Low Grade Myxoinflammatory Fibroblastic Sarcoma Of The Kidney - A Rare Entity

Barani Karikalan[1], Thanikachalam Pasupati[2], Sophia Merilyn George[2]

[1]Perdana University, Selangor, Malaysia

[2]Clinipath Pathology (M) Sdn Bhd, Klang, Malaysia

Abstract

Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare type of soft tissue sarcoma, rarely metastasize, usually of intermediate grade and commonly seen in the extremities. About 90% of the reported cases were seen to occur between ages 12 and 75, with an equal gender predilection. This tumor contains a mixed inflammatory cell component and fibroblastic component represented by epithelioid, spindled, and bizarre neoplastic cells in a background of myxoid and hyaline areas. Despite of its distinct histology, the lesion remains a diagnostic challenge due to its resemblance to varied inflammatory conditions that have a neoplastic behaviour. For precise diagnosis, elaborate clinical, radiological, and pathological evaluations are needed. We present a case of low grade MIFS in a 37-year-old female who presented with gross hematuria and renal mass.

Keywords: Myxoinflammatory, Fibroblastic, Sarcoma, Kidney

1. Introduction

Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare intermediate grade, rarely metastasizing fibroblastic sarcoma, commonly occurring in the 40th and 50th decades of life, with equal gender distribution. The lesion was first described in three independent case reports in 1998 (Meis-Kindblom and Kindblom 1998; Michal 1998; Montgomery et al. 1998). This tumor usually occurs in the soft tissue of the extremities, especially feet. On microscopy, MIFS is composed mainly of modified fibroblasts and has a tendency for local recurrence and distant spread (Weiss et al. 2013; Carter et al. 2014). Although previously identified in the lower extremities, it has recently been identified in the proximal extremities. This neoplasm has wide differential diagnosis (Meis et al.

2013; Miettinen et al. 2014). It is often misdiagnosed for many other reactive fibroinflammatory conditions and neoplasms with high metastatic tendency (Meis-Kindblom and Kindblom 1998; Hassanein et al. 2008). Hence, differential diagnoses of MIFS include tenosynovitis, ganglion cysts, spindle cell tumor and myxoid malignant fibrous histiocytoma. The pronounced inflammation and fibrous tissue proliferation found on microscopy in MIFS mimic a reactive coniditon. Myxoid background and scattered bizarre cells that are multi vacuolated occasionally may result in misdiagnosis as malignant fibrous histiocytoma or liposarcoma. An accurate diagnosis is hence essential to refrain unnecessary radical procedures and for proper patient management (Meis-Kindblom and Kindblom 1998). We report a case of a 37-year-old female who presented with gross hematuria and renal mass. After nephrectomy, histological and immunohistochemical analysis indicated a diagnosis of low grade MIFS. Our case will provide useful information regarding accurate diagnosis especially when presented in an unusual location.

2. Case report

A 37-year-old female presented with gross hematuria. Imaging studies showed a renal mass in the middle part of the right kidney extending into the pelvis. Right nephrectomy done. Gross examination of the right kidney with ureter weighing 209gms. The kidney measures 11.1 cm from upper to lower, 7.5 cm transversely and 3.2 cm anteroposteriorly. The ureter measures 12.6 cm, appears dilated and in the mid segment with a diameter of 1.3 cm. External surface shows flea bitten surface. The perinephric fat does not show significant abnormalities. The renal vessel measures 4.0 cm in length and 0.5 cm in diameter. On bisecting, the pelvicalyceal system is dilated with blood clots, the ureter shows no evidence of tumour, contains blood clot, and the proximal segment shows a stricture present 4.2 cm from the pelvicalyceal junction and 7.6 cm from the distal margin.

On further sectioning, there is evidence of a well circumscribed tumorous lesion, soft to firm in consistency at the mid pelvi calyceal system, protruding into the pelvis, measuring 2.1x1.7 cm [Fig1]. Rest of renal parenchyma appears normal. Microscopic examination showed a well-circumscribed, non-encapsulated lesion in the mid-pelvi calyceal system, exhibiting spindle-shaped fibres arranged in a haphazard, wavy and occasional fascicle like pattern with a predominant myxomatous stroma [Fig2 and Fig3]. Individual spindle shaped cells having centrally

placed vesicular nuclei, with indistinct cytoplasmic margins, occasionally displaying plump myoepithelial-like configuration is observed [Fig4]. Occasional large bizarre cells noticed [Fig5]. Scattered within the lesion, lymphocytes and plasma cells are observed.

