

## FIBROMYXOID SARCOMA IN *RATTUS NORVEGICUS*: CASE REPORT

### *SARCOMA FIBROMIXOIDE EM RATTUS NORVEGICUS: RELATO DE CASO*

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#### SUMMARY

Myxoid sarcoma comprises malignant tumors of myxoid origin. Low-Grade Fibromyxoid Sarcoma (LGFM) has benign histopathological characteristics, slow growth, but with high metastatic potential. There are at least 25 cases of LGFM in humans, being more common in the deep intramuscular region, mainly in the thigh and trunk, but it has also been described in the retroperitoneum, mesentery and renal capsule. In December 2022, a 2-year-old male Wistar rat (*Rattus norvegicus*) had difficulty walking and a nodule was noted in the dorsal region of the left pelvic limb, measuring 2.5 cm x 3 cm. In January 2023, amputation was performed and the morphological diagnosis obtained was myxoid sarcoma. In February 2023, formation was observed in the left renal capsule measuring 2cm, growing to 6cm in May 2023, with the same diagnosis as that of the limb. The tutors opted for the surgical removal of the neof ormation, however, the animal evolved to death, being referred for necroscopic examination. The case represents the first worldwide case of LGFM in Wistar, the second reported in animals.

**KEY-WORDS:** Sarcoma. Wistar. Histopathology. Neof ormation. Metastasis.

#### RESUMO

Sarcoma mixoide compreende os tumores malignos de origem mixoide. O Sarcoma Fibromixóide de Baixo Grau (SFBG) possui características histopatológicas benignas, crescimento lento, mas com alto potencial metastático. Existem ao menos 25 casos de SFBG em humanos, sendo mais comum em região intramuscular profunda, principalmente em coxal e tronco, mas também foi descrito em retroperitônio, mesentério e cápsula renal. Em dezembro de 2022 um rato Wistar (*Rattus norvegicus*), macho, 2 anos, apresentava dificuldade de locomoção e notou-se nódulo em região dorsal de membro pélvico esquerdo, medindo 2,5cm x 3 cm. Em janeiro de 2023 foi realizada a amputação e o diagnóstico morfológico obtido foi sarcoma mixóide. Em fevereiro de 2023, observou-se formação em cápsula renal esquerda medindo 2cm, crescendo até 6cm em maio de 2023, com o mesmo diagnóstico que o do membro. Os tutores optaram pela retirada cirúrgica da neof ormation, contudo, o animal evoluiu para o óbito, sendo encaminhado para o exame necroscópico. O caso representa o primeiro caso relatado do mundo de SFBG em Wistar, o segundo relatado em animais.

**PALAVRAS-CHAVE:** Sarcoma. Wistar. Histopatologia. Neof ormation. Metástase.

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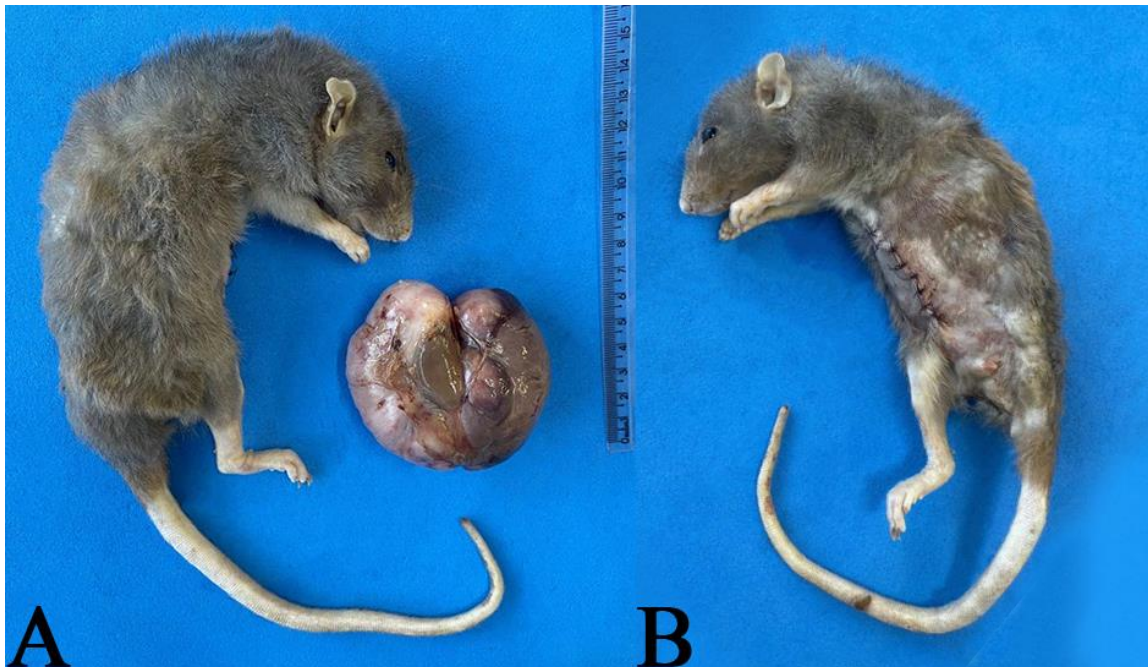
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## INTRODUCTION

