Short Communication

Disseminated Oral Melanoma with Brain and Gastrointestinal Tract Involvements in A Cocker Spaniel: A Case Report

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Abstract

A nine-year-old, male Cocker Spaniel with a history of surgical excision of oral melanoma located at the gingiva of the left maxilla was evaluated progressively over the course of 1 month post-surgery. The dog had shown signs of respiratory distress. Radiographic examination revealed diffusely pulmonary metastases. The respiratory distress progressively worsened and the dog died following excision of the oral mass. On necropsy, disseminated metastases to various organs including the lungs, heart, mediastinum, liver, kidneys, spleen, tonsil, lymph nodes, adrenal glands, thoracic wall, jejunum, pancreas, and brain were observed. Microscopically, the neoplastic cells were characterized by spindle to polyhedral phenotypes, having centrally located vesicular nuclei with prominent nucleoli, and melanin pigment accumulations in the cytoplasm. Neoplastic cells were seen within organ parenchyma as well as being found as emboli in blood and lymph vessels of those organs. The neoplastic cells demonstrated strongly cytoplasmic immunoreactivity to Melan A. Hematogenous dissemination is considered as an important route for distant metastases of oral melanoma. In this report, we describe the rare disseminated metastasis of an oral melanoma to the brain and gastrointestinal tracts, which are considered to be important sites of melanoma metastases in humans.

Keywords: blood-borne metastasis, brain, gastrointestinal tract, oral melanoma

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Introduction

Melanoma is a common neoplasm that account for 3% of all canine neoplasms and up to 7% of all malignancies in dog (Esplin, 2008; Smith et al., 2002). Melanoma is the second most common malignant neoplasm of the oral cavity in canids (Esplin, 2008; Ramos-Vara et al., 2000; Smith et al., 2002). Local recurrence and lymphatic metastasis to regional nodes and lungs are commonly seen in dogs (Head et al., 2002). On the other hand, the metastases to the other organs, especially to the brain, are only infrequently reported (Head et al., 2002; Kim et al., 2009; Ramos-Vara et al., 2000). In humans, malignant melanoma (MM) is the third most common metastatic neoplasm of the brain following neoplasms of the lungs and mammary glands (McWilliam et al., 2008; Sloan et al., 2009). MM also accounts for one third of all malignancy metastases to the gastrointestinal (GI) tract, especially the small intestine (Kim et al., 2005). However, only couple cases of MM metastases to the brain have been described in dogs (Kim et al., 2009; Snyder et al., 2008). Here, we report the dissemination of canine oral melanoma with the involvement of the brain parenchyma and GI tract, both considered to be important sites of melanoma metastases in humans but rare in dogs.

Materials and Methods

Case history: A nine-year-old, male Cocker Spaniel dog had been previously histopathologically diagnosed as oral melanoma at the gingiva of the left maxilla and surgical excision was performed. The ipsilateral mandibular lymph node was enlarged measuring 3x3 cm since the surgical removal of the gingival mass. Thereafter, the dog showed sign of the respiratory distress. Radiographic examination revealed diffuse pulmonary masses, which were interpreted to be metastasis from the primary melanoma. The respiratory distress progressively increased and the dog died within 1 month after surgical excision of the oral melanoma. A complete necropsy was performed. The lungs, heart, mediastinum, liver, kidneys, spleen, tonsil, lymph nodes, adrenal glands, thoracic wall, jejunum, pancreas, and brain were fixed with 10% buffered formalin. The fixed tissues were embedded into paraffin wax, cut at 4 µm thickness, and stained with haematoxylin and eosin (HE) and Masson Fontana. Immunohistochemistry was also performed using autoimmunohistochemistry stainer (Bond™ Polymer Refine Detection, Leica Biosystems, United Kingdom). The primary antibody was monoclonal mouse anti-human Melan A antibody (Clone A103, DAKO, USA).