Mitotic figures are negligible. No apparent necrosis is observed. Areas of haemorrhagic congestion with evidence of tumour infiltrating into the renal parenchyma is noted. There is also formation of lymphoid aggregates, juxtaposed to the tumour proper. Sections taken away from the tumorous lesion exhibit congested glomeruli with areas of small hemorrhagic congestion, in relation to the flea bitten appearance seen, grossly. A dilated pelvicalyceal system and distended proximal ureter, in relation to ureteric stricture is noticed. No apparent satellite nodules are observed. Both the renal vein and renal artery are acutely congested and free of tumor.

Immunohistochemical examination of the tumor revealed strong diffuse positivity is for Smooth muscle actin(SMA) and Vimentin. There is a total lack of expression for Desmin and Myogenin. CD34 is negative but highlights the vascular spaces, serving as internal control. Ki-67 shows a proliferative index of 5%. Owing to the strong expression of Vimentin, SMA and a low proliferative index, a diagnosis of low grade myxoinflammatory fibroblastic sarcoma was made. Presence of a myxomatous background with inflammatory cells is characteristically seen.

3. Discussion

MIFS, ia a new entity and a rarely metastasizing fibroblastic sarcoma, mainly seen in extremities of middle aged individuals and nearly equal gender distribution (Meis-Kindblom and Kindblom 1998; Montgomery et al. 1998; Meis et al. 2013; Brooks and Lee 2015). Only 10% of the cases were recorded to be below 12 or above 75 years of age (Lombardi 2013). The neoplasm has a noticeable inflammatory element and fibroblastic element composed of epithelioid neoplastic cells with abundant cytoplasm, enlarged nuclei with prominent nucleoli. However, extensive nuclear atypia and atypical mitotic figures are absent. Most patients are asymptomatic. The neoplasm has a preference to occur in the dorsal aspect of the hands and feet. The mass is typically ill-defined and raised and is more wide than deep. Clinically, the neoplasm may mimic an inflammatory swelling rather than a discrete tumor (Lang 2006; Miettinen et al. 2014). Hence, the lesion has many differential diagnoses that include various inflammatory and neoplastic conditions that have completely different patient management strategies (Meis et al. 2013; Miettinen et al. 2014).

However, in our case, due to the unusual renal location, our differential diagnoses include mainly renal tumors.

Macroscopically, the neoplasm typically measures about 1 cm to 5 cm, with the average size around 3 cm with a mucoid consistency, and is generally poorly circumscribed [6, 7] (Meis et al. 2013; Miettinen et al. 2014). Gross features of our case resembled those of reported cases (Meis-Kindblom and Kindblom 1998; Michal 1998; Montgomery et al. 1998). However, in our case, the location of the tumour is kidney, which is highly unusual. Microscopic characteristics of the tumor consist of three major elements: (a) multinodular pattern, alternating hypercellular regions with hypocellular myxoid areas; (b) mixed inflammatory cell infiltrate; and (c) large bizarre cells or vacuolated lipoblast-like cells (Chahdi et al. 2010). Histopathology of the tumor tissue in our case had all the features. Though the immunohistochemical features are nonspecific, immunohistochemistry is essential for absolute diagnosis of the tumor (Ieremia and Thway 2014). The tumor homes a large number of histiocytes, which are not large epithelioid cells, and that show positivity for CD163 and CD68. In around 10 to 15% of tumors, large atypical cells show focal positivity for EMA and keratin. The tumor cells are generally positive for vimentin, CD34, and AE1/AE3 and negative for desmin, α-SMA, CD34, and S-100 protein. A small number of tumours show positivity for smooth muscle actin (Laskin et al. 2014). Immunohistochemical findings in our case were almost similar to those reported previously (Meis et al. 2013; Miettinen et al. 2014).

