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**Journal Title:** Ophthalmic Plastic And Reconstructive Surgery

**Volume:** Volume 26, Number 2

**Publisher:** Lippincott, Williams & Wilkins | 2010, Pages 129-131

**Type of Work:** Article | Post-print: After Peer Review

**Publisher DOI:** 10.1097/IOP.0b013e3181b8efee

**Permanent URL:** <http://pid.emory.edu/ark:/25593/fhb0h>

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Final published version:

<http://ovidsp.tx.ovid.com/sp-3.11.0a/ovidweb.cgi?QS2=434f4e1a73d37e8c0a3e3482eb>

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*Accessed December 9, 2022 12:58 AM EST*



Published in final edited form as:

*Ophthalmol Plast Reconstr Surg.* 2010 ; 26(2): 129–131. doi:10.1097/IOP.0b013e3181b8efee.

## Myxofibrosarcoma of the Orbit

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### Abstract

A 27-year-old woman developed a rapidly progressive left orbital tumor which extended into the cranial fossa. MRI revealed a heterogenous enhancing lesion confined to the left frontal bone and superior orbit. An excisional biopsy was performed and examination of the specimen showed findings diagnostic of a high-grade myxofibrosarcoma. Myxofibrosarcoma is a fibroblast-derived soft tissue neoplasm with up to a 60% local recurrence rate and metastasis may be associated with intermediate to high grade tumors. Complete excision with postoperative adjuvant radiation therapy with chemotherapy was performed.

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Myxofibrosarcoma (MFS), formerly known as a myxoid or a myxoid variant of malignant fibrous histiocytoma (MFH), was first proposed in 1977 as a group of malignant lesions which show a broad spectrum of nuclear pleomorphism, cellularity and proliferative activity.<sup>1</sup> Over the ensuing years, this tumor has increasingly been recognized as a distinct neoplasm of fibroblastic origin without histiocytic differentiation. As a consequence, the category of so-called myxoid MFH was dropped by the World Health Organization classification in 2002, and MFS was added to the category of fibrous tumors.<sup>2</sup> MFS is a malignant mesenchymal tumor that occurs in older adults. The most common locations of MFS are the limb and limb girdle followed by the head and neck, retroperitoneum and mediastinum.<sup>3,4</sup> There has been one case described of MFS occurring in the orbit.<sup>5</sup> Herein, we report an additional case of myxofibrosarcoma of the orbit and briefly review the clinical, radiologica, and histopathologic characteristics of this tumor.

### Case Report

A 27-year-old woman complained of a painless lump in her left upper eyelid and left eyebrow area for the past six weeks. She had mild diplopia and no history of trauma or surgery. Her best corrected vision was 20/25 and 20/20, right and left eyes, respectively. Slit lamp examination was unremarkable. A 3×3 cm firm mass was palpable in the superotemporal orbital region. Magnetic resonance imaging (MRI) demonstrated a mass involving the frontal bone at the lateral superior aspect of the orbit, extending superiorly into the frontal bone.

A biopsy of the lesion was performed and histopathologic examination showed a tumor composed of loosely coherent sheets of cells, including elongated spindle-shaped cells with fusiform nuclei and prominent nucleoli and round cells with hyperchromatic, round nuclei. Some of these cells contained abundant eosinophilic cytoplasm. There were greater than 20

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mitotic figures per high power field in the tumor and there were bizarre mitotic figures present. Immunohistochemical stains were strongly positive for vimentin, for Ki67 in 20% of nuclei, and negative for desmin, myogenin, SMA and S100 in the tumor. The findings were consistent with a high grade myxofibrosarcoma.

The patient underwent a left fronto-orbital craniotomy for tumor resection. Intraoperatively, the tumor had a relatively well-defined capsule and was found to extend into the lateral orbital region. The bone in the frontal orbital area including the rim was substantially destroyed by the tumor. The histologic findings were as described above. Electron microscopic examination of the tumor showed scattered neoplastic cells, ranging from spindle shaped with round to oval nuclei, prominent nucleoli and heterochromatin to stellate diwht irregular nuclei. These cells contained prominent intracytoplasmic rough endoplasmic reticulum (RER), intracytoplasmic membrane bounded vacuoles and Golgi apparati.

