A case of giant cell tumour of soft parts in a horse

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Signalment:
Horse, British Warmblood mare, 12 years old

History:
The horse was examined by 608 Equine and Farm Vets for the evaluation of a small cutaneous lesion in the back area, on the right side of midline, at the level of the saddle.

Clinical Findings:
Clinical examination revealed normal vital parameters and excellent body condition. The mass was soft, non-alopecic, nodular, well circumscribed, approximately 2-3cm in diameter (Fig 1A).

Diagnostic procedures:
In order to determine the extent of involvement of the underlying tissues, ultrasound was performed. Results showed that the mass appeared as a well-defined, oval lesion within the subcutaneous tissue (Fig 1B). It measured ~50x20mm and was hypoechoic with homogeneous echotexture; it also ventrally displaced the fascia without evidence of infiltration of the surrounding tissue.

Fine needle aspiration (FNA) of the mass was performed. Results are shown below (Fig. 2 and 3).

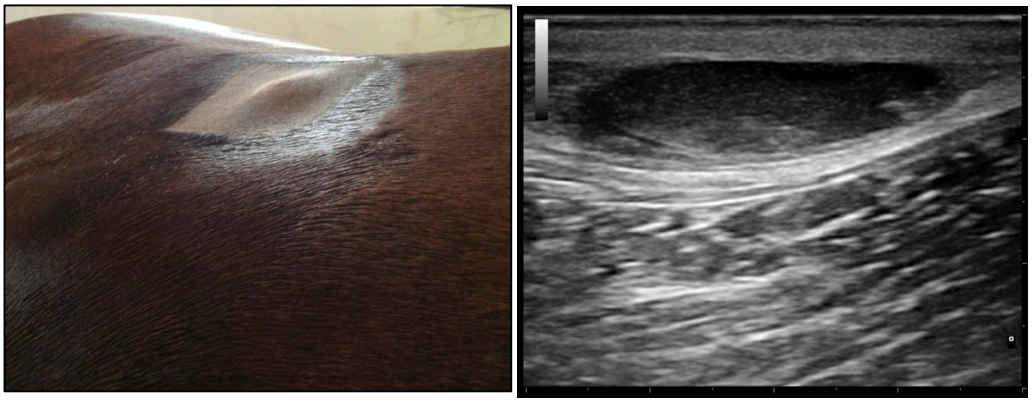

Fig. 1 (A,B). Macroscopic and ultrasonographic appearance of a subcutaneous dorsal mass in a horse.

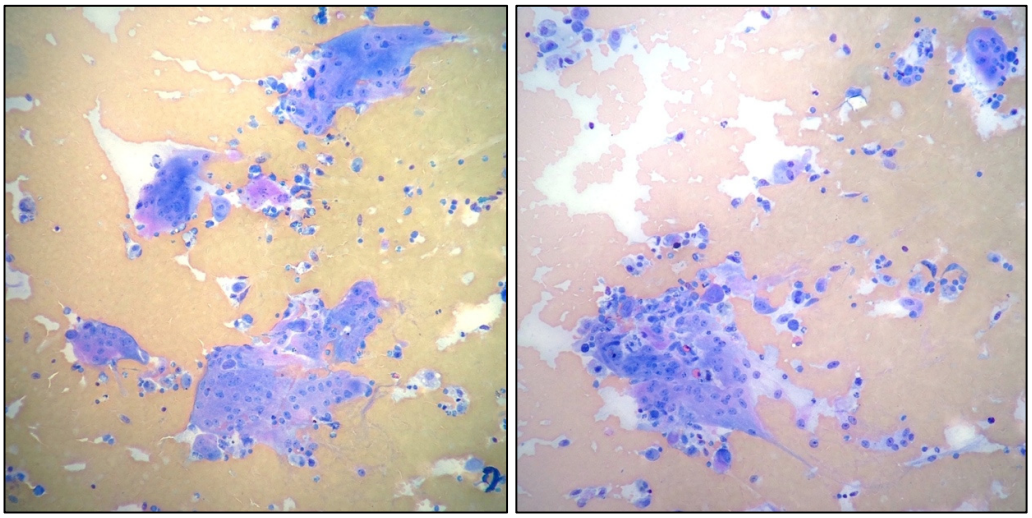

Fig. 2 (A, B) Fine needle aspirate from a subcutaneous dorsal mass in a horse. Mixed cell population on a hematic background. Prevalence of multinucleated giant cells, with lower numbers of mesenchymal spindle cells and macrophages. May-Grunwald Giemsa stained, x20