The pathogenesis of MIFS is not known yet. No infectious etiology has been recognised (Montgomery et al. 1998; Jurci et al. 2002; Miettinen et al. 2014). Cytogenetic studies have revealed an unbalanced translocation t(1;10)(p22;q24) and 3p amplification in the VGLL3 gene seem to occur repeatedly (Lambert et al. 2001; Jurci et al. 2002; Mansoor et al. 2004; Hallor et al. 2009; Antonescu et al. 2011). At the molecular level, the translocation was noted in the TGFBR3 gene at 1p22 and near the MGEAS locus at 10q24. Similar translocation is also recorded in hemosiderotic fibrolipomatous tumors (Hallor et al. 2009; Antonescu et al. 2011). Clinical course of the tumor is unpredictable, sometimes involving frequent multiple local recurrences. Local recurrence of MIFS is very common, with rare reports of distant spread (Meis et al. 2013; Miettinen et al. 2014). Hence, regular patient follow-up is required. In our case, since nephrectomy is performed, we didn't have to worry about local recurrence, but yet the rare possibility of distant metastasis is kept in mind and patient follow up have been planned accordingly. There are no

standard protocols available for the management of MIFS patients. Complete excision is recommended if this doesn't affect function-preservation. In the rest of cases, good results have been recorded with conservative surgery followed by postoperative radiation (Tejwani et al. 2010).

To conclude, MIFS is a rare intermediate grade, rarely metastasizing fibroblastic neoplasm, which is frequently mistaken for various benign lesions. Recently, the expectation of the clinical behaviour of MIFS has been made clear. However, early diagnosis of the tumor can be challenging. Hence, surgeons, radiologists, and pathologists must consider MIFS in their differential diagnosis of slow growing mass lesions to prevent misdiagnosis resulting in inappropriate patient management and delay in appropriate treatment.

