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Clinical Report

# Malignant (Anaplastic) Amelanotic/Hypomelanotic Melanoma in a Kurdish Gelding

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**ABSTRACT**

We report an 11-year-old Kurdish gelding with an anaplastic malignant melanoma arising from his right lateral of the neck, which developed over 6 weeks. A ~10 cm in diameter, firm, and non-ulcerated nodular subcutaneous mass located at the middle and proximal of the left side of the neck was detected in a physical examination. No evidence of local extent or metastasis was detected. Complete surgical excision was performed under general anesthesia. Gross morphology and histopathological examination of the mass confirmed an anaplastic malignant melanoma, in which the major part of the mass has little or no pigmentation. The gelding was euthanized due to tumor regrowth. The heterogeneity in pigmentation of equine melanocytic tumors can make diagnosis difficult in punch biopsy specimens. Anaplastic malignant melanoma is most often a very aggressive neoplasm and surgical excision was not effective in this case.

## Case Description

An 11-year-old grey Kurdish gelding was presented with a fast-growing soft tissue mass located on the right mid-cervical regions. It was first recognized by the owner 6 weeks prior to a veterinary consultation. He had not received any treatment. The gelding had no previous history of skin cancer, history of trauma or injection in the affected area of the neck. The gelding was bright, quiet, alert, responsive, and in a body condition score (BCS) of 6 (on a scale of 1–9).[1] Heart rate, respiratory rate, body temperature, and capillary refill time were within reference limits. An about 10 cm in diameter, firm, and non-ulcerated single nodular subcutaneous mass located at the middle of the right side of the neck was present (Figure 1). The mass was firmly attached to the lower tissues on palpation. No other lesions were identified on other parts of the body on physical examination. There was no evidence of metastasis to the abdomen, thorax or other distant sites

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following regional lymph nodes assessment, thoracic radiography and rectal examination. The gross tumor margins were determined via ultrasonographic examination, and the lesion invasion deeply into the subcutaneous tissue was not detected. The hematological and biochemical profiles were in the normal range. Based on the clinical and ultrasonographic findings, a single tumorous mass was suspected.

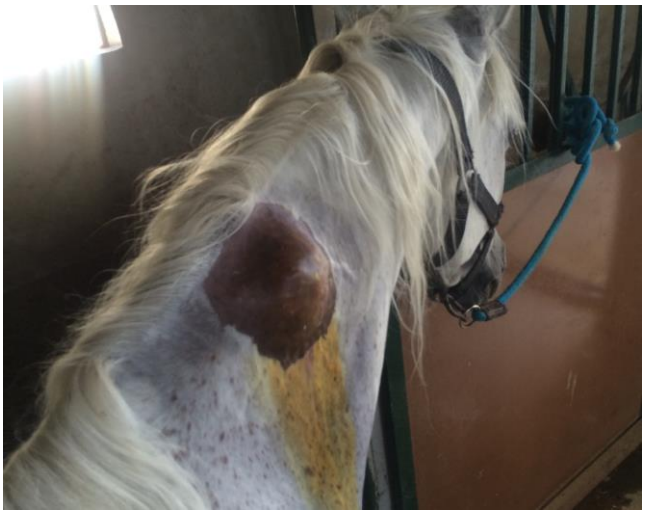

***Figure 1.*** Single nodular subcutaneous mass located in the middle of the right side of the neck in an 11-year-old Kurdish gelding.

## Treatment and Outcome

Regarding the location and size of the mass, no involvement of other sites and no evidence of metastasis, it was decided to perform complete surgical excision along with a safety margin of at least 1 centimeter under general anesthesia. Perioperative flunixin meglumine (0.5 mg/kg, IV), penicillin G procaine (20,000 IU/kg, IM), and gentamicin sulfate (6.6 mg/kg, IV) were administered. The entire removed mass was fixed in 10% formalin solution and sent for histopathological analysis.