Low-Grade Fibromyxoid Sarcoma (LGFM) is a rare metastasizing painless soft tissue tumor with deceptively benign histologic appearance, having features so bland that they are likely to be mistakenly considered benign (EVANS, 1987; TAKANAMI et al., 1999), being common in lower extremities and trunk (GJORGJOVA GJEORGJIEVSKI, 2021). Considering other malignant tumors as differential diagnoses, the most possible are malignant fibrous histiocytoma (equivalent to Grade 1 myxofibrosarcoma), low-grade fibrosarcomas (WEISS AND ENZINGER, 1977; MERCK et al., 1983) and low-grade myxofibrosarcoma (ANTONESCU AND BAREN, 2004). This type of tumor had been globally described in humans throughout the decades and, in 2019, it was described in a *Chelonid Alphaherpesvirus* (DÍAZ-DELGADO, 2019).

## CASE REPORT

In December, a 3-year-old Wistar rat, male, exhibited a nodule in tibia/fibula on the of the left pelvic limb measuring 4,3cm x 4,0cm, round, firm, whitish, adhered to the musculature, but without bone involvement. The limb was amputated and the morphological diagnosis was suggestive of Myxoid Sarcoma. Five months later, the animal presented a non-adherent left medial abdominal neoformation measuring 6 cm in ultrasound scan. It underwent surgery to remove this new formation but unfortunately died. The Wistar was submitted to the necropsic procedure (Figure 1A and 1B). In this avaluation, the Wistar rat had a regular, firm, smooth, whitish, round nodule measuring 7.2cm x 7.0cm x 4.2cm on the left kidney and adrenal gland.



**Figure 1** - Necropsy of the *Rattus norvegicus* with the (A) presentation of the neoformation with the left kidney and adrenal intact in the center of it and the (B) surgical points at the site of access to the abdômen. Note the absence of the right pelvic limb

## RESULTS AND DISCUSSION

In this report, macroscopically both of the neoformations were firm, ovoid, regular and white, meeting with the literature: LGFM is a lobulated, well-circumscribed mass with a cut surface tan-white trabeculated, ovoid and firm (EVANS, 1987).