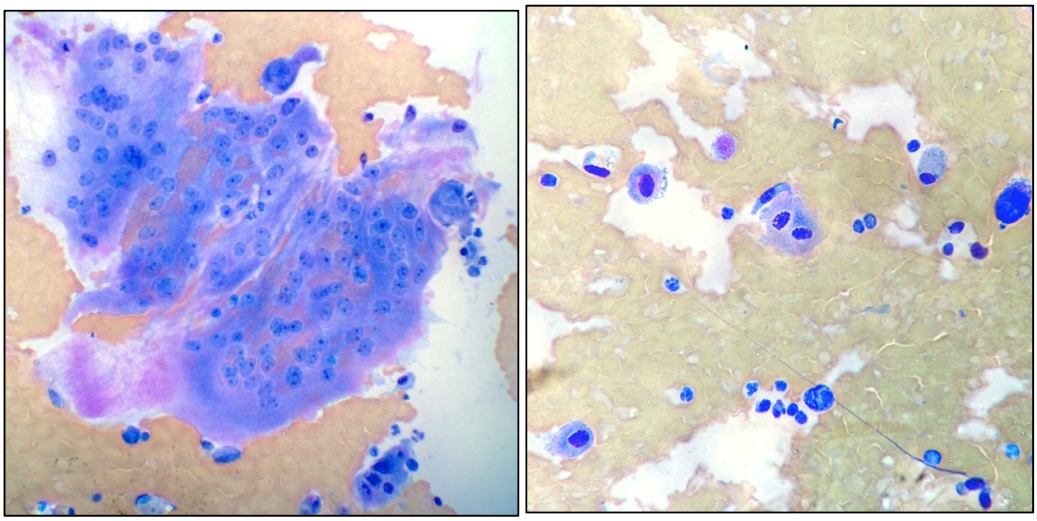

Fig. 3 (A, B) Fine needle aspirate from a subcutaneous dorsal mass in a horse. Multinucleated giant cells (A), mesenchymal spindle cells and macrophages (B) May-Grunwald Giemsa stained, x50

Questions:

1. What are your main differential diagnoses?
2. Which further tests would you suggest to confirm the diagnosis?

Further investigations and discussion

The aspirate from the subcutaneous mass was moderately cellular with adequate preservation. The background was clear with frequent red blood cells and small amounts of cellular debris. A mixed population of nucleated cells was seen throughout the smears, the majority being giant multinucleated cells and spindle-shaped mesenchymal cells; variable numbers of hemosiderin-laden macrophages, plasma cells

and lymphocytes were also noted. The spindle cell component was characterized by moderate amounts of elongated basophilic cytoplasm, with defined borders. Nuclei were oval, paracentral, with coarse granular chromatin and one or two prominent round nucleoli. Anisocytosis and anisokaryosis were moderate. Multinucleated giant cells had abundant basophilic cytoplasm, frequently forming multiple cytoplasmic tails. Nuclei were multiple, up to 50, round, with granular chromatin and prominent multiple small round nucleoli. Occasional neutrophils, likely blood derived, were also noted. These results were highly suggestive of a giant cell tumour of soft parts. A soft tissue sarcoma of other origin was also considered a possible differential.

Surgical excision was performed with a defocused bean carbon dioxide (CO2) laser under standing sedation (detomidine and butorphanol) and local anesthesia (lidocaine); this technique was preferred to conventional surgery in order to minimize the tissue handling and the possible contamination of the surgical bed with tumour cells. Methyl aminolevulinate photodynamic therapy (PDT) was performed at 12 and 19 days post-surgery in order to reduce the risk of local tumour recurrence.

