

MALIGNANT MELANOMA IN A COW

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A malignant melanoma located in the area of the ocular orbit and maxillary sinus of a 2,5 year old, female Brown Swiss cow is described. Complete clinical examination of the cow was performed and blood samples were taken for haematological analyses. According to the unfavorable prognosis, the cow was submitted for necropsy. After necropsy representative sections of tissue were sampled for gross and micro histopathology. Selected sections of tissue were stained with hematoxylin and eosin. Clinical examination of the cow revealed exophthalmus of the right eye, deviation of right maxillae and os faciale and progressive central nerve signs. At the necropsy a black tarry irregular mass, 10 cm in diameter was found in the area of the right orbit and maxillary sinuses protruding into the nasal conches and meninges. Multiple metastases were secondarily located in the heart, liver, spleen, lung and brain. Histologically the malignant melanoma was composed of melanocytic tumor cells and located in the described organs. Based on clinical and histological examinations we concluded, that the tumor mass was a malignant melanoma of the epithelioid type. The primary origin of the tumor was probably the right eye.

Key words: malignant melanoma, brain, cow

INTRODUCTION

Melanomas are benign or malignant neoplasms arising from melanocytes or melanoblasts. They occur in all domestic animals, but among the large domesticated species they are most significant in horses (Geisel and Wiest 1970, Howard 1994, Dobberstein and Tamaschke 1967, Moulton 1961, Radostits *et al.*, 1994, Schenker and Kronberger 1960, Weiss *et al.*, 1977). In cattle melanomas represent less than 2% of bovine tumors in general (Smith 1990). Most melanomas are benign, but malignancy is not uncommon. Causes for the development of melanoma are still unknown. Excessive exposure to sunlight is noted to be a risk factor in humans, but there is no evidence for that in domestic animals (Geisel and Wiest 1970). Genetic factors influencing the development of

melanomas were supposed for pigs of the Duroc-Jersey breed (Radostits *et al.*, 1994, Scott 1988).

These tumors occur in cattle at all ages. There is no definite breed or sex predilection, although they are more common in dark-skinned animals, especially Aberdeen Angus (Bückner 1994, Dobberstein and Tamaschke 1967, Rosenberger 1970, Smith 1990, Abraha *et al.*, 1997). Melanomas are usually solitary and infrequently multiple. They are customarily found in the skin of animals, but also in the iris, choroid, ciliary body and retina of the eye. In cattle they appear most frequently on the skin of feet and are usually benign (Harting 1987, Howard 1994). Malignant melanomas have been observed rarely in cattle. Metastases are most often observed in regional lymph nodes, lungs, spleen and liver (Smith 1990, Sockett *et al.*, 1984, Samija *et al.*, 1997). Melanomas are usually firm, nodular masses, located dermoepidermally or subcutaneously and grossly hyperpigmented (Ashley 1978, Smith 1990, Sockett *et al.*, 1984, Weaver and Miller 1994, Weiss and Rudolph 1977). With regard to the type of cells present, they are classified as epithelioid, spindle cell, epithelioid and spindle cell or dendritic types of malignant melanoma (Ashley 1978, Weiss and Frese 1974). Invasive growth into lymph vessels and small veins is often seen. Diagnosis of melanomas is based on histological and cytological evaluation. The presence of melanin pigment is the most valuable marker for the identification of melanocytic tumors. Serum S-100 protein is a potentially useful prognostic marker in cutaneous melanomas in humans (Abraha *et al.*, 1997, Hansson *et al.*, 1997). The aim of this article was to describe a case of malignant melanoma with secondary brain involvement in a cow.

MATERIALS AND METHODS

A 2.5 year old Brown Swiss cross-breed cow was admitted to the Clinic for Ruminants for evaluation of a bulging right eye, deviation of right maxillary sinuses and progressive nerve signs. Complete clinical examination of the cow was performed and blood samples were taken for haematological analyses. Also an agar gel immunodiffusion test for the presence of enzootic bovine leukosis (EBL) antibodies was done. The cow was emaciated due to problems with swallowing food and mastication. According to the unfavorable prognosis and the owners request, the cow was submitted for necropsy.

After necropsy a complete pathohistological examination was performed. For detailed examination of the head malformations several longitudinal and vertical cuts in the cranium were made. Tissue samples were taken and fixed in 10 % neutral buffered formalin at. After routine embedding in paraffin, 4 µm thick sections were cut and stained with haematoxylin and eosin (HE).

RESULTS

Clinical examination

Physical examination revealed that the cow had exophthalmus of the right eye with ventral rotation, deviation of maxillary sinuses and maxillae and progressive nerve signs such as abnormal head position, propulsion and hypersensitivity. The position and location of the left eye was normal and no

abnormality of the facial bone was observed. Ophthalmoscopic examination of the left eye revealed normal status. Due to marked exophthalmus and rotation of the eyeball it was impossible to examine the right eye. Values for body temperature, pulse/min, respiration/min and rumen contractions/5 min were within the normal reference range for adult cattle. Haematological examinations revealed anaemia, with lowered packed cell volume (23.9 %) and haemoglobin concentration (7.5 g/dl). The agar gel immunodiffusion test for EBL-antibodies was negative.

