MRI and CT of Low-Grade Fibromyxoid Sarcoma in Children: A Report From Children’s Oncology Group Study ARST0332

OBJECTIVE. The purpose of this article is to determine the MRI and CT features of low-grade fibromyxoid sarcoma in children.

MATERIALS AND METHODS. We retrospectively analyzed images of 11 pediatric patients with low-grade fibromyxoid sarcoma from a phase 3 clinical trial of nonrhabdomyosarcoma soft-tissue sarcoma (Children’s Oncology Group Protocol ARST0332). MRI and CT were performed in 10 and four patients, respectively. Location, size, margin, and composition on imaging were correlated with pathologic findings.

RESULTS. Tumors were located in the extremities in nine patients, and one tumor each was located in the tongue and lung. Tumors were deep in seven patients and superficial in four patients. All tumors were well defined, solitary, and nonmetastatic at presentation. Tumors were complex solid-cystic in eight patients and completely solid in three patients. On T1-weighted images, all tumors had at least some areas hypointense to muscles, and six had a split-fat sign. On STIR or T2-weighted images, eight tumors had areas hypointense to adjacent muscle, and eight tumors had fluid signal intensity. On contrast-enhanced MRI studies, eight tumors had thick enhancing internal septations, and three had peripheral nodular gyriform enhancement. When we correlated imaging to pathologic findings, areas with hypointense signal intensity on both T1- and T2-weighted images were likely related to fibrous component; areas with fluid signal intensity on T2-weighted images were likely related to myxoid component. On CT, all four tumors were hypodense to muscle, and one tumor showed punctate calcific foci.

CONCLUSION. Low-grade fibromyxoid sarcoma is hypodense to muscle on CT. MRI may identify both fibrous and myxoid components of this rare pediatric soft-tissue sarcoma.

Low-grade fibromyxoid sarcoma is a rare soft-tissue sarcoma characterized by a relatively benign histologic profile, with fibrous paucicellular and myxoid hypervascular zones [1]. In the short term (< 5 years), low-grade fibromyxoid sarcoma has an indolent clinical behavior but also a tendency for late local recurrence and metastasis [2]. It is more common in young and middle-aged adults but has increasingly been recognized in the pediatric population. Although in most cases it is localized to deep soft tissues of the extremities, these tumors can be seen in superficial subcutaneous tissues. The latter location is more commonly seen in children than in adults. On cytogenetic studies, these tumors have a t(7;16)(q34;p11) translocation [1]. Cross-sectional imaging, such as CT and MRI, has played a crucial role in the detection, evaluation of local extent, and staging of soft-tissue tumors.
CT and MRI of Pediatric Low-Grade Fibromyxoid Sarcoma

TABLE 1: Combined MRI and CT Features in 11 Pediatric Low-Grade Fibromyxoid Sarcomas

<table>
<thead>
<tr>
<th>Features</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shape, round to oval</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Morphologic features</td>
<td></td>
</tr>
<tr>
<td>Complex solid cystic</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Solid</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Intramuscular</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>4 (36)</td>
</tr>
<tr>
<td>Deep (lung)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Lower extremity</td>
<td>5 (45)</td>
</tr>
<tr>
<td>Upper extremity</td>
<td>4 (36)</td>
</tr>
<tr>
<td>Tongue muscles</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Diameter (cm), median (range)</td>
<td>6 (2–12)</td>
</tr>
<tr>
<td>Margin</td>
<td></td>
</tr>
<tr>
<td>Circumferentially well defined</td>
<td>9 (82)</td>
</tr>
<tr>
<td>Relatively well defined</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Infiltrating</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Involvement of adjacent structures</td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Skin</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Vessels</td>
<td>2 (18)</td>
</tr>
</tbody>
</table>

Note—Except where noted otherwise, data are number (%) of fibromyxoid sarcomas.

