard palates of a 1-year-old male terrier dog. The skin over the mass was alopecic and ulcerated. Histopathologically, the tissue sections consisted of sheets of neoplastic cells separated by narrow bands of fibrovascular stroma. The neoplastic cells were round to polyhedral with moderate, eosinophilic cytoplasm, and large clear nuclei. Mitotic figures were frequently observed. Immunohistochemically, the neoplastic cells were diffusely positive for neuron-specific enolase, but no detectable cellular staining was evident for S-100 protein. Regarding the histopathological and immunohistochemical features of the tissue sections, neuroendocrine carcinoma was concluded in this case.

Keywords Neuroendocrine carcinoma · Dog · Nasal cavity · Histopathology · Immunohistochemistry

Introduction

Neuroendocrine carcinoma is derived from the endocrine cells, which are disseminated in many tissues and organs

(Kulke and Mayer 1999). Neuroendocrine tumors are divided into well-differentiated, moderately differentiated, and poorly differentiated neoplasms (Sirsath et al. 2013).

The respiratory and digestive tracts are the most common sites of these cells. They are thought to derive from the undifferentiated precursor cells present in endodermal area and are designated as a diffuse endocrine system (Kulke and Mayer 1999). Neuroendocrine carcinomas have occasionally been reported in various tissues of dog, cat, and horse such as the intestines, liver, lungs, esophagus, and skin (Patnaik et al. 1981; Patnaik et al. 1990; Harkema et al. 1992; van Maanen et al. 1996; Sako et al. 2003), and most of these tumors are very invasive.

Occurrence of neuroendocrine carcinoma in the nasal cavity is uncommon in domestic animals and has only been reported in dog and horse (van Maanen et al. 1996; Koehler et al. 2012). It has been reported that most neuroendocrine carcinoma, in dogs, originate from the gastrointestinal tract, and these tumors often metastasize to the liver (Patnaik et al. 1981). The present study describes histopathological and immunohistochemical characteristics of a neuroendocrine carcinoma in the nasal cavity of a 1-year-old male terrier dog.

Case report

A 1-year-old male terrier dog was referred for clinical evaluation of a nasal mass. The dog had a clinical history of nasal discharge, stertor, and occasional sneezing. A mass of approximately 5×5×5 cm was located on the ridge of the nose, and the skin over the surface of the neoplasm was alopecic and ulcerated (Fig. 1). Swelling was also evident in the maxillary gingival, soft and hard palates, and in the oral cavity. After a few days, the animal died and was submitted for post-mortem examination. Appropriate tissue samples of the tumor were fixed in 10 % neutral buffered formalin, embedded in paraffin,

✉ F. Namazi
fnamazi@shirazu.ac.ir

¹ Department of Pathobiology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

² Department of Clinical Sciences, Faculty of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran

³ Department of Pathobiology, School of Veterinary Medicine, Lorestan University, Khorram Abad, Iran

⁴ School of Veterinary Medicine, Shiraz University, Shiraz, Iran



Fig. 1 Gross appearance of the nasal mass (*arrow*). The skin over the surface of the neoplasm was alopecic and ulcerated

sectioned at 5 μm , and stained with hematoxylin–eosin for light microscopic examination. In addition, an immunohistological analysis was performed for presence of neuron-specific enolase (NSE) and S-100 protein in the formalin-fixed paraffin-embedded tissues. The sections were dewaxed and processed with avidin-biotin-peroxidase complex (ABC) technique. Mayer's hematoxylin was used for counter staining. Appropriate external and internal controls were also used.

Grossly, the neoplastic mass occupied most of the nasal cavity and had destroyed the maxilla and invaded the turbinates and hard and soft palates. The mass was a solitary, white with a soft consistency. No metastases were observed in other organs and tissues. Microscopically, the tumor consisted of sheets of moderate size neoplastic cells separated by thin fibrovascular stroma. The neoplastic cells had round to polyhedral shapes with moderate amount of eosinophilic cytoplasm and large clear nuclei (Fig. 2). Mitotic figures were frequently observed.

Immunohistochemical analysis in most instances revealed that the cytoplasm of the neoplastic cells was diffusely

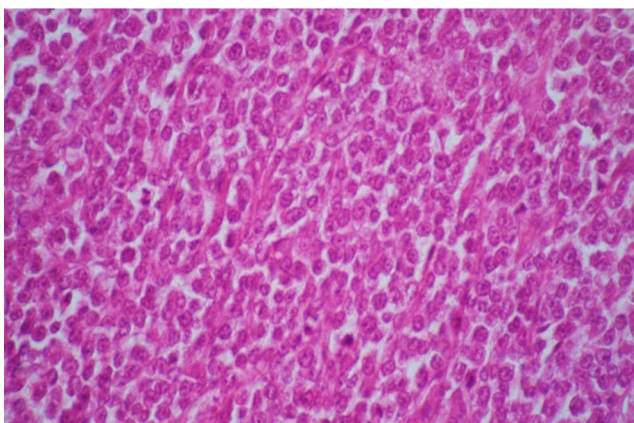


Fig. 2 Neuroendocrine carcinoma; round to polyhedral cells with moderate, eosinophilic cytoplasm, and round nuclei, arranged in sheets, H&E ($\times 180$)