Results and Discussion

Grossly, there was a healing wound at the surgical site noted on the gingiva of the left maxilla. The left mandibular lymph node was enlarged (up to 4 times normal size) with diffuse black discoloration on cut surface. Dark masses of variable sizes, measuring up to 5 cm were observed in various organs including the lungs, heart, mediastinum, liver, kidneys, spleen, tonsil, lymph nodes, adrenal glands, thoracic wall, jejunum, pancreas, and brain. In the brain, the multiple blackish masses were observed primarily in both the meningeal vessels as well as in the parenchyma of the cerebral cortex of the frontal and occipital lobes (Fig 1). Masses were also observed on the jejunal serosa and the mucosa was elevated by the invasion of the masses into the jejunal wall (Fig 2).

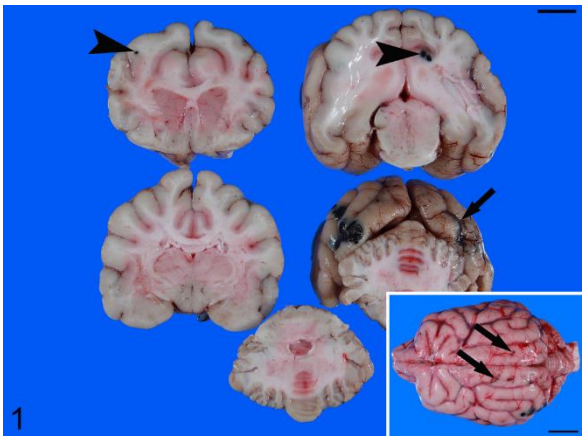

Figure 1 Multiple black masses were observed in the cerebral cortex (arrowhead) and meningeal vessel (arrow). Bar = 1 cm, inset. Bar = 2cm.

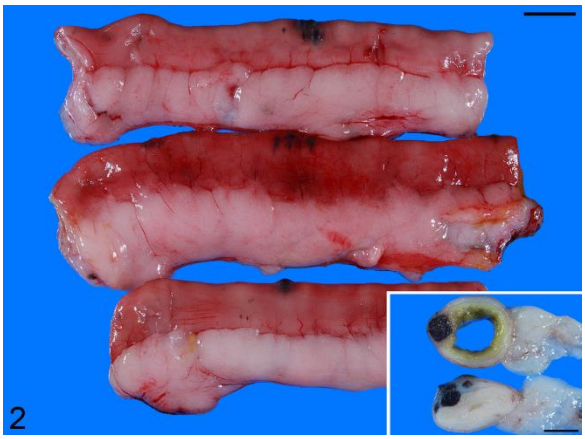

Figure 2 Multiple black masses were observed in the jejunal serosa. Bar = 1 cm. Inset. The black masses also occupied the jejunal wall. Bar = 0.5 cm

Microscopically, the neoplastic cells in all tissues demonstrated relative morphologic homogeny with spindle to polyhedral cells, arrange in dense cellular pattern. Neoplastic cells had central vesicular nuclei with prominent nucleoli, and coarse dark-brown pigmented cytoplasm corresponding to melanin pigment as demonstrated by Masson Fontana staining. Mitoses were commonly seen (3-4 mitoses/high power field). Multiple necrotic foci were seen in the center of the masses. In the brain, the neoplastic cells formed emboli in the meningeal vessels. Multifocally, the neuropil of the cerebral cortex was replaced and affected by multiple metastases, which compressed the adjacent parenchyma (Fig 3). The submucosa of the jejunum was expanded by the neoplastic cells and forming dome-like structure at various point along the mucosa (Fig 4). Moreover, the neoplastic cells were observed in both lymphatic and blood vessels of various organs. Immunoreactivity for Melan A was

noted to be very strong in the cytoplasm of the neoplastic cells (Figs 3 and 4). Melan A is considered as a sensitive and specific marker for canine melanocytic tumors (Ramos-Vara et al., 2000; Smith et al., 2002).

