



Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 93 Month: March Year: 2018

Answer Sheet

Title: Equine, skin, neoplasia, sarcoid.

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Microscopic Findings: Haired skin masses: Extensively effacing the dermis and subcutaneous tissue in the sections of all five submitted masses was an exophytic, poorly demarcated, densely cellular, non-encapsulated, malignant mesenchymal neoplasm composed of haphazard bundles and partial whorls of spindle cells supported by scant fibrous connective tissue (Figure 2). Neoplastic cells had thin light basophilic cytoplasmic processes with variably distinct cell borders. The nuclei were oval to elongate, with vesicular to coarsely stippled chromatin and generally inconspicuous nucleoli. Anisocytosis and anisokaryosis were moderate to marked; the mitotic index was low (2 mitotic figures in 10 high power fields). The overlying epidermis, which was irregularly hyperplastic with long, thin and branching rete ridges, was frequently ulcerated and replaced by hemorrhage and cellular debris, sometimes containing basophilic bacterial colonies. Degenerate neutrophils, fewer macrophages, and rare eosinophils infiltrated the exposed surfaces of the neoplastic masses. In the few areas where the extensively ulcerated, irregularly hyperplastic epidermis remained, neoplastic cells were variably palisading along the dermal-epidermal junction. The epidermis adjacent to the masses had moderate to marked orthokeratotic hyperkeratosis.

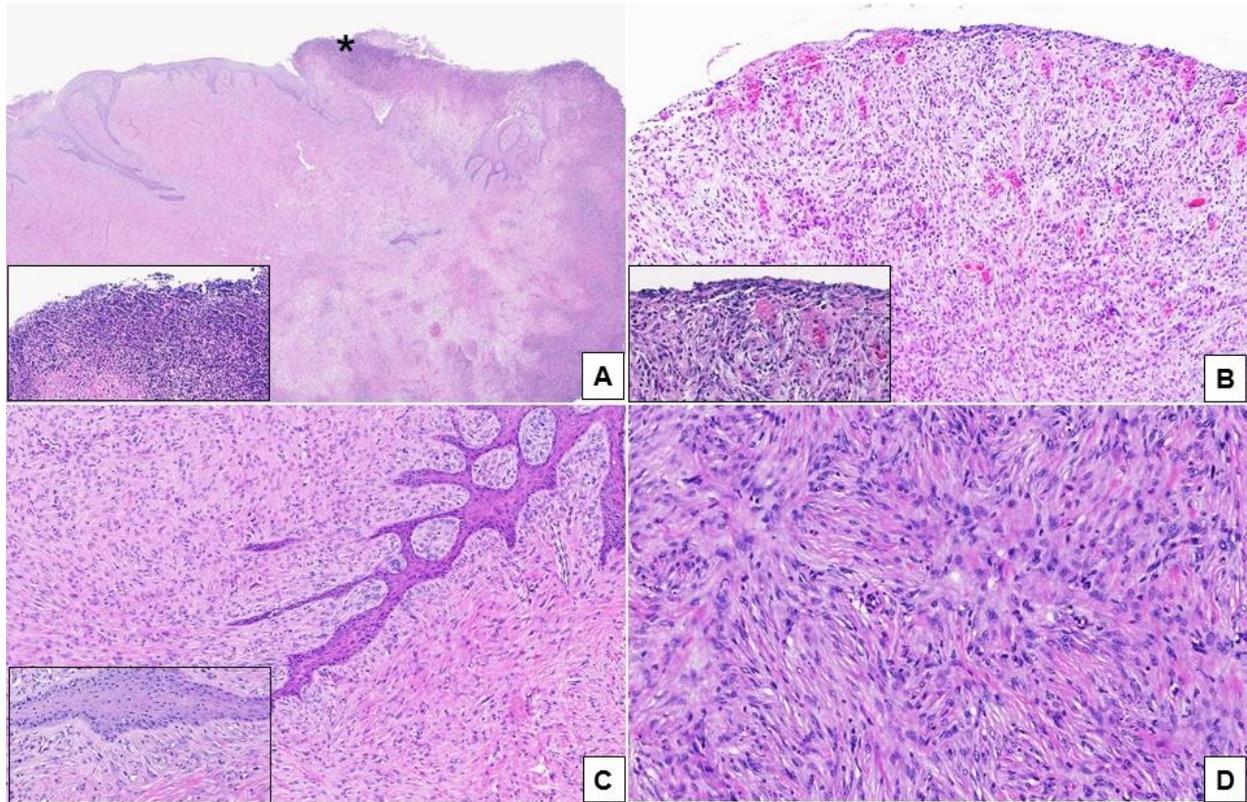


Figure 2. Horse, haired skin hindlimb masses. Spindle cell sarcoma consistent with Equine Sarcoid. (A) The dermis and subcutis are effaced by a malignant mesenchymal neoplasm. The overlying hyperplastic epidermis is multifocally ulcerated (asterisk). H&E, subgross microphotograph. Inset, 20x. (B) Higher magnification of A at the ulcerated areas with mild mixed superficial inflammatory cell infiltrate. H&E, 10x. Inset, 40x. (C) Prominent neoplastic spindle cell proliferation. The overlying intact epidermis is irregularly hyperplastic with multiple long, thin and branching rete ridges. H&E, 10x. Inset, the neoplastic cells are variably palisading along the dermal-epidermal junction 40x. (D) Neoplastic spindle cells are arranged in whorls, interlacing bundles, and haphazard arrays. H&E, 20x.