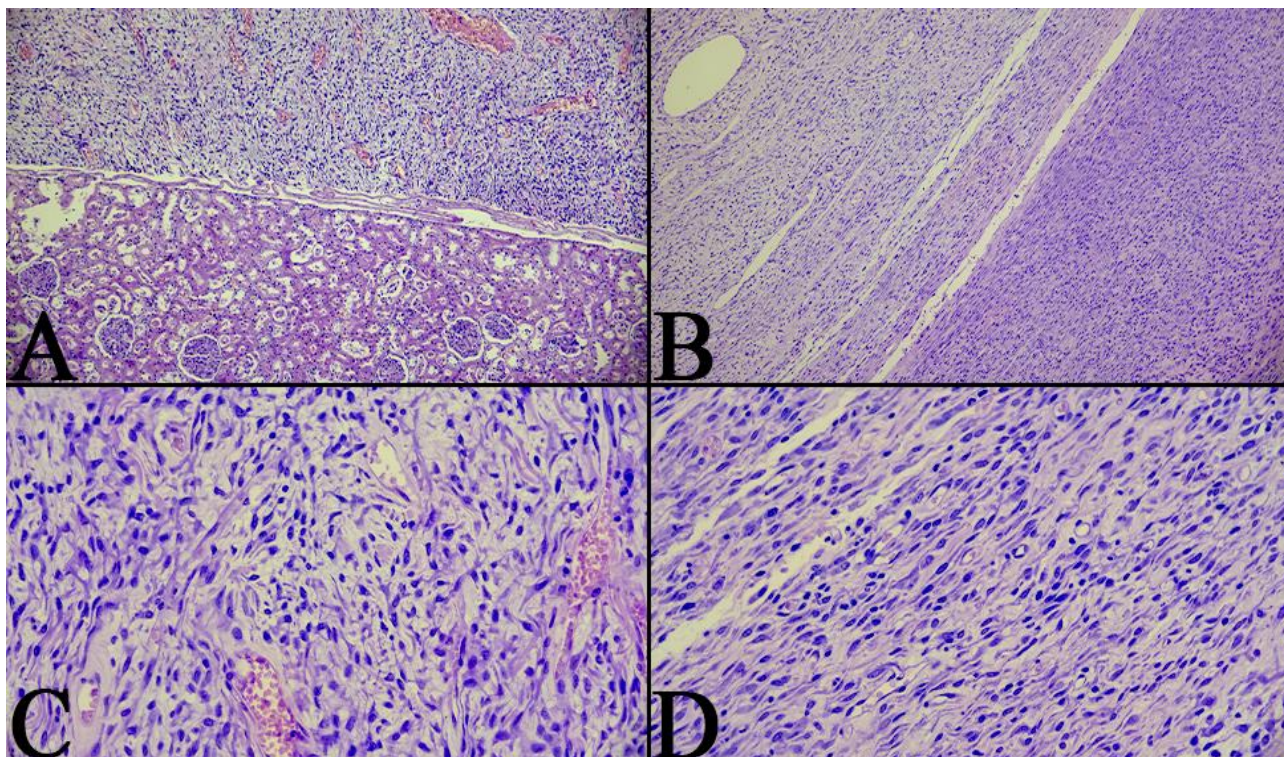
By the microscopy evaluation of the limp showed a well-defined proliferation of neoplastic mesenchymal cells arranged in multidirectional bundles, with a moderate myxoid matrix, sometimes with a collagenous appearance. Cytoplasm is elongated to fusiform. Nuclei are moderately pleomorphic, rounded with hyperchromatic chromatin and nucleoli sometimes

evident and small. This neoplasm had up to 7 mitotic figures in 10 high-power fields. In the center of the formation there are foci of necrosis with dystrophic calcification and low vascularity. Considering that this is the first and only site of the neoplasm by the time, the suggestive diagnosis of myxoid sarcoma was valid, once it is a difficult diagnosis considering all soft tissue sarcomas (DENNIS, 2011).

When the necropsy was performed, the kidney and adrenal gland were preserved (Figure 2A) and the formation contained a center with moderate cellularity, well-delimited and well-circumscribed, regular, non-encapsulated, composed by stellate to fusiform fibroblasts with benign appearing loosely arranged in swirling pattern

in the midst of a part fibrous part myxoid abundant matrix with an abrupt transition between them (Figure 2B, 2C and 2D). The cytoplasm was poorly delimited, eosinophilic and moderate, a central to peripheral, oval nuclei, with basophilic and sometimes hyperchromatic, lacy chromatin,

containing 0 to 1 conspicuous, small and central nucleolus. It showed moderate anisocytosis, anisokaryosis and cellular pleomorphism, low mitotic rate (1 to 5 mitotic figures in 10 high-power fields), with rare binucleations, and focally extensive areas of necrosis and low vascularity.



**Figure 2** - Histopathological of the tumor. (A) The formation was well-delimited, well-circumscribed, regular and non-encapsulated, preserving the left kidney and adrenal (HE. x4). (B) It had a abrupt transition between a part fibrous part myxoid abundant matrix (HE. X10). (C and D) Moderate cellularity with stellate to fusiform fibroblasts with benign appearing loosely arranged in swirling pattern. Moderate anisocytosis, anisokaryosis and cellular pleomorphism with rare binucleations (HE. x40).

This neof ormation has the same characteristics as the LGFM which are a bland-appearing fibroblastic spindle cells in a part fibrous part myxoid matrix with an abrupt transition between these two patterns. Cellularity is moderate to low, with benign-appearing fibroblastic spindle cells arranged in a whorled or swirling pattern. This tumor presents slight nuclear pleomorphism, little hyperchromatism and rare mitotic figures. Vascularity is low (EVANS, 1987 and 1993; TAKANAMI *et al*, 1999).