The patient completed 38 fractions of adjuvant radiation threatment and the first cycle of chemotherapy including adriamycin, doxorubicin, ifosfamide and mesna. The patient has had no physical nor radiologic evidence of tumor recurrence with six months follow-up.

## Discussion

Myxofibrosarcoma (MFS) is considered a distinct and definable clinicopathologic entity. MFS predominantly occurs in the lower and upper limbs of elderly people in the sixth to eighth decades. However, cases have been reported in patients under 20 years old<sup>6</sup> and our patient was 27. Previous studies have shown that this tumor arises equally in men and women.<sup>7</sup> Clinically, MFS often presents as a gradually enlarging painless mass, which may present as a subcutaneous multinodular growth or extend into the overlying dermis presenting as a cutaneous lesion. Our patient noticed a painless cutaneous lesion in the region of her superotemporal left orbit.

Histopathology in MFS include a multinodular proliferation of spindle-shpved or stellate fibroblasts withing a muyxoid stroma containing curvilinear blood vessels. The tumor cells are hyperchromatic and display moderate to marked nuclear pleomorphism.<sup>8,9</sup> Immunohistochemical staining of MFS shows diffuse strong positivity for vimentin consistent with fibroblastic differentiation<sup>3</sup> and negativ staining for cytokeratins, desmin, HMB45 and S-100. Ultrastructural findings include prominent RER, well-developed Golgi apparati and a moderate number of mitochondria.<sup>3</sup> The pathologic differential diagnosis of MFS incudes pleomorphic rahbdomyosarcoma, myxoid liposarcoma, melanoma, myoepithelial carcinoma and metastatic carcinoma. These entities were excluded in our case because of histologic, immunohistochemical and ultrastructural features.

There is some controversy regarding grading this tumor as there are both three and four tiered grading systems. On scheme classifies MFS as grades I–IV according to the degree of tumor cellularity, cellular atypia and prevalence of mitotic figures<sup>8</sup> whereas another system classifies MFS as low, intermediate and high grade (Table 1).<sup>9</sup> Complete excision with tumor free margins is the recommended treatment for MFS. Tumor response to therapy may be monitored with MRI.<sup>10</sup> When negative margins cannot be obtained, a combination of postoperative radiation therapy and systemic chemotherapy are recommended, especially for high-grade MFS.<sup>3,8,9</sup>

The local recurrence rate of MFS is 50% to 60%, and recurrent lesions often progress to higher grades with increased metastatic potential.<sup>1,7,9</sup> Studies have showed that the risk to metastasis and tumor-related death correlate with the anatomic depth of the primary lesion and histologic grade. Lung and bone are the most common sites of metastasis, although spread to regional lymph nodes may occur.<sup>3,8,9</sup> Orbital MFS is rare, although it may have been classified as

myxoid MFH in the past. Due to its high recurrence rate and risk of metastasis, patients with orbital MFS should be treated aggressively and followed closely.

## Acknowledgments

Supported in part by and unrestricted departmental grant from Research to Prevent Blindness, Inc.

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**Table 1**Myxofibrosarcoma Grading System<sup>9</sup>

	<b>Low Grade</b>	<b>Intermediate Grade</b>	<b>High Grade</b>
Cellularity	hypocellular architecture with vacuolated myxoid matrix	more cellular with predominantly myxoid matrix	hypercellular architecture with small myxoid areas
Cellular atypia	mild to moderate nuclear pleomorphism and hyperchromasia	discernable nuclear atypia	marked cellular pleomorphism and nuclear atypia
Mitotic activity	occasional mitoses	higher mitotic rate	conspicuous mitotic figures with bizarre nuclear features