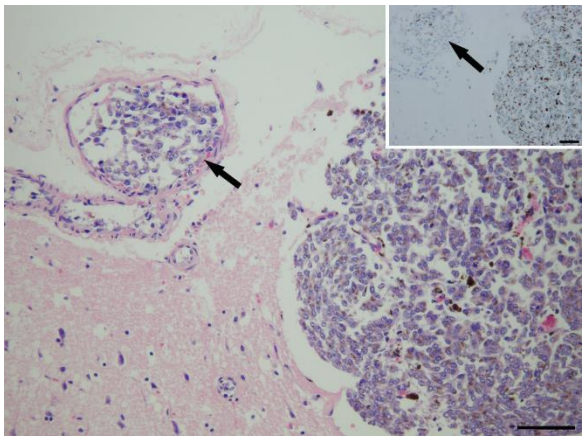

Figure 3 Multiple metastatic mass from the primary oral melanoma were noted in the cerebral cortex compressing the adjacent neuropil . Neoplastic emboli were seen in meningeal vessels (arrow). (HE stain, Bar = 80 µm**).** Inset, the neoplastic cells were cytoplasmically immunoreactive to Melan A within the metastatic nodules and the meningeal vessels (arrow). (IHC, DAB, hematoxylin, Bar = 40 µm)

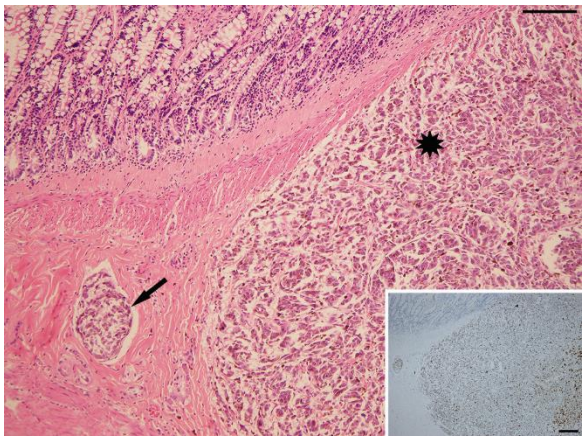

Figure 4 Metastatic melanoma within the submucosa causing elevation of the mucosa (asterisk). A neoplastic embolus was seen in the lymph vessel (arrow). (HE stain, Bar = 200 µm). Inset**,** the neoplastic cells demonstrated cytoplasmic immunoreactivity to Melan A in the cytoplasm in the metastatic nodules and the lymph vessel (arrow). (IHC, DAB, hematoxylin, Bar = 100 µm)

Oral melanoma is considered to be a malignancy that favors the gingiva (Head et al., 2002; Ramos-Vara et al., 2000; Smith et al., 2002). Recurrence is frequently occurred after surgical removal (Smith et al., 2002). Regional lymph node, lungs, and the heart are the primary predilection sites for distant metastases (Head et al., 2002; Ramos-Vara et al., 2000; Smith et al., 2002). Brain metastasis is the third most common sites of MM metastases in humans (Sloan et al., 2009), and is considered to carry a poor prognosis (McWilliam et al., 2008). Unlike the human cases, only 3% of canine oral melanoma metastasized to the brain (Snyder et al., 2008). The pattern of multiple brain metastases was observed in the present case, which is consistent with what has been previously described (Kim et al., 2009; Snyder et al., 2008).) It is notable that the pattern of metastasis in this dog did not result in clinical signs relating to neoplasia induced neurogical deficits (Kim et al., 2006; Schwartz et al., 2011). A recent study noted that up to 50% of the dogs diagnosed with neoplastic brain metastases/invasion did not show seizure activity, indicating that neurological signs should not be considered a requirement for diagnosis of brain metastases (Kim et al., 2009; Schwartz et al., 2011). When it occurs, seizures are typically seen in conjunction with neoplastic spread within the frontal lobe (Schwartz et al., 2001). GI tract has been reported to be the sixth most common sites of melanoma metastasis and mainly occurred in the small intestine (Brummel et al., 2005; Kim et al., 2006). The metastasis of melanoma the small intestine has been reported to cause intussusception and perforation of the intestinal wall (Brummel et al., 2005; Kim et al., 2006). The present case also revealed multiple metastases of melanoma in the submucosa of jejunum leading to elevation of the mucosa. Hematogenous metastasis is the main route for spread of melanoma, which was frequently observed in the present study (Kim et al., 2006). Furthermore, hematogenous route was also facilitated mammary gland metastasis of melanoma (Yang et al., 2011). The using of contrast enhanced computed topography (CT) and magnetic resonance imaging are considered as a standard method for confirmed diagnosis of brain metastases of MM in human (McWilliams et al., 2008). CT also favors for early detection of GI tract metastases of MM (Kim et al. 2006).

