

Hepatic Malignant Melanoma in a Goat, Primary or Metastatic?

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ABSTRACT

This report presents a case of malignant melanoma without a confirmed primary tumor in a six-year-old, female, hairy goat (*Capra hircus*). Macroscopically, multicentric localizations of tumor lesions were seen in liver, hepatic lymph nodes, spleen and lungs. Histopathologically, these lesions were diagnosed as malignant melanoma. Variable intracytoplasmic melanin pigments were observed in tumor cells. In addition to these findings, occasional multinucleated giant cells and common mitotic figures were detected. For immunohistochemistry, avidin-biotin-peroxidase complex (ABC) method was used with primary antibody to Melan-A and diagnosis of malignant melanoma was confirmed by immunohistochemistry. This case demonstrates the difficulties in determining a primary tumor site of a malignant melanoma in a goat.

Key words: Malignant melanoma, Pathology, Immunohistochemistry Melan-A, Goat.

INTRODUCTION

Malignant melanoma is a malignant tumor of melanocytes and generally seen in older animals (1, 2). It is common in dogs and very rare in other domestic animals such as horses, swine, cattle, cats and goats (1, 3). Primary malignant melanoma appears most often in the skin and less frequently in the choroid layer of the eyes, under the nail, in the leptomeninges, oral cavity, nasal mucosa, pharynx, esophagus, bronchus, vaginal or anorectal mucosa and is the most important malignant tumor having the potential to metastasize to the gastrointestinal tract in humans (4). In animals, malignant melanomas are frequently seen on the skin of the head, limbs and other frequently affected sites including the mucous membranes and mucocutaneous junctions such as in the oral cavity (5). It is often locally invasive and metastases frequently occurs to regional lymph nodes and lungs. However, metastasis of malignant melanomas in animal to other body sites such as brain, heart, spleen and liver is uncommon (1). This report presents a case of malignant melanoma in a hairy goat (*Capra hircus*) without a confirmed primary tumor site.

MATERIALS AND METHODS

A six-year-old, female, hairy goat was presented for necropsy to Department of Pathology, Faculty of Veterinary Medicine, University of Mehmet Akif Ersoy, Burdur, Turkey. Tissue samples were fixed in 10% neutral buffered formalin, processed routinely, sectioned at 5 µm, and stained with hematoxylin and eosin (HE). Selected sections were stained for immunohistochemistry and processed according the manufacturer's instructions. For immunohistochemistry, avidin-biotin-peroxidase complex (ABC) method was used with primary antibody against Melan-A (Melan-A antibody, DAKO, Clone A103, Carpinteria, CA, USA). The reaction product was visualized by DAB [3, 3'-diaminobenzidine chromogen (Zymed, South San Francisco, CA, USA)] and counterstained with Harris' hematoxylin.

CLINICAL HISTORY

The goat had lived in a farm from the time of birth without any health problems until two weeks before death. It showed

respiratory distress and inappetence. There were not clinical symptoms suggestive of a liver tumor such as icterus. The goat died two weeks after the initial clinical signs. The owner stated that the goat's body condition was excellent before illness but slight cachexia was observed at necropsy.

Macroscopic Findings

The necropsy material was examined in detail for cause of death and possible primary and metastatic tumor lesions. At the post mortem examination the goat was diagnosed with severe hepatomegaly. The liver contained numerous widely distributed firm black pigmented tumor nodules. In addition, other tumor nodules were only seen in hepatic lymph nodes,



Figure 1: Gross appearance of malignant melanoma shows firm and black pigmented tumor nodules arising from the liver, hepatic lymph nodes and lungs.

spleen and lungs (Figure 1). These lesions ranged in size from 0.5 to 4 cm in diameter. In particular, liver nodules were detected frequently, but only three nodules were detected on the lungs. There was no evidence of ocular and dermal primary lesions in any other common site for primary or metastatic spread of malignant melanoma.