Morphologic Diagnosis:

Haired skin masses: Spindle cell sarcoma consistent with Equine Sarcoid (Mixed, Fibroblastic and Verrucous forms)

Discussion: Sarcoids are the most common skin tumors of horses, accounting for up to 90% of skin tumors.¹³ They are locally aggressive, non-metastatic fibroblastic tumors that can become more proliferative and invasive if traumatized.^{7,9,13} The most common involved locations are head, limbs, and ventral trunk, but sarcoids can also develop elsewhere on the body.¹³ Young horses between 1 and 7 years of age are at increased risk; reports involving older horses are rare.¹³

A clinical classification into five distinct types has been proposed for sarcoids: occult, verrucous, fibroblastic, nodular, and mixed.¹⁵ A sixth type (malevolent/malignant) was proposed, being characterized by marked local invasiveness and presumptive lymphatic infiltration based on palpable peripheral cords of tumor.¹⁰ However, histologic comparison of the various tumors did not show any difference among these groups, suggesting a weak correlation between clinical classification and histologic lesions.¹²

Histopathology is necessary for definitive diagnosis of sarcoids.¹³ Histopathologic findings are characterized by the proliferation of neoplastic spindle cells arranged in bundles and whorls in the dermis, with a “picket fence” pattern at the dermo-epidermal junction and hyperplasia and hyperkeratosis of the overlying epidermis, with thin long epidermal rete peg extensions into the tumor.¹² Ulceration of the overlying epidermis with secondary bacterial infection and inflammatory cell influx is frequent and makes the distinction between exuberant granulation tissue and sarcoid more difficult.¹³ The histologic similarities between inflamed sarcoids and exuberant granulation tissue can easily lead to misdiagnosis. Exuberant granulation tissue is a common condition in horses, with similar site predilection but very different clinical approaches.^{16,17} The distinction between these two lesions can therefore be easily blurred when dealing with chronic ulcerated lesions, particularly in the presence of variable degrees of secondary tissue damage due to an assortment of prior treatments.

Equine sarcoids have been associated with infection with bovine papillomaviruses (BPV) types 1, 2 and 13^{11,14} and is, thus, considered the most important papillomavirus-induced lesion in the horse.¹³ Martens et al. (2000) demonstrated the presence of BPV DNA in all 50 sarcoid cases included in their study: 74% were positive for BPV1 and 26% for BPV2. Nevertheless, the pathogenesis of sarcoids is not yet well understood since normal horse skin can also be positive for BPV DNA by polymerase chain reaction (PCR) testing.^{2,18} There is a widespread occurrence of BPV in the horse population and, as a result, latent viral infection needs to be considered in PCR-positive cases.² As a result, bovine papillomaviral infection alone does not seem to be enough for the development of sarcoids. A combination of factors should therefore be considered in the pathogenesis of sarcoids, including exposure to the viral agent, cutaneous trauma, and genetic predilection of Appaloosas, Quarter Horses, Arabians, Thoroughbreds, and Franches-Montagnes.^{4,13}

Differential diagnoses of sarcoid include peripheral nerve sheath tumors, fibromas, fibrosarcomas, and other spindle cell neoplasms. And, as already stated above, particularly in ulcerated chronic lesions, exuberant granulation tissue should also be ruled out. The distinction between the latter and sarcoid is very important since their clinical

approaches are very different. Complete excision of the tumor is curative⁹ but recurrence is common in inadequately excised masses.⁹ Spontaneous regression of sarcoids has rarely been reported.¹ Sarcoids therefore generally require association of surgical excision with chemotherapy or immunotherapy.^{8,10} They do not metastasize, however.⁹

Recent research has revolved around establishing standardized diagnostic procedures for equine sarcoids. Ten tumors initially diagnosed as schwannomas were positive for BPV 1 or 2 via PCR, had strong positive expression of vimentin and were negative for S-100 via immunohistochemistry, leading to reclassification of these tumors as atypical forms of sarcoids.³ However, broader studies comparing equine sarcoids to other spindle cell tumors found a high variability in S100 immunolabeling and BPV PCR results.⁵ An alternative diagnostic test, albeit expensive and therefore still seldomly performed, has been developed using an in situ hybridization technique to locate BPV nucleic acids in the nuclei of proliferating fibroblasts.⁶ This new technique also represents a way to further investigate the role of BPV in the pathogenesis of sarcoids.

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