

Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 103 Month: August Year: 2018

Answer Sheet

Title: Giant cell tumor of soft tissue in a horse.

Contributors: Tatiane Terumi Negrão Watanabe¹, DVM, MS, PhD; Charles T. McCauley², BS, DVM, ABVP, ACVS; Clarisa Krueger², BS, DVM, MS; Rudy Bauer¹, BS, DVM, PhD, DACVP. ¹Louisiana State University School of Veterinary Medicine, Department of Pathobiological Sciences and Louisiana Animal Disease Diagnostic Laboratory, Baton Rouge, LA 70803, USA. ²Louisiana State University School of Veterinary Medicine, Department of Veterinary Clinical Sciences, Baton Rouge, LA 70803, USA.

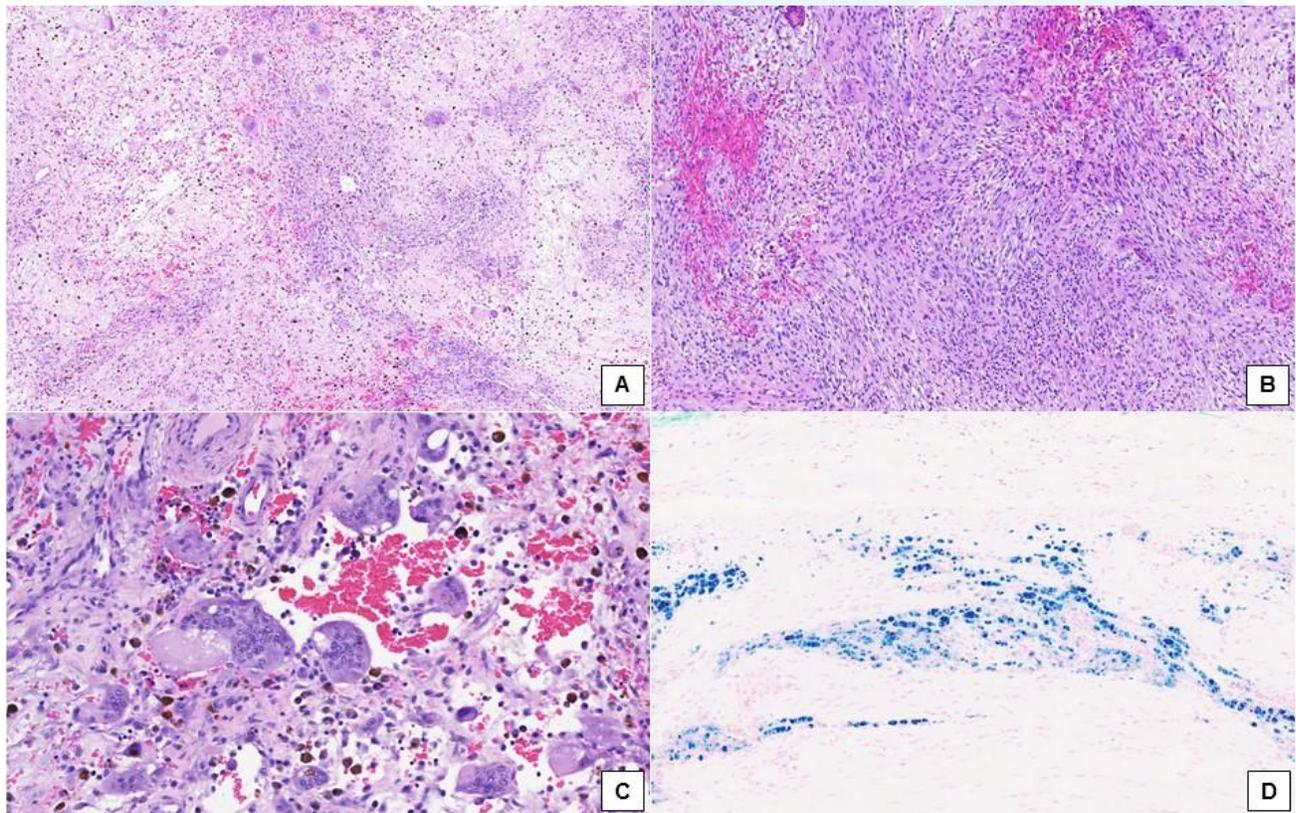


Figure 2

Microscopic Findings: Subcutis (proximal right rear leg): The mass was characterized by a non-encapsulated, well-demarcated, expansile, moderately cellular neoplasm of haphazardly arranged spindle cells in bundles and streams supported by a scant fibrovascular stroma (Figure 2A). Neoplastic cells were spindle-shaped with indistinct cell borders and variable amount of homogeneous to vacuolar eosinophilic cytoplasm. The nuclei were round to polygonal, often indented with finely to coarsely stippled chromatin and up to two small basophilic nucleoli. Anisocytosis and anisokaryosis were moderate (Figure 2B). Mitotic figures were two per ten high power fields. Interspersed among the spindle cells were frequent multinucleated giant cells with abundant cytoplasm and up to 51 nuclei (Figure 2C), often associated with numerous variably sized light brown crystals consistent with hemosiderin (positive with Gomori Prussian Blue stain) (Figure 2D). There were multifocal areas of necrosis and hemorrhage. Low numbers of lymphocytes and rare plasma cells were scattered throughout the neoplasm and infiltrating the surrounding tissue.