 Patients or their guardians signed informed consent or assent as appropriate. All tumors were reviewed centrally by two expert pediatric pathologists to confirm the histologic subtypes of nonhodgkinosarcoma soft-tissue sarcoma. Of the 18 subjects with low-grade fibromyxoid sarcoma, 11 underwent MRI or CT of the primary tumor before tumor resection. CT and MR images of these 11 subjects were reviewed retrospectively by a study radiologist central reviewer and a pediatric radiology fellow. MR images were obtained in 10 subjects (Table 1), three of whom also underwent contrast-enhanced MDCT with coronal and sagittal reconstructions. One subject underwent only CT of the primary tumor. Demographics, clinical data, and pathology reports were reviewed, and pathologic findings were correlated with imaging findings to the extent possible. Clinical and imaging evidence for local recurrence and metastasis were sought during a 5-year planned follow-up period.

MRI

The standard MRI protocol included unenhanced T1-weighted and fat-saturated T2-weighted or STIR axial and coronal, unenhanced T1-weighted axial, and contrast-enhanced fat-saturated T1-weighted axial and coronal sequences. Additional sagittal images were acquired in some subjects to better show the tumor extent.

On MR images, the radiologist reviewers assessed the anatomic location, size, shape, margin, homogeneity, and signal intensity patterns on T1-weighted and STIR or T2-weighted fat-saturated sequences; contrast enhancement patterns on T1-weighted fat-saturated sequences; and peritumoral edema, hemorrhage, necrosis, and depth of involvement (skin, muscle, bone, joint, and neurovascular invasion). Tumor dimensions were measured in the cephalocaudal, transverse, and anteroposterior planes.

Four terms were used to visually classify the tumor margin: “circumferentially well-defined” when we were able to appreciate well-demarcated margins in over 90% of the tumor surface, “relatively well-defined” when well-demarcated margins were seen in 70–90% of the tumor surface, “discrete mass with poorly defined margins” when well-demarcated margins were seen in less than 70% of the tumor surface and there was no infiltration of surrounding structures, and “infiltrating margins” when tumor was clearly seen invading adjacent structures.

Tumor signal homogeneity was classified subjectively on both T1- and T2-weighted images as homogeneous when more than 95% of the tumor volume showed uniform signal intensity, as mildly inhomogeneous when 75–95% of the tumor volume showed uniform signal intensity, as moderately inhomogeneous when 50–75% of the tumor volume showed uniform signal intensity, and as complex when less than 50% of the tumor volume showed uniform signal intensity.

On T1-weighted MR images, we classified signal intensity of tumor components into four categories: hypointense in areas where tumor had signal intensity less than that of adjacent muscles, isointense in areas with signal intensity the same as that of muscles, areas with signal intensity brighter than that of muscles but less bright than that of subcutaneous fat, and areas with signal intensity equal to that of fat.

On STIR or T2-weighted fat-saturated images, we classified the signal intensity of tumor components into four categories: hypointense in areas with signal intensity less than that of adjacent muscles, isointense in areas with signal intensity the same as that of muscles, areas brighter than muscles but less bright than fluid, and areas with signal intensity as bright as that of fluid.

A cystic mass was defined as having a homogeneous hypointense signal on T1-weighted images and homogeneous hyperintense signal, similar to that of fluid, on T2-weighted images, with no enhancing component on contrast-enhanced images. A complex cystic mass was defined as having predominantly cystic signal with some enhancing solid components or internal septations. A solid mass was defined as having inhomogeneous (predominantly iso- to hypointense) signals on T1-weighted images and inhomogeneous (iso- to hyperintense, but less than fluid) signal on T2-weighted images with enhancement on contrast-enhanced images.

We also evaluated contrast enhancement in tumors by comparing unenhanced and contrast-enhanced T1-weighted fat-saturated images. Tumors with peritumoral regions having T1-hypointense and T2-hyperintense signals were designated to exhibit peritumoral edema. Areas with T1-hyperintense signal and T2-hyperintense or T2-hypointense signal that did not suppress on fat-saturated images were characterized as internal hemorrhage. Nonenhancing areas within the tumor were characterized as necrosis. We also evaluated invasion of surrounding structures, such as muscles, vessels, bones, nerves, and joints.