The lesion was submitted for histopathological examination and confirmed the cytological diagnosis (Fig 4 and 5). The mass was well demarcated, partially encapsulated, expansile, densely cellular and was composed of loosely woven spindle cells, frequently haphazardly arranged, and large numbers of multinucleated giant cells. Clusters of lymphocytes, plasma cells, and hemosiderin-laden macrophages were also noted. No mitotic figures were seen in 10 high power fields (40x). The neoplasm extended to the deep and lateral margins. Immunohistochemistry for vimentin was performed and was positive confirming the mesenchymal origin of the cell population (Fig. 6).

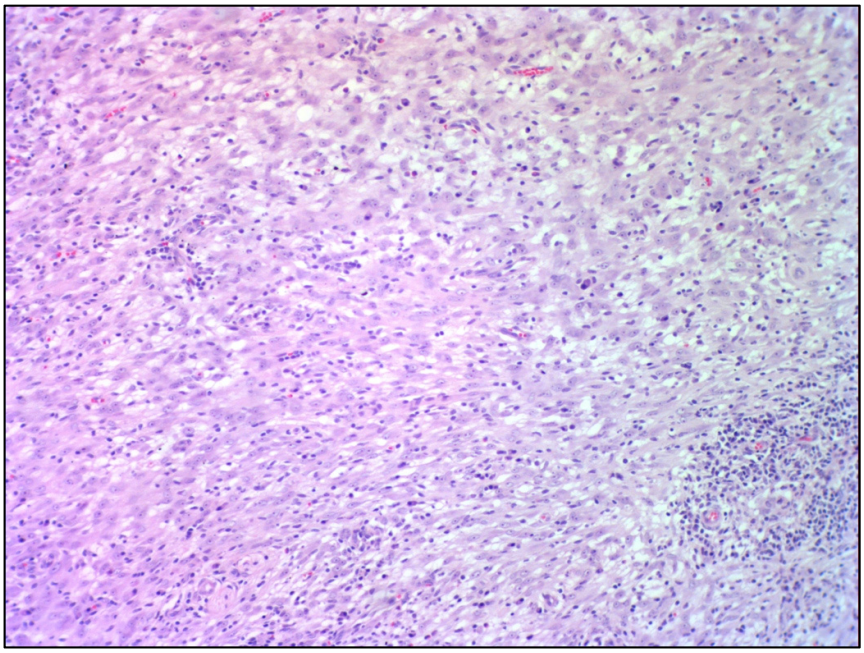

Figure 4 Subcutaneous dorsal mass, horse, histological section.
Moderately to densely cellular neoplasm composed of spindle cells with indistinct cell borders, moderate amounts of eosinophilic cytoplasm, and oval nuclei. Scattered moderate numbers of lymphocyte infiltrate, often cuffing vascular profiles. H&E, 10x.

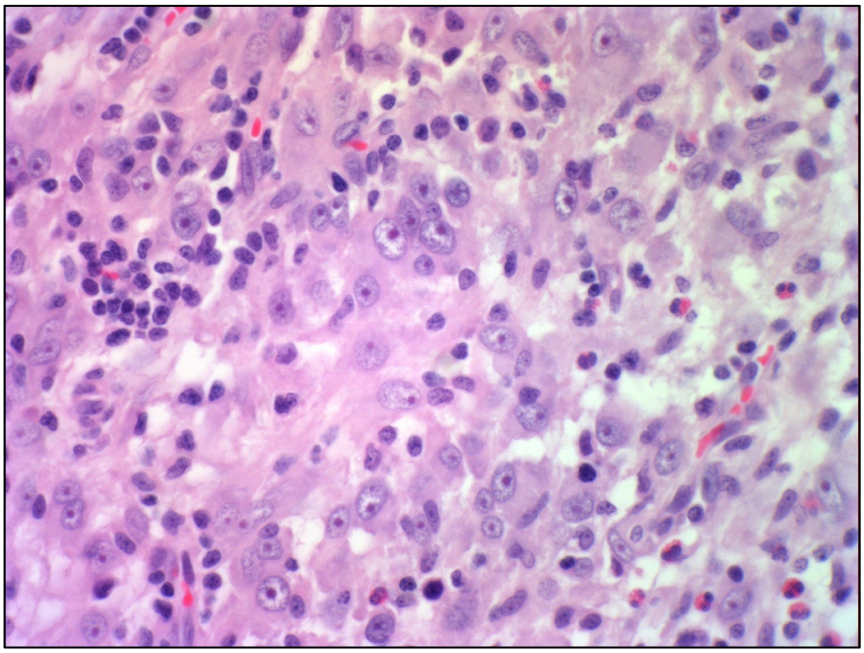

Figure 5 Subcutaneous dorsal mass, horse, histological section.
Centrally a multinucleated giant cell with six nuclei is present. Mild to moderate anisokaryosis is observed. Nuclei are ovoid with finely stippled chromatin and a prominent nucleolus. Lymphocytes can be seen infiltrating between the indistinct spindle cells of the neoplasm. H&E, 40x