The possible differential diagnoses are benign neoplasms (EVANS, 1987; TAKANAMI *et al*, 1999), malignant fibrous histiocytoma, low-grade fibrosarcomas (WEISS AND ENZINGER, 1977; MERCK *et al*, 1983) and low-grade myxofibrosarcoma (ANTONESCUS AND BAREN, 2004). Although when comparing the neof ormation of this Wistar rat with them, this case had blander cells and lower pleomorphism to be considered a malignant fibrous histiocytoma or a low-grade fibrosarcoma (HANSEN *et al*, 2006). The last possible diagnoses is low-grade myxofibrosarcoma, with a multinodular growth pattern (ANTONESCUS & BAREN, 2004) and without metastasis, characteristics that were not seen in this present case, because this neof ormation suggests a

metastasis of the one found on the left pelvic limb (MERCK *et al*, 1983 and ANGERVALL *et al*, 1977), once they are composed of the same cellularity and both of them were lobulated and well-circumscribed formation, not being a benignant neoplasm either (CAVALLARO AND GEHARD, 2001).

Although this neoplasm has only been reported in humans, the same pattern of cellular organization is seen in this present case. Therefore, it is the first reported case of LGFM in a Wistar rat of the world.

## CONCLUSION

To obtain the diagnosis of Low-Grade Fibromyxoid Sarcoma, the metastatic power of the neoplasm and its benign appearance must be considered. In this case, the possible metastasis to the renal capsule region and the benign arrangement of the neoplasm were crucial for the diagnosis of LGFM, since the macroscopic and microscopic characteristics of this case are in line with the description of other species. Therefore, despite the challenge, this is the first reported case of LGFM in a *Rattus norvegicus* in the world.

## REFERENCES

- ANGERVALL, Lennart; KINDBLÖM, Lars-Gunnar; MERCK, Christer. Myxofibrosarcoma: a study of 30 cases. **Acta Pathologica Microbiologica Scandinavica Section A Pathology**, v. 85, n. 2, p. 127-140, 1977.
- ANTONESCU, Cristina R. & BAREN, Ann. Spectrum of low-grade fibrosarcomas: a comparative ultrastructural analysis of low-grade myxofibrosarcoma and fibromyxoid sarcoma. **Ultrastructural pathology**, v. 28, n. 5-6, p. 321-332, 2004.
- CAVALLARO, Ugo & CHRISTOFORI, Gerhard. Cell adhesion in tumor invasion and metastasis: loss of the glue is not enough. **Biochimica et Biophysica Acta (BBA)-Reviews on Cancer**, v. 1552, n. 1, p. 39-45, 2001.
- DENNIS, M. M. et al. Prognostic factors for cutaneous and subcutaneous soft tissue sarcomas in dogs. **Veterinary Pathology**, v. 48, n. 1, p. 73-84, 2011.
- DÍAZ-DELGADO, Josué et al. Primary multicentric pulmonary low-grade fibromyxoid sarcoma and chelonid alphaherpesvirus 5 detection in a leatherback sea turtle (*Dermochelys coriacea*). **Journal of Comparative Pathology**, v. 168, p. 1-7, 2019.
- EVANS, Harry L. Low-grade fibromyxoid sarcoma: a report of two metastasizing neoplasms having a deceptively benign appearance. **American journal of Clinical Pathology**, v. 88, n. 5, p. 615-619, 1987.
- EVANS, Harry L. Low-grade fibromyxoid sarcoma. A report of 12 cases. **The American Journal of Surgical Pathology**, v. 17, n. 6, p. 595-600, 1993.
- GJORGOVA GJEORGJIEVSKI, S., FRITCHIE, K., THANGAIAH, J. J., FOLPE, A. L., & DIN, N. U. Head and neck low-grade fibromyxoid sarcoma: a clinicopathologic study of 15 cases. **Head and Neck Pathology**, 1-10, 2021.
- HANSEN, T., KATENKAMP, K., BRODHUN, M., & KATENKAMP, D. Low-grade fibrosarcoma—report on 39 not otherwise specified cases and comparison with defined low-grade fibrosarcoma types. **Histopathology**, 49(2), 152-160, 2006.
- MERCK, C., ANGERVALL, L., KINDBLÖM, L. G., & ODÉN, A. Myxofibrosarcoma. A malignant soft tissue tumor of fibroblastic-histiocytic origin. A clinicopathologic and prognostic study of 110 cases using multivariate analysis. **Acta pathologica, microbiologica, et immunologica Scandinavica. Supplement**, 282, 1–40, 1983.
- TAKANAMI, Iwao; TAKEUCHI, Ken; NARUKE, Masao. Low-grade fibromyxoid sarcoma arising in the mediastinum. **The Journal of Thoracic and Cardiovascular Surgery**, v. 118, n. 5, p. 970-971, 1999.
- WEISS, Sharon Whelan; ENZINGER, F. M. Myxoid variant of malignant fibrous histiocytoma. **Cancer**, v. 39, n. 4, p. 1672-1685, 1977.