![Fig. 1—12-year-old boy with low-grade fibromyxoid sarcoma arising in lung. Axial CT image of chest with lung window shows tumor that is hypodense (36 HU) compared with muscles (63 HU) on mediastinal window (not included) in anterior segment of left lower lobe.](image-url)
The anatomic location, size, shape, margin, homogeneity, and density of tumors were assessed on contrast-enhanced CT images. We categorized density of the tumor as hypodense (less than that of adjacent muscle), isodense (equal to that of muscle), and hyperdense (more than that of adjacent muscle). Areas of calcification and hyperdense hemorrhage within the tumor and the presence and pattern of contrast enhancement were recorded.

**Pathologic Review**

In this study, the gross specimens were not available for radiologic-pathologic correlation. All tumors were, however, reviewed centrally by two expert pediatric pathologists to confirm the histologic subtypes of low-grade fibromyxoid sarcoma. The gross and microscopic pathologic features of low-grade fibromyxoid sarcoma were obtained from reports issued by local institutions.

**Results**

Subjects ranged in age from 3 to 18 years with a median of 13 years. The male-to-female ratio was 2.6:1. All 11 low-grade fibromyxoid sarcomas were nonmetastatic at presentation. There was no evidence of local recurrence or metastasis in our subjects during short-term follow-up of 0.5–6 years (median, 2.7 years). Table 1 summarizes the combined MRI and CT findings. By MRI and CT, nine tumors were circumferentially well defined (> 90% of the tumor surface). Low-grade fibromyxoid sarcoma was located in the lower extremity in five patients, the upper extremity in four patients, and in the tongue muscles and the lung in one patient each. There was involvement of the pelvic region in two of the three lower extremity tumors. Of the four upper extremity tumors, three were located in the region of the shoulder girdle and one was in the upper arm. Two unusual locations were the lung (Fig. 1) and tongue muscles (Fig. 2). On MRI and CT,
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The maximum diameter of tumor was 2–12 cm with a median of 6 cm. In nine low-grade fibromyxoid sarcomas, the margin was circumferentially well defined (well-demarcated margins in > 90% of the tumor surface), and one of the tumors was relatively well defined (well-demarcated margins in 70–90% of the tumor surface). Infiltrating margins were seen in one of the tumors involving muscles of the shoulder (Fig. 3).

MRI (10 Subjects)

None of the low-grade fibromyxoid sarcomas appeared uniformly homogeneous on T1- and T2-weighted images. Two tumors showed mild inhomogeneity, four showed moderate inhomogeneity, and four had a complex appearance.

On T1-weighted images, all low-grade fibromyxoid sarcomas had at least some areas with signal intensity less than that of adjacent muscle and equal to that of cortical bone. In six tumors (Table 2), the predominant signal intensity was isointense to muscle (Fig. 4). In three tumors, the predominant signal intensity was hypointense to muscles but more than that of cortical bone (Fig. 5). One of the tumors showed predominant signal intensity greater than that of muscle but less than that of the subcutaneous fat. Five of the six tumors located in the intramuscular compartment of the extremities showed a split-fat sign (Fig. 5). None of the tumors showed hemorrhagic components.

On STIR or T2-weighted fat-saturated images, eight low-grade fibromyxoid sarcomas had at least some hypointense areas (Table 2). Eight tumors had areas of fluid signal intensity. Four tumors had predominant signal intensity equal to that of fluid (Fig. 6). In five tumors, the predominant signal intensity was equal to that of muscle (Fig. 5). Of the three completely solid tumors, two were isointense and one was hypointense to muscle on fluid-sensitive sequences. Peritumoral edema (Fig. 5) was present in seven cases. Thick (> 3 mm) internal septations were seen in four tumors.

On contrast-enhanced T1-weighted fat-saturated images, all 10 low-grade fibromyxoid sarcomas revealed mild-to-moderate inhomogeneous contrast enhancement. Thick enhancing internal septations were seen in four sarcomas. Areas with T1 and T2 hypointensity and areas with fluid signal on STIR or fat-saturated T2-weighted images showed variable enhancement. In three tumors with a completely solid appearance, peripheral nodular gyriform enhancement was seen (Figs. 2 and 3).