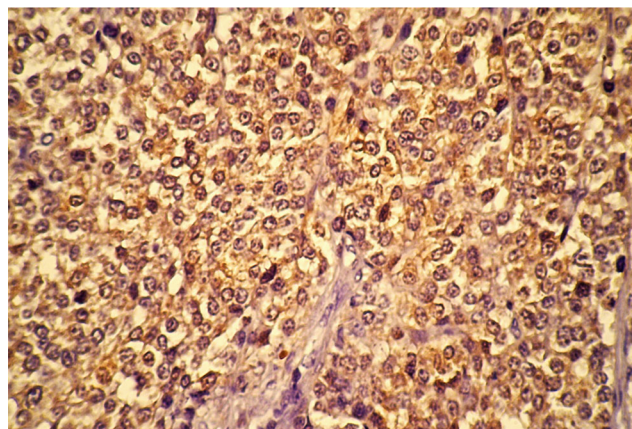


Fig. 3 Neuroendocrine carcinoma. The neoplastic cells show diffuse positive staining for neuron-specific enolase, IHC ($\times 180$)

positive for neuron-specific enolase (Fig. 3), but they were negative for S-100 protein. On the basis of the histopathological and immunohistochemical findings, the tumor was diagnosed a neuroendocrine carcinoma.

Discussion

Neuroendocrine tumors are rare in dogs and arise from the distributed neuroendocrine cells, which produce peptides and amines in various organs. Neuroendocrine carcinomas have been classified as a separate class from the epithelial or mesenchymal tumors of the nasal or paranasal tissues (Wilson and Dungworth 2002). Neuroendocrine carcinomas have been reported occasionally in various tissues of dogs such as lungs and liver (Patnaik et al. 1981; Harkema et al. 1992). In the present study, the neoplastic mass in the nasal cavity was diagnosed as neuroendocrine carcinoma by histopathological and immunohistochemical examinations. Previous studies of the canine nasal tumors have shown that adenocarcinomas are predominant among the carcinomas (Wilson and Dungworth 2002). However, neuroendocrine carcinoma of the nasal cavity is a rare tumor in animals (Patnaik 1983).

In most instances, it is difficult to diagnose the neuroendocrine tumors of the nasal cavity from other neoplasms by light microscopical examination (Wilson and Dungworth 2002). Immunohistochemical and electron microscopical examinations are useful for the differential diagnosis of these neoplasms in human patients and animals (Hara et al. 2002). Neuron-specific enolase is an acid-soluble protein isolated from the brain tissue and is found in the cytoplasm of all neuroendocrine cells and most neural cells. Neuron-specific enolase seems to be a useful and ideal marker which can be used to distinguish the endocrine from the non-endocrine tumors (Tapia et al. 1981). In the present case, the strong cytoplasmic positivity of the tumor cells for neuron-specific enolase revealed neuroendocrine differentiation. Van Maanen

et al. (1996) showed that the neuron-specific enolase is also a suitable marker for equine neuroendocrine carcinomas.

Although the olfactory neuroblastoma is an uncommon tumor, it has been reported more often than nasal neuroendocrine carcinoma (Hara et al. 2002). In human olfactory neuroblastomas, it has been shown that the cells located at the periphery of the neoplastic cell nests are positive for S-100 protein (Hirose et al. 1995). It has been reported that the neuroendocrine carcinomas, including the respiratory and gastrointestinal neuroendocrine tumors were not immunolabeled for S-100 protein in both human and animals (Barwick, 1990). In the present study, the neoplastic cells did not stain with S-100 protein, and this result is consistent with the previous studies (Patnaik et al. 2002).

The biologic behavior of these tumors is variable and very unpredictable in different species. A correlation between the tumor site and malignancy rate has been reported in the human intestinal neuroendocrine carcinomas (Van Maanen et al. 1996). The neuroendocrine carcinomas in dogs mostly metastasize to the liver (Patnaik et al. 1981). The present neuroendocrine carcinoma had not metastasized to other parts.

To the best of our knowledge, although there are rare reports of the occurrence of neuroendocrine carcinoma in 7- to 13-year-old dogs (Konno et al. 1998; Koehler et al. 2012), this is the first reported case of a neuroendocrine carcinoma in a young terrier. Therefore, it seems this tumor can happen in the young terrier dogs, too.

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