11288: Histologic Response of Infiltrative Myxofibrosarcomas and Undifferentiated Pleomorphic Sarcomas to Pre-Operative Radiotherapy

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Abstract (740 words)

Background:

Infiltrative growth pattern is often observed in superficial myxofibrosarcoma (MFS) and undifferentiated pleomorphic sarcoma (UPS). According to the past literatures, radiographic infiltration of superficial MFS and UPS on magnetic resonance (MR) images indicates a high possibility of histologic infiltration. In recent years, this growth pattern has become widely recognized as a primary risk factor for local recurrence and possibly distant metastases. However, the role of radiotherapy (RT) as adjuvant therapy remains uncertain.

Questions/Purposes:

The aims of this study are to clarify the efficacy of preoperative RT strategy for infiltrative MFS and UPS by examining pathologic findings and patients' clinical outcomes, and to reveal current issues concerning pre-operative RT on infiltrative MFS and UPS.

Patients and Methods:

From 1996 to 2014, 252 soft tissue sarcomas diagnosed as malignant fibrous histiocytoma (MFH), MFS, or UPS were surgically treated at our institution. Ninety-six patients initially excised outside were excluded. Among the remaining 156 cases, MR images were available for review in 101 cases. Of the 101 cases, 19 cases had a subcutaneous or on-fascia tumor, but one case amputated without RT was excluded. The total of 18 cases were included in this study. These cases were pathologically reviewed and re-labeled as MFS or UPS according to the World Health Organization (WHO) classification published in 2013. All the 18 cases fit either of MFS or UPS.

MR images before RT were reviewed in terms of the maximum diameter and peripheral growth pattern of the tumors. If a tumor extends on a fascial plane or into subcutaneous fat tissue for 2 mm or more from the edge of the main mass on gadolinium-enhanced, fat-saturated T1-weighted MR imaging, then the tumor is considered 'infiltrative'.

Specimens of all the cases were microscopically reviewed. Firstly, overall histologic response to RT was measured on the 4-grade scale proposed by Willett CG et al. in 1987, by the ratio of necrosis or severe

cellular alteration; the ratios of less than 50%, 50–80%, more than 80% but not 100%, and 100% were classified as +1, +2, +3, and +4, respectively. In this evaluation, grades +3 and +4 were considered as good response (GR), and the rest as poor response (PR). Then, the peripheral area, where an infiltrative growth pattern was observed on pre-RT MR images with contrast, was graded regarding the degree of viable tumor cells remaining in the area. We classified a case with no viable tumor cells in the infiltrative area as grade A, while a case with some but fewer viable tumor cells than initial biopsy as grade B, and that with similar tumor viability to initial biopsy as grade C. For cases with viable tumor cells remaining in the infiltrative area, how far viable tumor cells extended from the edge of main mass was also measured on glass slides. These two pathologic results (GR vs. PR, and grade A vs. grade B or C) were compared between MFS and UPS using Fisher's exact test.

Clinical outcomes were reported in terms of patient survival, local recurrence, and distant metastasis.

Results:

Eighteen cases included six MFSs and 12 UPSs. All the cases were non-metastatic at the first presentation. Radiographically, all cases except for three UPSs were infiltrative. Histologic GR was observed in ten (83%) UPS but only one (17%) MFS case. Among the 15 radiographically infiltrative cases, viable tumor cells remained in the infiltration after RT in seven (47%) cases (MFS: 5/6, UPS: 2/9). In these seven cases, the distance from the edge of the main tumor mass to the furthest extension of viable tumor cells was almost the same as that of pre-RT radiographic infiltration (Table 1, 2). There was a statistically significant correlation between myxofibrosarcoma and both of histologic PR and residual viable tumor cells in the infiltration according to Fisher's exact test (p = 0.01 and 0.04, respectively).

Two cases (11%) had local recurrence; one recurred in the field of RT (case 4), while the other did outside (case 5). Both of them had histologic PR and viable tumor cells in the radiographic infiltration (Table 1).