Bone involvement of the scapula was seen in association with a tumor arising from the infraspinatus muscle (Fig. 3). Skin involvement was seen in one tumor in the inguinal-scrotal region. Vascular encasement involving small branches of major extremity vessels was seen in two tumors located in the deep muscular compartment. None of the tumors showed joint or obvious nerve encasement.

CT (Four Patients)

On contrast-enhanced CT, all four low-grade fibromyxoid sarcomas were hypodense to adjacent muscles. Tumors were located in the subcutaneous plane in two subjects, in the lung parenchyma in one patient, and in the tongue muscles in one patient. All four tumors showed mild inhomogeneous contrast enhancement (Figs. 2 and 7). The tumor involving the tongue had internal punctate calcific foci (Fig. 2).

Pathologic Review (11 Patients)

Because gross tumor specimens were not available for central pathologic review, pathology reports from the local institutions of the excised tumors were reviewed. All tumors were described as well circumscribed, round to oval, and gray-white with a whorled appearance without hemorrhage. The maximum diameter of tumor varied by report, from 2 to 12 cm, with a median of 6 cm. On microscopy, tumors showed two distinct zones—a paucicellular fibrous zone and a hypervascu-
lar myxoid zone with an abrupt transition between these zones. Some tumors contained hyalinizing spindle cells with giant rosettes. Fascicular and whorled arrangements were noted in all tumors. In most tumors, mitotic figures were less than 10 per 10 high-power fields, and cellular atypia was rare. No areas of necrosis or hemorrhage were identified. This finding was correlated with the lack of high-density hemorrhage on MRI and CT.

Cytogenetic studies were performed in five tumors, all of which showed the characteristic t(7;16)(q34;p11) translocation. The resection margin was negative in all patients, except in one tumor arising from the left shoulder.

Discussion

Low-grade fibromyxoid sarcoma was first described in 1987 and was initially thought to exhibit bland histologic features but aggressive clinical behavior. Subsequently, many studies revealed that low-grade fibromyxoid sarcoma usually has a relatively benign course and occurs most commonly in young and middle-aged adults. An increasing number of cases have been reported in pediatric patients [1,3].

On histologic analysis, these tumors have a low mitotic rate, two distinct zones (myxoid and fibrous), bland regular spindle cells, and a swirling or whorled pattern [2]. Myxoid zones are typically hypercellular with prominent vascularity, whereas fibrous zones are hypocellular [1,2]. The transition between myxoid and fibrous zones may be gradual or abrupt [1]. Hyalinized spindle cell tumor with giant rosettes is now considered to be a variant of low-grade fibromyxoid sarcoma that also shows collagen rosettes [1,3,4]. Cytogenetic studies show that the t(7;16)(q34;p11) translocation results in a chimeric fusion protein derived from the FUS gene on chromosome 16p11 and the BFB2H7 gene on 17q33 being seen in both low-grade fibromyxoid sarcoma and hyalinized spindle cell tumor with giant rosettes [1]. All low-grade fibromyxoid sarcomas are positive for Muc-4, an immunohistochemical marker that is very sensitive for the diagnosis of this tumor [5]. Low-grade fibromyxoid sarcomas are also positive for vimentin, actins, CD 68, and epithelial membrane antigen and negative for CD34, keratins, and S-100 protein [1].

Low-grade fibromyxoid sarcomas are commonly located in the lower extremity, shoulder, trunk, inguinal regions, upper extremity, and vulvovaginal regions [1–3]. In our study, most tumors were seen in the lower and upper extremities, including the shoulder. Two unusual locations in our study were in the lung parenchyma and tongue musculature. Low-grade fibromyxoid sarcoma is commonly deep and intramuscular in young and middle-aged adults. In the pediatric population, a superficial subcutaneous location has been reported to be more common (37%), compared with less than 10% in large series including all ages [1]. In our pediatric cohort, deep intramuscular (6/11 [55%]) and subcutaneous locations (4/11 [36%]) were observed. The reported median size of tumor ranges from 4.2 to 9.4 cm, which is in agreement with a median size of 6 cm seen in our study.