Microscopic Findings

Microscopically, tumor areas were found in multicentric localizations and pleomorphic melanocytes were present in various morphological patterns including solid sheets, nests and bundles with interstitial fibrovascular stroma. The anaplastic tumor cells were round to oval and varied in size. They had variable nuclear pleomorphism including nuclear hyperchromasia and irregularities with multiple prominent nucleoli and moderate cytoplasm. Intracytoplasmic dark brown melanin pigments were seen in the tumor cells (Figures 2 and 3). In some areas of tumor, occasional multinucleated giant cells were observed. Mitotic figures were generally common and the mitotic index was 3-5 mitoses/high powered fields (40x). In the tumor stroma, mononuclear cell infiltrations and hemorrhages were seen.

Immunohistochemical Findings

Immunohistochemically, most of the tumor cells displayed positive cytoplasmic immunoreactions for Melan-A (Figure 4). Staining with Melan-A antibody was always diffusely cytoplasmic and never nuclear. The Melan-A positive cells were homogeneously distributed throughout the tumoral masses.

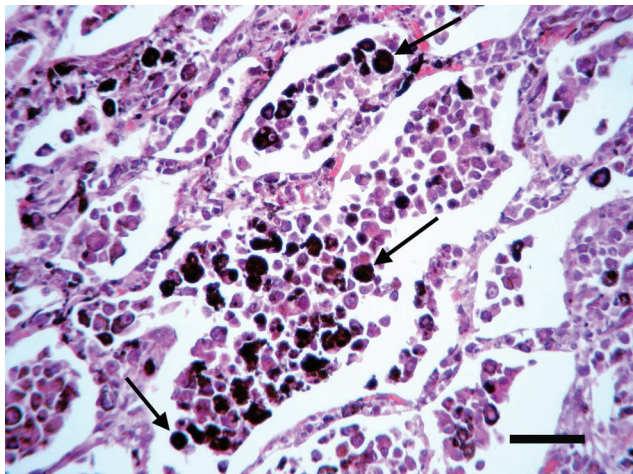


Figure 2: Malignant melanoma. Intracytoplasmic melanin pigments in the tumor cells of lung (arrows). HE, bar= 50 μ m.

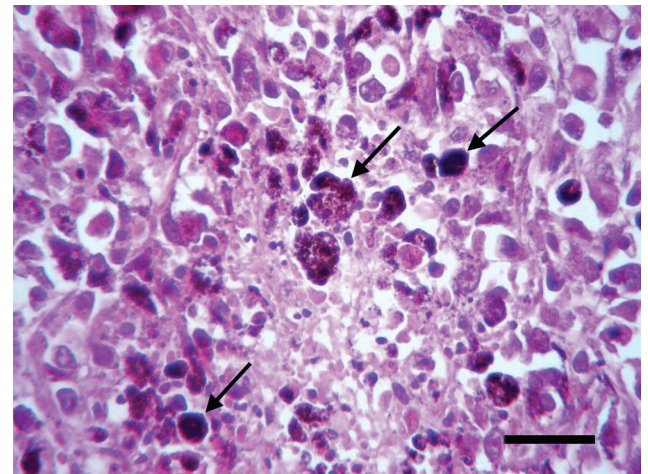


Figure 3: Malignant melanoma. Dark brown melanin pigments in the cytoplasm of tumor cells of liver (arrows). HE, bar= 30 μ m.