The gross appearance was indicative of a tumorous, multilobular, firm, fleshy mass. The mass had a variegated appearance, with areas of pigmentation intermingled with non-pigmented regions. The central base of the mass attached to the neck muscles was heavily melaninized. Some parts surrounding this area was poorly (sparsely) pigmented. A major part of the mass was pale yellow and unpigmented with melanin (Figure 2). Histopathological examination revealed marked pleomorphic to fusiform cells and mitotic activity. Mitoses averaged 5/high power field. Amounts of intracytoplasmic melanin varied greatly -heavy pigmentation to little or no pigmentation in different parts of mass. Gross morphology and histopathological evidence led to a diagnosis of malignant amelanotic melanoma.

Post-operative complications in the short-term follow up was seroma accumulation in the surgical site. A large 30 cm in diameter multinodular tumorous mass regrew at the excision site during the 6 months post-operation (Figure 3). Due to the location and numerous sizes of the tumor as well as its deep extension into the subcutaneous tissue, surgical removal was not considered to be an option. The prognosis was poor and the owner accepted to euthanize the gelding. In post mortem examination, there was no evidence of metastases within local lymph nodes or other organs. There were no other significant lesions. The gross appearance of the recurrent mass included multilobulated, irregular, fleshy, firm, pale tan and confluent. Histopathological evidence was consistent with a malignant (anaplastic) amelanotic tumor.

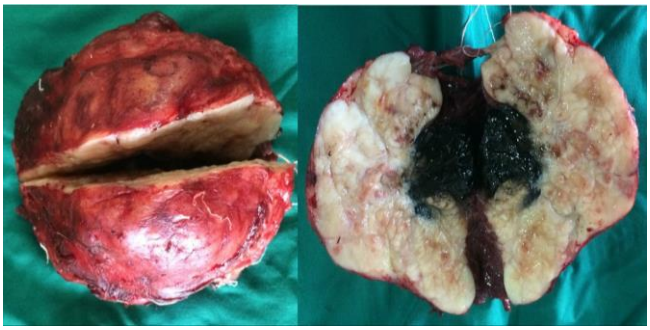

***Figure 2.*** Cross section of the surgically excised anaplastic malignant melanoma in an 11-year-old Kurdish gelding. The tumor mass was fleshy, multilobular. Also, major part of the mass was unpigmented or poorly pigmented with melanin.

***Figure 3.*** Clinical presentation of a multinodular and large anaplastic malignant tumor, with regrew at the excision site during the 6 months post operation.

## Clinical Relevance

Melanocytes are dendritic cells derived from neuroectodermal melanoblasts that migrate during embryogenesis to the epidermis, dermis, and other sites (eg, eye, inner ear, meninges). Through the process of melanogenesis, these cells produce a pigment called melanin, which can be found in the skin, eyes, and hair.[2] Melanomas are tumors that arise from the malignant transformation of normal melanocytes. The etiology of melanocytic tumor development is still not completely understood but is believed to be secondary to genetic mutations in the melanin metabolism molecular pathway.[3] Also, an association between increased ultraviolet radiation exposure and tumor growth has been suggested.[4] Melanomas are among the most common skin tumors in horses (second only to sarcoid), comprising between 3.8% and 15.0% of all skin tumors.[2] Although melanomas have been diagnosed in horses of all colors, a marked predisposition has been extensively reported in gray horses over 15-years-old.[2,5,6]

Equine melanocytic tumors have been recognized as slow-growing, low-grade neoplasms. Although most cutaneous melanomas are benign at initial presentation, if left untreated, up to two-thirds can progress to overt malignant behavior capable of extensive local invasion and widespread metastasis.[2,7] The most common location for melanocytic neoplasms are the undersurface of the tail, perineal region, and prepuce.[8] Less commonly affected sites include the periorbital, head/neck, parotid region, guttural pouches, commissures of the lips, and limbs.[9] From these primary locations, metastasis may occur by either hematogenous or lymphatic spread to any region of the body.[2]Smaller melanocytic tumors typically cause no clinical signs. Larger tumors may obstruct the rectum or prepuce and parotid melanomas can prevent neck flexion, or impinge the upper airway. Necrosis of the tumor and overlying skin may result in substantial open wounds with a tarry black discharge and bleeding.[4]