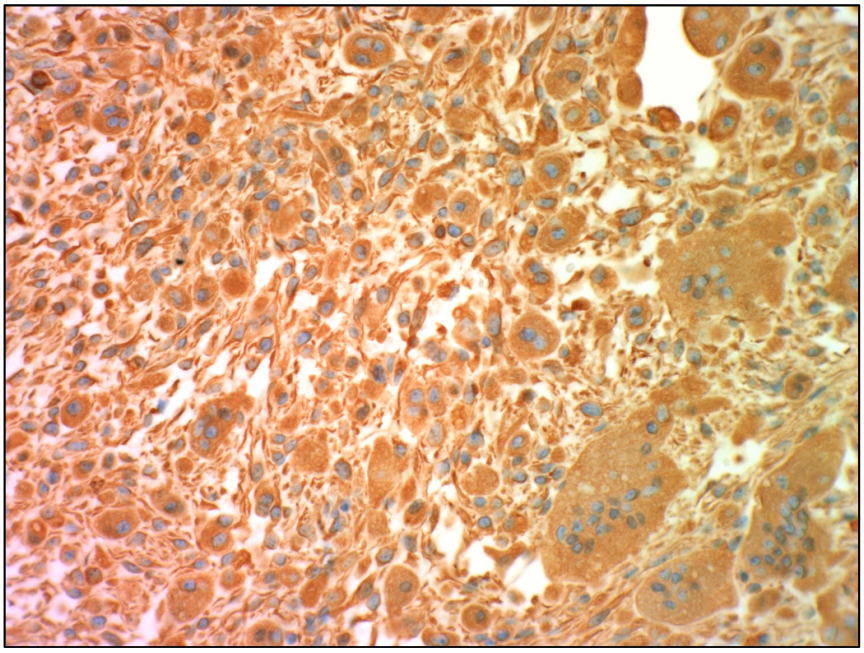

Figure 6 Subcutaneous dorsal mass, horse, histological section. IHC Vimentin.
Mesenchymal spindle cells and multinucleated giant cells show strong positive cytoplasmic immunoreactivity for vimentin. Basic alkaline phosphatase red and hematoxylin, 20x.

Treatment:
After surgery was performed, regular reexaminations were undertaken. At 1 month

from surgery, the surgical site is healing properly with no evidence of recurrence (Fig. 7)

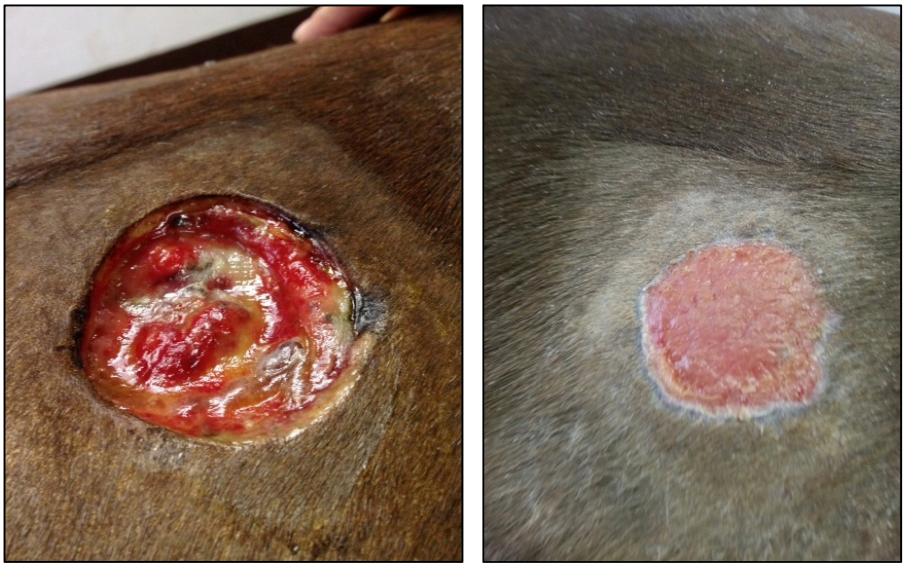

Figure 7 (A,B) Macroscopic appearance of the surgical site after the removal of the mass, 1 week (A) and 1 month (B) after the surgery.