Conclusions:

(1) Pre-operative radiotherapy can improve local control for infiltrative UPS.

(2) In contrast, MFS cells in the infiltration are more likely to remain viable even after pre-operative RT.

(3) Some infiltration can exceed 3cm, which is currently a standard extra-length of RT field from the edge of main mass. Therefore pre-operative RT planning for infiltrative UPS and MFS should be strictly based on MRI rather than CT.

Table 1. Summary of 18 cases in this study

Case No.	Age, sex	Dx	T location	T depth	IGP	Initial T size	Willet grading	HIP	LR/Met[a]	FU (month)	Status
1	88, M	UPS	Forearm	OF	+	30 mm	+3	B	–	88	CDF
2	78, F	UPS	Lower leg	OF	+	70 mm	+2	A	–	86	CDF
3	66, M	MFS	Scapula	SC	+	50 mm	+2	B	–	69	CDF
4	83, M	MFS	Forearm	OF	+	53 mm	+1	B	LR (32)	75	AWD
5	76, F	UPS	Lower leg	OF	+	43 mm	+1	B	LR (31)	72	NED
6	81, F	UPS	Thigh	SC	–	82 mm	+4	N/A	–	60	CDF
7	54, F	UPS	Lower leg	SC	–	60 mm	+4	N/A	–	63	CDF
8	73, F	MFS	Lower leg	SC	+	57 mm	+2	B	–	58	CDF
9	82, M	UPS	Pelvis	OF	+	40 mm	+4	A	–	59	CDF
10	47, F	UPS	Lower leg	OF	+	38 mm	+3	A	Met (28)	57	AWD
11	68, M	MFS	Lower leg	SC	+	24 mm	+2	A	Met (3)	47	NED
12	63, M	UPS	Lower leg	OF	+	42 mm	+4	A	–	34	CDF
13	66, F	UPS	Thigh	OF	+	43 mm	+4	A	–	17	CDF
14	41, F	UPS	Shoulder	SC	–	55 mm	+3	N/A	Met (18)	23	AWD
15	66, F	MFS	Shoulder	OF	+	41 mm	+3	B	–	16	CDF
16	68, F	UPS	Lower leg	OF	+	48 mm	+4	A	–	14	CDF
17	84, F	MFS	Lower leg	OF	+	31 mm	+1	C	–	13	CDF
18	51, M	UPS	Thigh	OF	+	20 mm	+3	A	–	7	CDF

Dx diagnosis, *MFS* myxofibrosarcoma, *UPS* undifferentiated pleomorphic sarcoma, *T* tumour, *OF* on-fascia, *SC* mainly subcutaneous, *IGP* infiltrative growth pattern, *N* necrosis, *HIP* histologic infiltration pattern, *N/A* not applicable, *LR* local recurrence, *Met* metastasis, *FU* follow-up, *CDF* continuous disease free, *AWD* alive with disease, *NED* no evidence of disease

Table 2. The maximum length of viable tumor cell extension from the edge of the main mass on specimen for the 7 cases with tumor viability in the radiographic infiltrated area

	Infiltration on MRI [a] (before RT)	Infiltration on MRI [a] (after RT)	Histologic infiltration (after RT)	Margin
Case 1 (UPS)	10 mm	ND	10 mm	Wide
Case 3 (MFS)	7 mm	78 mm	4 mm	Wide
Case 4 (MFS)	29 mm	28 mm	25 mm	Positive
Case 5 (UPS)	25 mm	ND	30 mm	Wide
Case 8 (MFS)	7 mm	51mm	12 mm	Wide
Case 15 (MFS)	27 mm	17 mm	20 mm	Wide
Case 17 (MFS)	33 mm	43 mm	24 mm	Wide

ND no data available for evaluation

[a] Radiographic infiltration was measured on gadolinium-enhanced, fat-saturated T1-weighted MRI.