In conclusion, the disseminated oral melanoma in this animal, with involvement of the brain and GI tract was diagnosed based on the pathological findings and confirmed through immunoreactivity to Melan A in the cytoplasm of the tumor cells. Although, oral melanoma with brain metastasis has involved a poor prognosis, early detection might be considered as a critical factor towards the promotion of quality of life by implementation of combined specific and palliative treatments such as radiation, chemotherapy, and stereotactic radiosurgery (McWilliams et al., 2008).

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บทคัดย่อ

การแพร่กระจายไปทั่วของมะเร็งชนิดเมลาโนมาของช่องปากที่แพร่กระจายไปยังสมองและทางเดินอาหารในสุนัขพันธุ์คอกเกอร์สเปเนียล: รายงานสัตว์ป่วย

สว่าง เกษแดงสกลวุฒิ* แคทลียา จันทร์ขาว อนุเทพ รังสีพิพัฒน์

สุนัขพันธุ์คอกเกอร์สเปเนียล เพศผู้ อายุ 9 ปี มีประวัติเป็นมะเร็งชนิดเมลาโนมาที่เหงือกของขากรรไกรบนด้านซ้ายและได้รับการผ่าตัดเอาก้อนมะเร็งออก ภายหลังการรักษาสุนัขแสดงอาการหายใจลำบากและตรวจพบการแพร่กระจายของก้อนมะเร็งในปอด จากการตรวจทางรังสีวิทยา ต่อมาสุนัขแสดงอาการหายใจลำบากมากขึ้นและเสียชีวิตภายใน 1 เดือนหลังการผ่าตัดเอาก้อนมะเร็งออก การตรวจทางมหพยาธิวิทยาพบมีการแพร่กระจายของมะเร็งชนิดเมลาโนมาของช่องปากไปยังอวัยวะต่างๆได้แก่ ปอด หัวใจ มีดิเอสตินัม ตับ ไต ม้าม ทอนซิล ต่อมน้ำเหลือง ต่อมหมวกไต ผนังช่องอก ลำไส้เล็กส่วนกลาง ตับอ่อน และสมอง การตรวจทางจุลพยาธิวิทยาพบเซลล์มะเร็งที่มีรูปร่างยาวรีถึงรูปทรงมีหน้าหลายหน้า มีนิวเคลียสแบบเวสซิคุลาที่มีนิวคลิโอลัสที่ชัดเจนและมีเม็ดสีเมลานินในไซโตพลาสมของเซลล์มะเร็งแทรกอยู่ในเนื้อเยื่อของอวัยวะต่างๆ และพบเซลล์มะเร็งในหลอดน้ำเหลืองและหลอดเลือด เซลล์มะเร็งให้ผลบวกต่อแอนติบอดีชนิดเมแลน เอ ด้วยวิธีอิมมูโนฮีสโตเคมี การแพร่กระจายทางหลอดเลือดเป็นทางที่สำคัญในการแพร่กระจายไปยังอวัยวะต่างๆของมะเร็งชนิดเมลาโนมาของช่อง-ปาก ผลการศึกษาครั้งนี้เป็นการรายงานการเกิดการแพร่กระจายมะเร็งชนิดเมลาโนมาของช่องปากไปยังสมองและทางเดินอาหาร ซึ่งเป็นตำแหน่งที่เกิดการแพร่กระจายได้บ่อยของมะเร็งชนิดเมลาโนมาในมนุษย์

คำสำคัญ: การแพร่กระจายทางหลอดเลือด สมอง ทางเดินอาหาร มะเร็งชนิดเมลาโนมาของช่องปาก

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