Figure 2. Horse, subcutaneous mass. Giant cell tumor of soft tissue. (A) Moderately cellular neoplasm of haphazardly arranged spindle cells in bundles and streams supported by a fibrovascular stroma. There are multifocal areas of necrosis and hemorrhage. H&E, 5x. (B) Higher magnification of the Figure 2A. Neoplastic spindle cells have indistinct cell borders and variable amount of eosinophilic cytoplasm. There are scattered small numbers of lymphocytes. H&E, 10x. (C) Frequent numbers of multinucleated giant cells are intersperse among the spindle cells, often associated with numerous variable sized light brown crystals. H&E, 20x. (D) Majority of the brown pigment is positive for iron. Gomori Prussian Blue stain, 10x.

Morphologic Diagnosis: Haired skin, subcutis: Giant cell tumor of soft tissue.

Typical microscopic findings: Spindle-cell proliferation, numerous multinucleated giant cells, abundant numbers of hemosiderin-laden macrophages, multifocal areas of hemorrhage and necrosis.

Discussion: Giant cell tumor of soft tissue is a rare neoplasm (1% of all cutaneous neoplastic lesions of equids)¹⁰ potentially having a locally aggressive behavior but with low metastatic potential,^{1,3,6} reported in many domestic species^{2,4,5,10} and also described in humans³. In horses, this neoplasm is described mainly affecting mature animals (average age is 6.8 years⁵; however, other studies suggest 10 years or older¹, and in one report the average age was 12.9 years¹⁰). No breed predisposition is evident.¹⁰ Sex predisposition is variably described (no sex predisposition¹⁰ vs more males being affected¹). Additionally, low numbers of cases precludes adequate report of long-term prognosis.^{1,5,9} Complete surgical excision with adequate margins and a combination of laser surgery with adjunctive therapy are likely considered curative.^{1,2,5,8}

The histogenesis and origin for this tumor remains controversial and unclear. Initially it was reported as being a malignant counterpart of the benign giant cell tumor of tendons and tendon sheaths; however, this concept is not fully accepted, since other reports demonstrated the lesions are not located within the bones, joints, or adjacent to tendons or synovial tissue.^{3,6} Therefore, giant cell tumor of soft tissue is considered a unique and distinct entity. Two forms (superficial and deep categories) of the neoplasm were described in humans based on the localization and growth pattern.⁶ Cats and dogs seem more prone to have the deep form, whereas, horses tend to have the superficial pattern.^{1,4,9}

Macroscopically, the superficial form of the neoplasm is characterized by being relatively small, firm, raised, solitary, superficial, and attached to subcutaneous tissue. In horses, giant cell tumors of soft tissue tend to be distributed predominantly on the hind limbs,^{1,10} as observed in the present case; however, other locations throughout the body have been described including the superficial fascia and subcutis of the jugular groove, thigh, stifle, elbow, thorax, shoulder, abdomen, muzzle, and dorsum.^{1,2,4,5,8,9} Microscopically, the cells have features more typical for a low grade sarcoma with relatively low mitotic index. In contrast, the deep form is often a larger mass, involving the fascia and skeletal muscle with high metastatic potential, presence of cellular atypia and high mitotic index. Therefore, the latter form has been referred to as anaplastic sarcoma with giant cells or undifferentiated pleomorphic sarcoma with giant cells and not classified as giant cell tumor of soft tissue or giant cell tumor of low malignant potential.³

Spindle cells and multinucleated giant cells involved in giant cell tumor of soft tissue have strong cytoplasmic immunoreactivity for vimentin supporting a mesenchymal origin.^{2,4} Histiocytic origin or secondary recruitment of a histiocytic cell population was suspected based on the cellular phenotyping and positive immune reaction for CD18.^{1,9} Osteoclastic origin has been proposed in humans.⁷ Occasional cytokeratin, smooth muscle actin and rarely S-100 protein immunopositivity has been described in humans.⁶

The final diagnosis can be achieved by either fine-needle aspirates for cytological examination; however, in case of lack of sufficient exfoliation of neoplastic cells during the aspiration, histopathology is required.²

References:

1. Bush JM, Powers BE. Equine giant cell tumor of soft parts: a series of 21 cases (2000–2007). *J Vet Diagn Invest.* 2008;20(4):513–516.
2. Cian F, Whiteoak S, Stewart J. A case of giant cell tumor of soft parts in a horse. *Vet Clin Pathol.* 2016;45(3):501–504.
3. Fletcher CDM, Bridge JA, Hogendoorn P, Mertens F. *WHO Classification of Tumors of Soft Tissue and Bone.* 4th

ed. Lyon: IARC press; 2013.

4. Ford GH, Empson RN, Plopper CG, Brown PH: Giant cell tumor of soft parts: a report of an equine and a feline case. *Vet Pathol.* 1975;12:428-433.
5. Hamir AN. Equine giant cell tumor of soft tissues. *Cornell Vet.* 1989;79(2):173-177.
6. Holst VA, Elenitsas R. Primary giant cell tumor of soft parts. *J Cutan Pathol.* 2001;28:492-495.
7. Lau YS, Sabokbar A, Gibbons CL, Giele H, Athanasou N. Phenotypic and molecular studies of giant cell tumors of bone and soft tissue. *Hum Pathol.* 2005;36:945-954.
8. Marryatt PA. Malignant giant cell tumor of soft parts in a mare. *Can Vet J.* 2003;44(9): 743-745.
9. Pool RR, Thompson KG. Tumors of joints. In: Meuten DJ, ed. *Tumors in Domestic Animals.* 4th ed. Iowa: Iowa State Press; 2002:199-244.
10. Schaffer PA, Wobeser B, Martin LE, Dennis MM, Duncan CG. Cutaneous neoplastic lesions of equids in the central United States and Canada: 3,351 biopsy specimens from 3,272 equids (2000-2010). *J Am Vet Med Assoc.* 2013;242(1):99-104.

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