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Concurrent occurrence of malignant melanoma and amyloidosis in a horse

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Summary

In a 16-year-old mare of mixed breed, with gray coat, which was used for 2 years for production of polyvalent anti-snake antiserum, some nodules appeared on the underside of the tail and perineum. The animal gradually became weakened and showed weight loss and eventually, was euthanatized. Based on necropsy findings and histopathologic examination, affection to malignant melanoma was confirmed. By applying Congo red for detection of amyloidosis, deposition of amyloid within the wall of arterioles of spleen and a small amount inside the hepatocytes were observed.

Key words: Horse, Malignant melanoma, Amyloidosis, Histopathology

Introduction

Amyloidosis is a condition characterized by the deposition of an amorphous, predominantly extracellular, eosinophilic material called amyloid in various body tissues and organs (Bancroft and Gamble, 2002). It may be seen as microscopic deposits, as plaques or confluent masses that may progressively replace the parenchyma of the affected organs, and the accumulation of amyloid protein in extracellular space that compresses the adjacent structures. The normal tissue eventually atrophies or becomes necrotic due to pressure or lack of blood supply, resulting in gradual loss of function and eventual death (Jones and Hunt, 1983; Jubb *et al.*, 1985; Feldman *et al.*, 2000; MacGavin *et al.*, 2001; Bancroft and Gamble, 2002). Most cases of amyloidosis in domestic animals are idiopathic but appear to be of the reactive systemic type. The deposits of amyloid may be found in many organs such as the liver or spleen, but the kidney is the organ most commonly involved in amyloidosis. Amyloidosis occurs in horses used for antiserum production (Jubb *et al.*, 1985).

The melanocytic tumors of domestic animals include a group of neoplasms

composed of melanin-producing cells (melanocytes). One of the main functions of melanin is the protection of the skin from the harmful effects of sunlight. Melanocytes are normally found in various ocular structures, in addition to the skin and may also be present in the meninges, adrenal gland and in the intima of the heart and blood vessels in some species (Jones and Hunt, 1983; Jubb *et al.*, 1985; MacGavin *et al.*, 2001; Meuten, 2002). Melanocytic tumors are relatively common in the dog, horse and certain breeds of swine. They are less frequent in cattle and goats and quite rare in cats and sheep. In the horse melanocytic tumors represent 6% to 15% of the skin tumors. There is a striking relationship between the incidence of melanocytic tumors and gray coats in the horse, though occasionally they are found in horses with other hair color. There is an increasing tendency for development of melanocytic tumors as the gray horses grow older so that approximately 80% of gray horses over 15 years have developed clinically recognizable melanocytic growths. It has been suggested that all gray horses eventually become affected with melanocytic tumors if they live long enough (Jubb *et al.*, 1985; MacGavin *et al.*, 2001;

Meuten, 2002). Melanocytic tumors in the horse are usually multiple and generally originated in the skin. The most common sites are the perineum and the underside of the root of the tail; other areas are affected much less frequently. Malignant melanomas can metastasize via lymph channels and blood, probably regardless of their origin. Regional lymph nodes are the first sites affected. The lung is one of the most common sites of visceral involvement. Widespread metastasis occurs in many cases (Jones and Hunt, 1983; Jubb *et al.*, 1985; MacGavin *et al.*, 2001; Meuten, 2002).

Case history

A 16-year-old mare of mixed breed, with gray coat, which was used for two years for production of polyvalent anti-snake antiserum, showed the sign of inflammation in the root of the tail. Gradually, some nodules appear on the underside of the tail, which became ulcerated and infected. Antibiotic therapy had no effect on the course of the disease. Later, other nodules appeared on the perineum and vulva. The animal gradually became weakened and showed weight loss. Eventually, rely on the history and the clinical signs, it was

suspected to have malignant melanoma and therefore euthanized. Necropsy was performed (Jubb *et al.*, 1985; Meuten, 2002).