Post mortem examination

The cow was submitted for necropsy within 12 hours of euthanasia. A black, jelly boundless mass of irregular form up to 10 cm in diameter was located in the area of the right orbit and maxillary sinuses (Figure 1). The tumor mass extended into the right nasal meatus. Moreover, the left nasal hole was also filled with tumor tissue. Involved lymph nodes, lungs, liver, spleen and heart contained multiple irregular black areas varying in size from 0.5 to 3.0 cm in diameter. Metastases were disseminated on the surface and parenchyma of these organs.



Figure 1. Periocular area of the right eye as primary location of malignant melanoma (arrow). From this area the tumor mass has grown into the maxillary sinus and nasal meatus, causing their deviation.

Histopathological findings

The malignant melanoma was composed of melanoblastic tumor cells of the epithelioid type. The tumor was a black pigmented mass without any stroma and membranes. Younger immature forms of melanoblastic tumor cells with a large amount of dark brown to black pigment were differentiated. Neoplastic cells had infiltrated within lymphatic and blood vessels through the serosal surface and into the parenchyma of regional lymph nodes, liver, lung, spleen, heart and brain. In these tissues, nests of less differentiated variably sized epithelioid tumor cells were randomly distributed and infiltrated through the primary tissue. Infiltrates of neutrophils, macrophages and lymphocytes were visible around nests of tumor cells. In the brain tissue black pigmented tumor cells were observed in the lumen of blood vessels.

DISCUSSION

The described changes in the cow were characteristic for malignant melanoma. Malignant melanomas are very rare in cattle. The periocular area of the right eye was considered to be the primary location of the tumor. From this area the tumor mass had grown into the maxillary sinuses and nasal meatus, causing their deviation. Secondary neoplastic masses metastasized into the regional lymph nodes, lungs, spleen, liver, heart and brain. The malignancy of the tumor was macroscopically evident from the infiltrative growth into surrounding tissue, the spread by serosal membranes into other organs and accumulation in soft irregular black pigmented masses without membranes and base.

The exophthalmus and ventral rotation of the right eye, deviation of the right facial bones and progressive nerve signs were consequences of tumor pressure and growth into the involved tissue. Haematological examinations detected only lowered packed cell volume and haemoglobin values.

Post mortem findings in the other organs were the result of spread and infiltration of melanoblastic tumor cells through lymphatic and blood vessels. The spread of tumor to the meninges and brain tissue can be explained by passage of tumor cells into blood vessels around the ocular nerve (Figure 2). The ocular nerve is surrounded by an external membrane s.c. *dura mater* and internal membrane s.c. *pia mater*. They are separated by the space between (Banić 1988, Ellenberger and Baum 1977). Tumor cells could have passed through vessels located in *pia mater* into the brain tissue. The permeability of meninges is mechanically damaged by infiltration of tumor cells. In humans malignant melanomas of the choroid extend along the scleral canals into the orbit, but less frequently extrabulbar spread is by way of the optic nerve (Ashley 1978).

Metastases are characteristic for malignant melanomas and they are usually located in regional lymph nodes, lungs and liver. The spread of tumor cells within blood vessels is demonstrated by the finding of melanoblastic tumor cells in the lumen of blood vessels on histological smears. Nests of tumor cells were located perivascularly and infiltrated between cells of primary tissue. Increased numbers of macrophages, neutrophils and lymphocytes were established around tumor cells as an expression of the inflammatory reaction, probably secondarily to the neoplastic event. The tumor cells were classified as the epithelioid type of malignant melanoma and determined as some mature melanoblasts but mainly as very immature cells (small and diffuse black colored). Because of the strong



Figure 2. Black pigmented tumor cells in the brain tissue in the lumen of blood vessels (black arrow)
Haematoxylin - eosin x 100

black pigmentation we were not able to distinguish the cell structure of the melanoblasts. Usually epithelioid melanomas are not excessively pigmented (Weiss and Frese, 1974).

The etiology of malignant melanomas is still unknown. We consider that the primary location of the tumor mass was the chorioid tissue in the right eye. This can explain the metastases through the ocular nerve into the brain tissue and the marked exophthalmus of the right eye as a consequence of peribulbar tumor growth. Malignant melanoma of the choroid is an infrequent neoplasm but represents the most common intraocular malignant tumor in man (Ashley 1978). According to the available literature, this is the first reported case of malignant melanoma in a cow with secondary brain involvement.

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MALIGNI MELANOM KRAVE

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U ovom radu je prikazan slučaj malignog melanoma kod krave smeđe švajcarske rase stare 2,5 godine. Posle kompletnog kliničkog i hematološkog pregleda, zbog nepovoljne prognoze, izvršena je eutanazija i obdukcija životinje. Kliničkim pregledom su utvrđeni egzoftalmus desnog oka, devijacije kostiju lica i progresivni nervni simptomi. Obdukcijom je u predelu desne orbite ustanovljena crna tumorozna masa koja je dolazila do konhi i moždanih ovojnica. Sekundarne metastaze su otkrivene na srcu, u jetri, slezini, plućima i mozgu. Analizom histoloških preparata je utvrđeno prisustvo melanocita i zaključeno da je u pitanju maligni melanom epitelioidnog tipa koji je primarno nastao u desnom oku.