Discussion:

Giant cell tumour of soft parts (GCTSP) is a rare neoplasm, reported in several domestic species, including cats and horses. In the equine species, it represents 1% of all cutaneous neoplasia.

It affects mostly adult animals, with the majority of horses over the age of 10 years. There is no apparent sex or breed predilection, although in a previous retrospective study on 21 cases of GCTSP males were overrepresented. These tumours usually appear as firm, raised, solitary and superficial masses, attached to the superficial subcutaneous tissue. They have been described in several regions of the body (jugular groove, thigh, stifle, elbow, thorax, shoulder, abdomen, muzzle) although there seems to be a predilection for the hind limbs. Metastatic potential for these tumours in horses appears to be very low and surgical excision with clean margins is considered to be resolutive. Local recurrence after incomplete surgical resection has been reported.

Diagnosis can be achieved by fine needle aspiration of the mass since the cytological features are considered characteristic. However, the use of cytology as a diagnostic technique may be limited by the poor tendency of these masses to exfoliate cells during the aspiration, as frequently observed in mesenchymal lesions. In those cases, histopathology is required.

The classification of giant cell tumours of soft parts has been subject of continuous debate in the last decades and its histogenesis remains controversial even nowadays.

First reports in humans and cats referred to this tumour as malignant giant cell tumour of the tendon sheath, since tendons and their sheaths appeared to be the main sites of origin. However, further studies showed that the malignant giant cell tumour of soft parts may arise in different locations and should not be regarded as the malignant counterpart of the benign giant cell tumour of tendons and tendon sheaths, but as a distinct entity with a different origin.

Giant cell tumour of soft parts was then referred to as giant variant of malignant fibrous histiocytoma. This classification was also applied to domestic animals and is still in use in veterinary medicine. In human medicine, there has been a further differentiation into superficial and deep forms, according to the localization and pattern of growth. Deep

tumours are typically large, involving the fascia and the skeletal muscle and have a high metastatic potential. Cells display marked features of atypia, and mitotic activity may be very high. Superficial forms are instead smaller in size, occur within the subcutaneous tissue and superficial fascia and rarely metastasize. Neoplastic cells have minimal anaplastic features and a relatively low mitotic index. Deep forms have been observed mostly in cats, whereas in horses only superficial forms have been reported to date.
Given the different and distinctive behavior of this neoplasia and its subtypes (superficial and deep), the last edition of the human WHO Classification of Tumours of Soft Tissue and Bone reclassified it. The superficial (and benign) form has now been located in the category fibrohistiocytic tumours as giant cell tumour of soft tissue (or giant cell tumour of low malignant potential). The malignant counterpart, previously called deep form, has now been renamed undifferentiated pleomorphic sarcoma with giant cells and reclassified under the undifferentiated / unclassified sarcomas. It includes a group of sarcomas of various cellular origins, and may represent anaplastic variants of different forms (i.e. fibrosarcoma, liposarcoma, histiocytic sarcoma).

The histogenesis of the giant cell tumour of soft parts is currently unknown, although is it is generally accepted that this tumour represents a soft tissue sarcoma. The positive expression of neoplastic cells to vimentin in the majority of cases confirms this. Some authors claim a histiocytic origin, given the cytological features of the mononuclear cells, resembling histiocytic elements, their phagocytic activity and the positivity of multinucleated giant cells to CD18. Other authors suggest a fibroblastic lineage. Recent studies considered a possible osteoclastic origin of the multinucleated component, since those two types of cells have similar microscopic and ultrastructural features and share some hydrolytic enzymes. For this reason this tumour is also referred as osteoclastoma.

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