On imaging, low-grade fibromyxoid sarcomas are solitary and well circumscribed at presentation, but they tend to present as multiple infiltrating masses at recurrence [6]. All of the tumors in our study were solitary at presentation and most were well circumscribed and round to oval in shape.

On MRI, low-grade fibromyxoid sarcoma is inhomogeneous owing to two distinct internal zones: myxoid and fibrous. Low-grade fibromyxoid sarcoma has been reported to show areas of low signal intensity on both T1- and T2-weighted sequences because of
the fibrous component [7–11]. In our study, most of the tumors had an inhomogeneous appearance on T1- and T2-weighted images. In all tumors, we found internal components that were hypointense to muscle on T1-weighted images. In agreement with prior reports, we found that most T1-hypointense foci (8/10 [80%]) were also hypointense on T2-weighted images, likely corresponding to fibrous tissue. On CT, low-grade fibromyxoid sarcomas have low-attenuation components that are hypodense to the skeletal muscle, likely due to the myxoid component and extracellular matrix [6, 8, 10, 11]. Though calcification has been reported in these tumors, it is not very common [6, 7, 11, 12] and was seen in only one tumor in our study.

We observed a complex solid-cystic appearance in most (9/11 [82%]) of the tumors in our study. The complex solid-cystic appearance is probably related to the histologic profile of the tumor, in which myxoid zones appear cystic and fibrous zones appear as solid nodular or septate areas. A somewhat similar imaging appearance in the form of intralesional nodules with hyperintense signal had previously been reported in low-grade fibromyxoid sarcoma [6]. A few tumors in our study (3/11 [27%]) were entirely solid but no tumor was entirely cystic.

The split-fat sign on T1-weighted images was seen in 50% (5/10) of our subjects with an intramuscular tumor. None of the prior studies or case reports has reported this finding in low-grade fibromyxoid sarcoma. However, this sign was seen in three cases on review of the T1-weighted images included in some case reports [12–14]. The split-fat sign (best appreciated on T1-weighted images) represents a rim of fat surrounding a tumor, such as a peripheral nerve sheath tumor, that is located in the intermuscular space. Low-grade fibromyxoid sarcomas are considered to be malignant fibroblastic neoplasms. It is not surprising that low-grade fibromyxoid sarcoma that occurs in muscles may exhibit this sign.

On fluid-sensitive sequences, a distinct gyriform pattern with multiple folded layers of predominantly low-signal-intensity areas mimicking brain gyri was reported in a prior study [6]. We observed a similar gyriform pattern in two tumors that were completely solid. Peritumoral edema was seen on T2-weighted images in 70% (7/10) of our subjects. This imaging feature has not previously been described or seen on images in previous case reports. However, most of the images from prior reports did not include a fat-suppressed T2-weighted or STIR sequence. In our study, vascular encasement of small branches of major extremity vessels was seen in two subjects, and bone and skin invasion were observed in two different subjects. Though areas of internal hemorrhage have been reported in low-grade fibromyxoid sarcoma [14], no tumor in our study showed imaging evidence of hemorrhage.

On T1-weighted fat-saturated contrast-enhanced studies, low-grade fibromyxoid sarcoma has been reported to show inhomogeneous contrast enhancement, reflecting the two distinct internal zones with varying vascularity [6, 13]. All tumors in our study showed inhomogeneous contrast enhancement. Tumors with a complex solid-cystic appearance showed either enhancing solid components

**Fig. 6**—12-year-old boy with right groin mass. A, Axial T1-weighted image of pelvis shows hypointense mass (arrow) in subcutaneous plane of right groin. B, On axial T2-weighted fat saturation image, mass shows almost entirely fluid signal intensity. Notice T2-hypointense nodular component (arrow) along posterior margin of mass. C, Axial contrast-enhanced T1-weighted fat-saturated image shows peripheral enhancement with nonenhancing central component in this complex cystic mass. Notice nodular enhancement (arrow) along posterior margin of mass. Synovial sarcoma should be considered in differential diagnosis of soft-tissue tumors with cystic appearance.