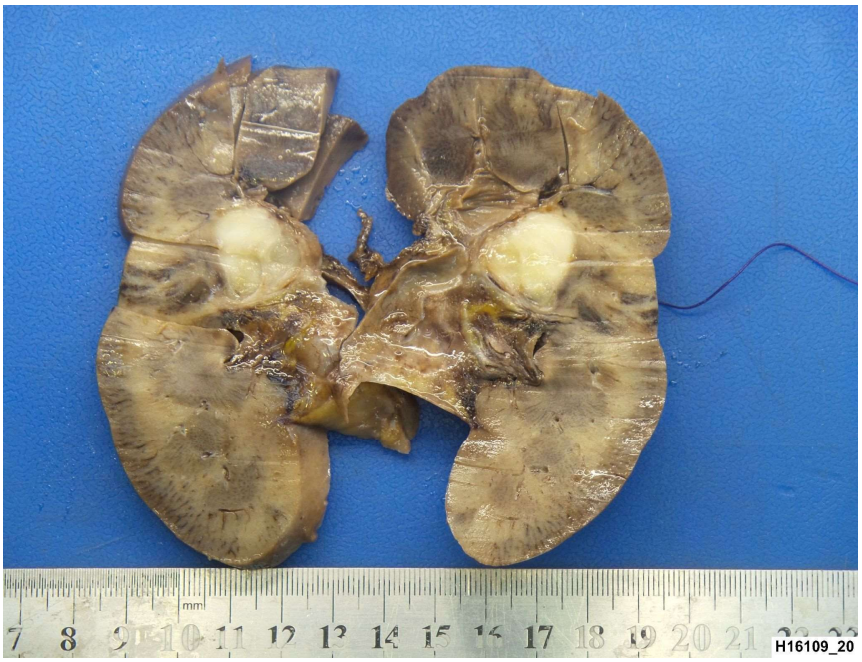

Fig. 1: Grey-white gross tumour

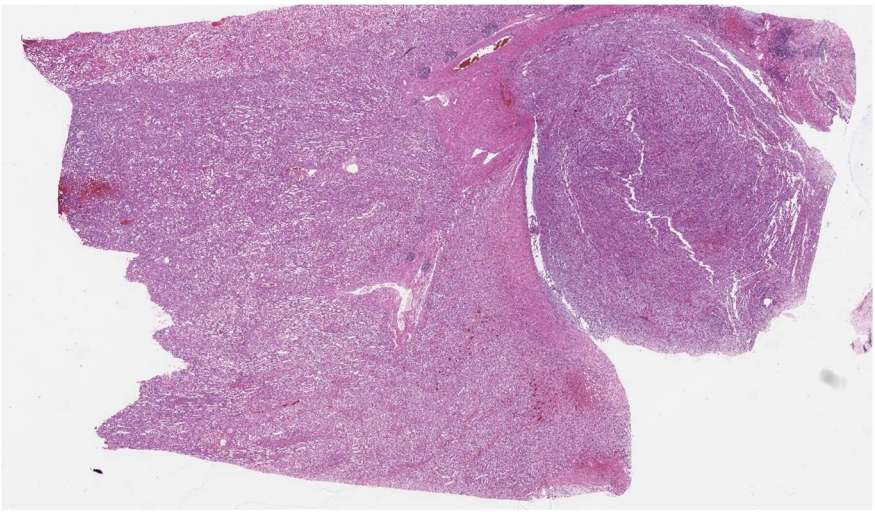

Fig. 2: Circumscribed tumour; H&E

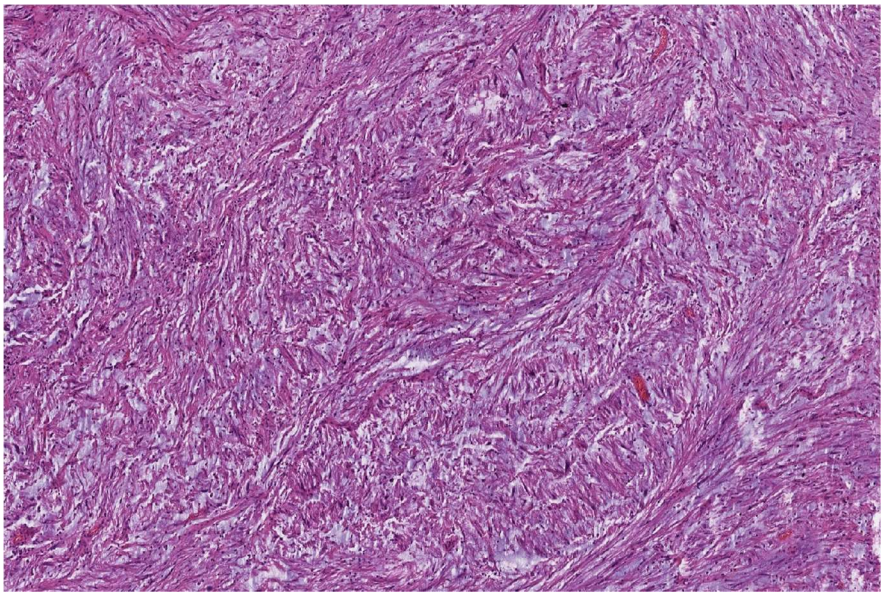

Fig. 3: 10X; Myxoid tumour; H&E

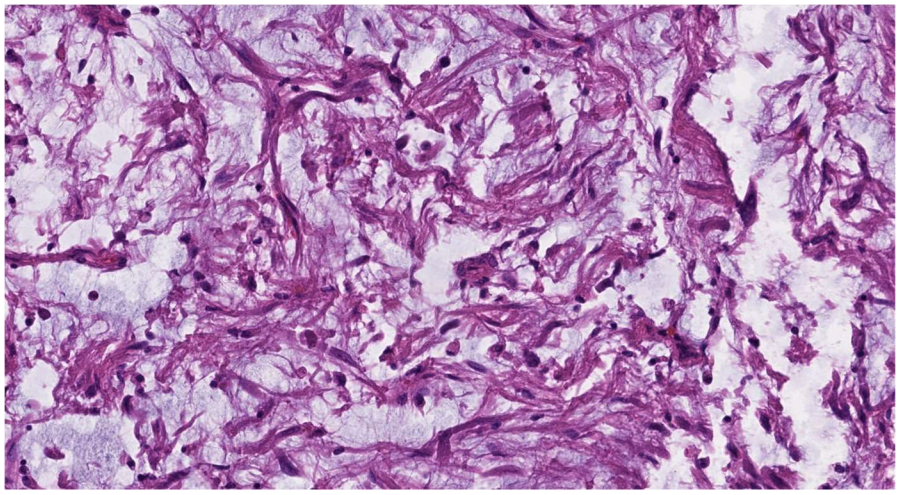

Fig. 4: Spindle shaped tumour cells along with inflammatory cells in a myxomatous background; 40X; H&E