The term equine melanoma or melanocytic tumor encompasses all histologic and clinical variants from the benign to the most anaplastic malignant variants. Four distinctive manifestations of equine melanocytic tumors have been defined based on clinical presentation, histologic examination, tendency to become malignant, and response to surgical excision.[1] Benign melanocytic nevi or benign melanocytoma (tumor cells located in the superficial dermis or at the dermo-epidermal junction),[2] dermal melanomas (single neoplastic nodule located in the deep dermis, and appear histologically as small, homogeneous, indistinct round or dendritic tumor cells containing condensed chromatin and dense cytoplasmic pigmentation, They demonstrate minimal malignant criteria),[3] dermal melanomatosis (multiple to confluent neoplastic nodules in the deep dermis),[4] anaplastic malignant melanoma (neoplastic cells with marked pleomorphism, moderate to a high number of mitotic figures, variable pigmentation, and invasion).[10,11] In the present gelding, gross morphology and histopathological finding of primary mass were consistent with anaplastic malignant melanoma.

Both malignant and benign neoplasms may be highly pigmented or lack pigment. The color of the neoplasm of melanoma depends on the amount of melanin within the cells and varies from black through various shades of brown to gray, pale tan, and white.[6,12,13] Size and degree of pigmentation are not reliable indicators of the malignant potential or prognosis of these melanocytic neoplasms.[12] Also, malignant melanoma cannot be differentiated from melanocytoma on gross examination. The tumor tissue submitted in this case (a major part of the primary and all of the part of recurrent tissue) represented an amelanotic malignant melanoma. Although the diagnosis of melanocytic neoplasms in horses is typically straightforward due to heavy pigmentation, equine melanomas may be amelanotic or poorly pigmented.[6,14] The absence of pigmentation in the tumor may result in diagnostic confusion. Also, the heterogeneity in pigmentation can make diagnosis difficult in punch biopsy specimens. Furthermore, the variety of histologic appearances of equine melanocytic neoplasms makes them difficult to distinguish from schwannoma and equine sarcoid.[11]

Diagnosis of melanocytic neoplasia in poorly pigmented melanocytic neoplasms in horses can be challenging and relies on histopathological or cytological examination of tumor cells. Immunohistochemistry is only necessary when melanin cannot be found on routine H&E evaluation of the neoplasm that is widely used to confirm a diagnosis of melanoma in human and veterinary medicine. Commonly used antibodies are Melan-A, S100, TRP-1, TRP-2, and PNL2.[4] PNL2 is the marker of choice in equine melanomas and it is expressed in 100% of equine melanocytic neoplasms. Electron microscopy has been used to identify premelanosomes in

amelanotic tumors, but is rarely useful for routine diagnosis.[15]

Malignant melanomas are often rapidly growing and can be fatal. There is a local invasion into the subcutaneous tissue, thus, surgical margins should be carefully evaluated for the presence of neoplastic melanocytes. At least 1 mm of uninvolved tissue is suggested for lateral and deep margins. Those masses removed with cautery/lasers often have distortion of the tissue at the margins, making an accurate evaluation of these margins difficult or impossible. It has been suggested that excision of large (ranging from 4 to 20 cm diameter) melanocytic tumors in horses is a viable treatment option that is locally curative with minimal complications.[4] However, it has been indicated that anaplastic malignant melanoma in horses often occurs on the tail and that, with rare exceptions, it is an aggressive tumor leading to death within a year of diagnosis. Surgical excision, including tail amputation and medical therapy (cimetidine) do not appear to be effective in most cases of anaplastic malignant melanoma in horses.[13]

Findings of the present study suggested that anaplastic malignant melanoma might have little or no pigmentation and heterogeneity in pigmentation and could make diagnosis difficult in punch biopsy specimens. Furthermore, surgical excision was not effective for the treatment of anaplastic malignant melanoma of the neck in this grey gelding.

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