**Fig. 7**—10-year-old boy with left shoulder tumor. Coronal contrast-enhanced CT scan reveals slightly hypodense mass in left supraclavicular region with thin peripheral rim (arrow) that is isodense to surrounding muscles. Histologic examination shows solid mass without cystic or necrotic changes.
or enhancing thick (>3 mm) internal septations. As on the fluid-sensitive sequences, the two tumors that were entirely solid showed a gyriform enhancement pattern on contrast-enhanced T1-weighted fat-saturated images. Areas with hypointense signal on T1- and T2-weighted images showed variable contrast enhancement, from minimal to intense. This finding may be a reflection of the degree of fibroblastic activity versus frank fibrosis in these tumors, similar to that observed in desmoid tumors [15]. Areas with fluid signal intensity on STIR or T2-weighted images showed variable enhancement, largely related to the degree of vascularity of the myxoid component of the tumor.

Differential diagnoses for low-grade fibromyxoid sarcoma of the extremity and trunk in the pediatric population include rhabdomyosarcoma, synovial sarcoma, Ewing sarcoma, family tumors, nerve sheath tumors, and solitary fibrous tumor. Apart from some cystic synovial sarcomas, these tumors usually appear solid on imaging and show inhomogeneous contrast enhancement. Rhabdomyosarcoma, myxoid neurofibroma, primitive neuroectodermal tumors, and synovial sarcoma can be distinguished from low-grade fibromyxoid sarcoma by the absence of fibrous tissue and, therefore, lack of T1- and T2-hypointense areas. Solitary fibrous tumors can mimic low-grade fibromyxoid sarcoma, although they lack the T2-bright myxoid component.

Studies with short-term follow-up have shown that, if widely excised, these tumors have relatively low local recurrence (9%) and metastatic (6%) rates. These studies also report that the local recurrence rate of superficial tumors is the same as that of deep tumors, although metastases occurred less frequently with superficial tumors [1,3]. In contrast, prior studies with long-term follow-up have shown that low-grade fibromyxoid sarcoma has high local recurrence (68%) and metastatic (41%) rates [2]. Because these tumors have an indolent nature, they may recur up to 15 years after completion of therapy, with a median time to recurrence of about 3.5 years [2]. The lung, pleura, and chest wall are the most commonly reported sites of metastasis, followed by bone and liver [2]. Neither local recurrence nor metastasis was found in our subjects during short-term follow-up of 0.5–6 years (median, 2.7 years). Because low-grade fibromyxoid sarcoma may recur many years after treatment, long-term follow-up is recommended.

Limitations of our study included a relatively small sample despite a 5-year data collection period from all Children’s Oncology Group institutions, underscoring the rarity of this cancer in children and young adults. Because of the nature of data collection for this study, an exact spatial correlation between radiologic and gross pathologic appearances of the tumor was not possible. However, local pathologic descriptions of the excised tumors provided valuable information regarding tumor composition, which could be correlated to imaging features. Another study limitation is the relatively short-term follow-up of our subjects.

**Conclusion**

Low-grade fibromyxoid sarcoma is a rare soft-tissue neoplasm that is increasingly being recognized in pediatric populations. MRI features of a complex solid-cystic tumor with fibrotic tissue that appears hypointense to muscle on T1- and T2-weighted images and exhibits a variable degree of enhancement can be very helpful in suggesting this diagnosis before biopsy. Solid-cystic lesions show enhancement of solid components or thick internal septations. Tumors that are predominantly solid may show peripheral nodular gyriform enhancement. Areas with fluid signal intensity on STIR or T2-weighted images may show variable enhancement likely related to the vascularized myxoid component of the tumor. In our study, all tumors underwent complete surgical resection with negative margins (except in one) and showed no evidence of local recurrence or metastasis on short-term follow-up.

**References**