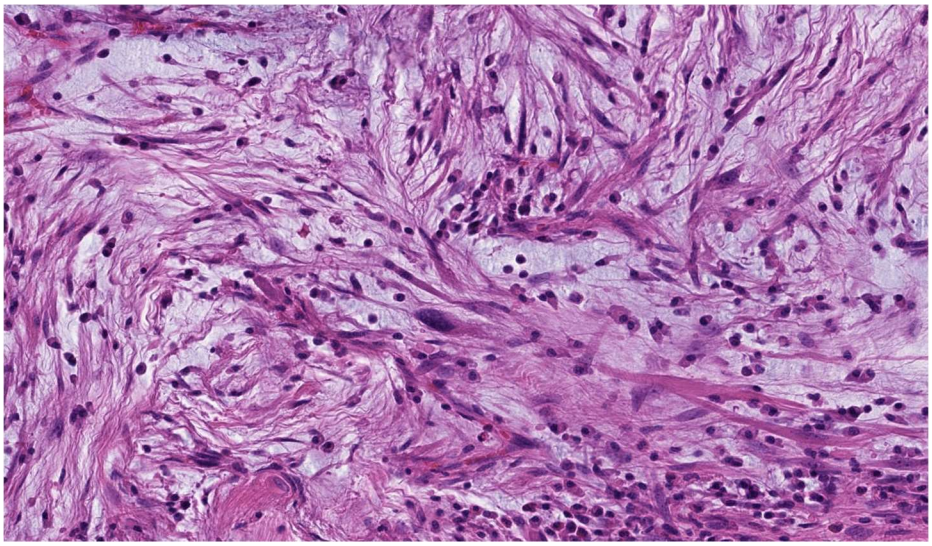

Fig.5: Occasional bizarre cells; 40X; H&E

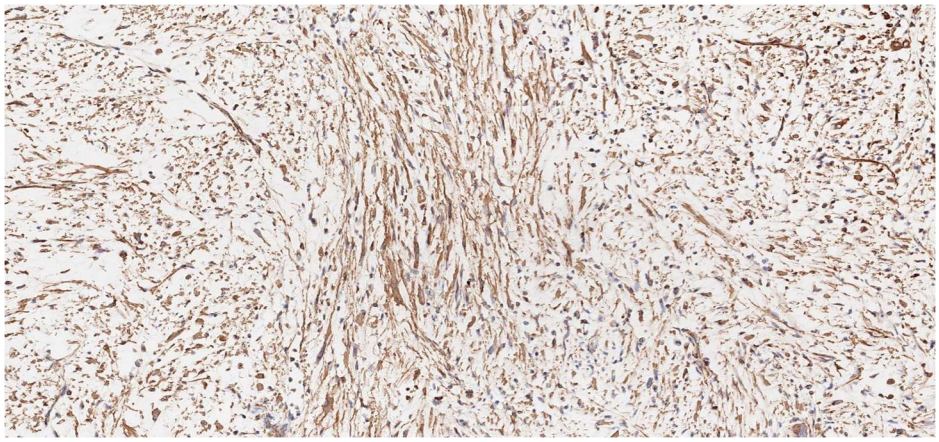

Fig. 6: Vimentin +ve; 20X

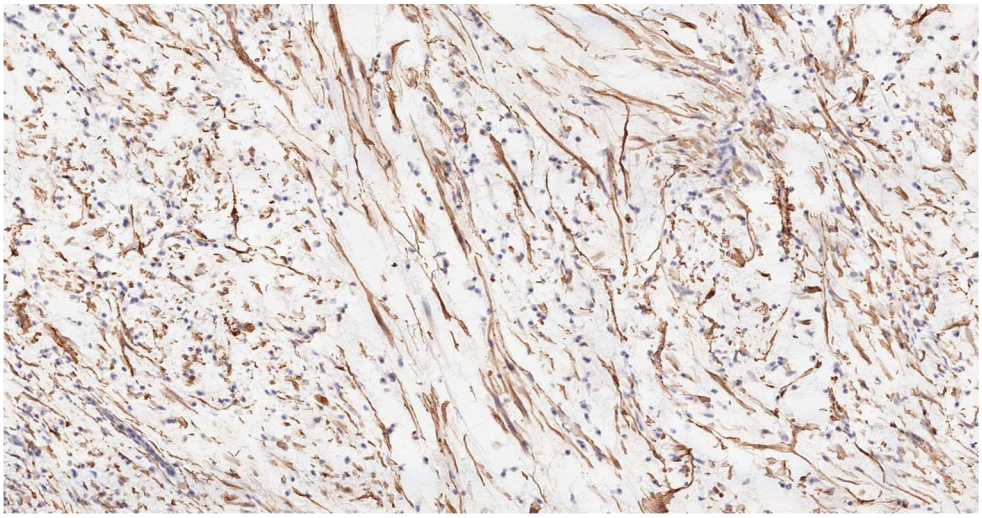

Fig. 7: SMA +ve; 20X

References

Antonescu, C. R., Zhang, L., Nielsen, G. P., Rosenberg, A. E., Dal Cin, P., & Fletcher, C. D. (2011). Consistent t(1;10) with rearrangements of TGFBR3 and MGEA5 in both myxoinflammatory fibroblastic sarcoma and hemosiderotic fibrolipomatous tumor. Genes, chromosomes & cancer, 50(10), 757–764. https://doi.org/10.1002/gcc.20897

Brooks, J. S., & Lee, S. (2015). Contemporary diagnostics: sarcoma pathology update. Journal of surgical oncology, 111(5), 513–519. https://doi.org/10.1002/jso.23853

Carter, J. M., Sukov, W. R., Montgomery, E., Goldblum, J. R., Billings, S. D., Fritchie, K. J., & Folpe, A. L. (2014). TGFBR3 and MGEA5 rearrangements in pleomorphic hyalinizing angiectatic tumors and the spectrum of related neoplasms. The American journal of surgical pathology, 38(9), 1182–1992. https://doi.org/10.1097/PAS.0000000000000212.

Chahdi, H., Damiri, A., Oukabli, M., Albouzidi, A., Bouabid, S., & Lazrek, K. (2010). Acral myxoinflammatory fibroblastic sarcoma. Orthopaedics & traumatology, surgery & research : OTSR, 96(5), 597–599. https://doi.org/10.1016/j.otsr.2009.11.018