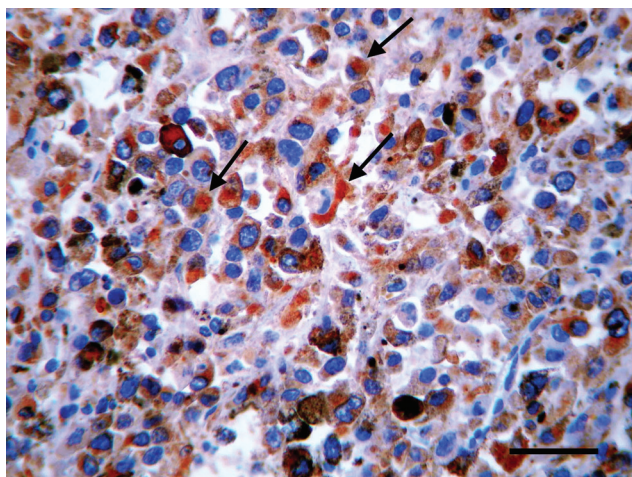


Figure 4: Malign melanoma. Immunohistochemical staining for Melan-A showing cytoplasmic positivity in tumor cells. ABC method, Harris hematoxylin counterstain, bar= 30 μ m.

The intensity of staining was higher in central areas of the tumors. It was not uncommon for positive cells to be heavily laden with melanin. Those cells with both melanin and the DAB product had a brown-green cytoplasm.

DISCUSSION

Melanocytic tumors originate from epidermal melanocytes or melanoblasts which are of neuroectodermal origin (6, 7, 8). The behavior of malignant melanomas in humans is that of rapid growth and high aggressiveness with a fast spread from the primary tumor site by metastasis. The primary malignant melanomas may be located on limbs (22%), the trunk (40%), head and neck (15%), and in 16% of cases in humans from an unknown site (9). In addition, primary malignant melanomas of gastrointestinal tract and gallbladder are reported to be extremely rare (10, 11). In the goat, primary sites for malignant melanomas are reported from the skin, coronary band of the hoofs and the horn buds (12, 13). Metastases often spread hematogenously or via lymphatics to regional lymph nodes, liver, small intestines, heart, brain, spleen and lungs (14, 15).

In this report, multiple melanotic tumor lesions were seen on the serosal and cut surface of liver, hepatic lymph nodes, spleen and lungs. Before making the diagnosis of primary intestinal malignant melanoma, other primary melanomas must be eliminated (16). In extensive investigation of the cadaver, no tumor lesion was seen on the skin, in the uveal tract, oral cavity, mucocutaneous junction of the lips, other mucosal sites, coronary band of the hoofs, the horn buds

and internal organs except in the liver, hepatic lymph nodes, lungs and spleen.

Previously reported metastatic tumors are generally presented as well-defined multiple tumor lesions in different organs (17). In the presented case, because of the multiple localization of well-defined tumor lesions in the multiple organs, it is considered that these lesions were metastases of malignant melanoma. In our case, due to the lack of a primary site for a malignant melanoma, the source of primary tumor could not be determined.

The possibility of a primary intestinal malignant melanoma was considered. This location has been reported to be extremely rarely in the gastrointestinal tract of humans (10, 11). It has been proposed that differentiated ectodermic cells may approach the distal ileum and colon via the omphalomesenteric duct, thus serving as the precursor of primary intestinal melanomas (18). According to this hypothesis it is thought that the possible primary site of the tumor may be the intestines with hematogenously and/or lymphatics metastases to hepatic lymph nodes, liver, spleen and lungs, as in this case. However, in the case presented here no tumor lesions were detected in the intestines. However there is a possibility that a primary tumor in the intestines might have regressed before the appearance of metastases or were too small to be diagnosed by conventional clinical and laboratory techniques.

The Melan-A protein is a melanocytic differentiation antigen and previous studies have shown that Melan-A to be the most frequently demonstrated antigen in metastatic melanomas including lymph node (19, 20). In a previous case of malignant melanoma case in a goat, Melan-A is used for confirmation of melanocytic differentiation with tumor cells staining positive (21). In this case, tumor cells in sections were demonstrated to be positively immunoreactive for Melan-A thus confirming the diagnosis of a melanoma using immunohistochemistry.

In conclusion, this case in a goat is presented in view of its rare occurrence in the liver, spleen, lungs and hepatic lymph nodes without a confirmed primary tumor site.

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