Results

Root of the tail had several nodules different in size on the ventral side, which in some parts were ulcerated. There were similar nodules on the perineum and vulva. In longitudinal section of the tail, some black nodules were observed (Fig. 1). Moreover, a big mass was found in the caudal part of the right kidney. No specific lesion or tumorous mass was observed on the surface and cross section of the kidneys. The liver was enlarged with round edge and had multiple nodules on its surface. In cross sections, these nodules had different size and color (pale to deep black). The spleen was enlarged and had several nodules, some of which were as large as a small orange. In the mediastinal lymph nodes and lung, there were multiple metastatic masses (Fig. 3), some of which were black and could be separated from the parenchyma. No specific gross changes were observed in other organs. In histopathological examination,

Fig. 1: Malignant melanoma masses are seen in longitudinal-section through the root of the horse tail (arrows)

Fig. 2: Malignant melanoma in the skin of the horse. Turmeric cells are seen inside the dermis in one part disintegrated epidermis and causes ulceration (arrow). (H&E ×200)

Fig. 3: Metastatic mass of the malignant melanoma in the lung of the horse. Arrow points to a turmeric mass inside a bronchiole. (H&E ×200)

Fig. 4: Amyloid deposits are seen within the wall of arterioles of the spleen (arrows). (Congo red ×400)

there were anaplastic melanocytes in some parts of the skin. However, in other parts grew enough to disintegrated epidermis and ulceration (Fig. 2). Addition of infection caused inflammation in ulcerated lesions. The anaplastic melanoma cells showed considerable pleomorphism, ranging from cuboidal to fusiform in shape. In the skin, the cells were predominantly fusiform. There were bizarre giant cells between anaplastic cells. The mitotic figures were rare. The cells tend to lie in alveolar form or in irregular branching strands. The melanin contents of the cells in turmeric masses were significantly variable in different parts; in most parts considerable amounts were found.

By applying the Congo red dye, deposition of amyloid within the wall of arterioles of spleen (Fig. 4) and in a much smaller amount, inside the hepatocytes were observed. No amyloid deposit was observed in the kidneys.

Discussion

The age, gray coat and development of malignant melanoma on the perineum and the site of involvement (underside of the

root of the tail) in this horse, were all in agreement with earlier reports (Jubb *et al.*, 1985; MacGavin *et al.*, 2001; Meuten, 2002). Presence of anaplastic melanoma cells in mediastinal lymph nodes revealed that metastasis via lymph channels were already occurred (Meuten, 2002). Moreover, numerous turmeric nodules in the lung and liver showed that these organs are at higher risk of metastasis (Jones and Hunt, 1983; Jubb *et al.*, 1985; MacGavin *et al.*, 2001; Meuten, 2002). It is probable that the large mass on the caudal part of the right kidney was in fact a lymph node that was metastasized early from perineum into the pelvic cavity.

Absence of amyloid deposit in the kidneys was in contrast to reports that revealed early involvement of kidney in such a condition (Jones and Hunt, 1983; Feldman *et al.*, 2000; Bancrft and Gamble, 2002). Amyloid infiltration of the liver in horses occurs chiefly in those used for the production of hyperimmune serum (Jubb *et al.*, 1985; MacGavin *et al.*, 2001; Meuten, 2002). As we observed, amyloid is deposited primarily in the parenchyma about the portal branches that predisposed the liver to rupture (Jubb *et al.*, 1985; MacGavin *et al.*, 2001; Meuten, 2002). Amyloidosis of the

spleen occurs as part of generalized amyloidosis. The deposition of amyloid occurs first in the small arteries of the lymphoid sheaths (Jones and Hunt, 1983; Jubb *et al.*, 1985; MacGavin *et al.*, 2001). In our case, no amyloid deposit was observed in other organs. This is also in contrary to many reports disclosing deposition of amyloid in other organs. This might be attributed to the short time this animal was used for production of antiserum. Based on our results, it is likely that the spleen shows the sign of amyloidosis earlier than kidney. Although some plasma cell disease such as multiple myeloma, causes amyloidosis (myeloma-associated amyloidosis) and there is also amyloidosis associated with aging (Bancroft and Gamble, 2002), repeated injection of antigen (snake venom) to the horse can cause amyloidosis. Nevertheless, we believe that concurrent occurrence of amyloidosis and malignant melanoma was perhaps accidental.

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