Hallor, K. H., Sciot, R., Staaf, J., Heidenblad, M., Rydholm, A., Bauer, H. C., Aström, K., Domanski, H. A., Meis, J. M., Kindblom, L. G., Panagopoulos, I., Mandahl, N., & Mertens, F. (2009). Two genetic pathways, t(1;10) and amplification of 3p11-12, in myxoinflammatory fibroblastic sarcoma, haemosiderotic fibrolipomatous tumour, and morphologically similar lesions. The Journal of pathology, 217(5), 716–727. https://doi.org/10.1002/path.2513

Hassanein, A. M., Atkinson, S. P., Al-Quran, S. Z., Jain, S. M., & Reith, J. D. (2008). Acral myxoinflammatory fibroblastic sarcomas: are they all low-grade neoplasms?. Journal of cutaneous pathology, 35(2), 186–191. https://doi.org/10.1111/j.1600-0560.2007.00789.x

Ieremia, E., & Thway, K. (2014). Myxoinflammatory fibroblastic sarcoma: morphologic and genetic updates. Archives of pathology & laboratory medicine, 138(10), 1406–1411. https://doi.org/10.5858/arpa.2013-0549-RS

Jurcić, V., Zidar, A., Montiel, M. D., Frković-Grazio, S., Nayler, S. J., Cooper, K., Suster, S., & Lamovec, J. (2002). Myxoinflammatory fibroblastic sarcoma: a tumor not restricted to acral sites. Annals of diagnostic pathology, 6(5), 272–280. https://doi.org/10.1053/adpa.2002.35738

Lambert, I., Debiec-Rychter, M., Guelinckx, P., Hagemeijer, A., & Sciot, R. (2001). Acral myxoinflammatory fibroblastic sarcoma with unique clonal chromosomal changes. Virchows Archiv : an international journal of pathology, 438(5), 509–512. https://doi.org/10.1007/s004280000376

Lang, J. E., Dodd, L., Martinez, S., & Brigman, B. E. (2006). Case reports: acral myxoinflammatory fibroblastic sarcoma: a report of five cases and literature review. Clinical orthopaedics and related research, 445, 254–260. https://doi.org/10.1097/01.blo.0000201158.67443.a2

Laskin, W. B., Fetsch, J. F., & Miettinen, M. (2014). Myxoinflammatory fibroblastic sarcoma: a clinicopathologic analysis of 104 cases, with emphasis on predictors of outcome. The American journal of surgical pathology, 38(1), 1–12. https://doi.org/10.1097/PAS.0b013e31829f3d85

Lombardi, R., Jovine, E., Zanini, N., Salone, M. C., Gambarotti, M., Righi, A., Balladelli, A., Colangeli, M., & Rocca, M. (2013). A case of lung metastasis in myxoinflammatory fibroblastic sarcoma: analytical review of one hundred and thirty eight cases. International orthopaedics, 37(12), 2429–2436. https://doi.org/10.1007/s00264-013-2048-5

Mansoor, A., Fidda, N., Himoe, E., Payne, M., Lawce, H., & Magenis, R. E. (2004). Myxoinflammatory fibroblastic sarcoma with complex supernumerary ring chromosomes composed of chromosome 3 segments. Cancer genetics and cytogenetics, 152(1), 61–65. https://doi.org/10.1016/j.cancergencyto.2003.10.004

Meis-Kindblom, J. M., & Kindblom, L. G. (1998). Acral myxoinflammatory fibroblastic sarcoma: a low-grade tumor of the hands and feet. The American journal of surgical pathology, 22(8), 911–924. https://doi.org/10.1097/00000478-199808000-00001M.

Meis, J. M., Kindblom, L. G., and F. Mertens, F. (2013) WHO Classification of Tumours of Soft Tissue and Bone: Myxoinflammtory fibroblastic sarcoma. Fletcher, C. D. M, Bridge, J. A., Hogendoorn, C. W., Mertens, F. Eds. pp. 87–88, IARC Press, Lyon, France.

Michal M. (1998). Inflammatory myxoid tumor of the soft parts with bizarre giant cells. Pathology, research and practice, 194(8), 529–533. https://doi.org/10.1016/S0344-0338(98)80041-1

Miettinen, M., Fetsch, J. F., Antonescu, C. R., Folpe, A. L., and Wakely, P. E. J. (2014) Tumors of the Soft Tissues: Inflammatory myxohyaline tumor od distal extremities (acral myxoinflammatory fibroblastic sarcoma). Silverberg, S. G. Ed. pp. 190–192. American Registry of Pathology, Silver Spring, Md, USA.

Montgomery, E. A., Devaney, K. O., Giordano, T. J., & Weiss, S. W. (1998). Inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg-like cells: a distinctive lesion with features simulating inflammatory conditions, Hodgkin's disease, and various sarcomas. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc, 11(4), 384–391.

Tejwani, A., Kobayashi, W., Chen, Y. L., Rosenberg, A. E., Yoon, S., Raskin, K. A., Rosenthal, D. I., Nielsen, G. P., Hornicek, F. J., & Delaney, T. F. (2010). Management of acral myxoinflammatory fibroblastic sarcoma. Cancer, 116(24), 5733–5739. https://doi.org/10.1002/cncr.25567

Weiss, V. L., Antonescu, C. R., Alaggio, R., Cates, J. M., Gaskin, D., Stefanovici, C., & Coffin, C. M. (2013). Myxoinflammatory fibroblastic sarcoma in children and adolescents: clinicopathologic aspects of a rare neoplasm. Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society, 16(6), 425–431. https://doi.org/10.2350/13-06-1353-CR.1.