Malignant Soft-Tissue Tumors of Foot and Surgical Treatment

Abstract

Background: Malignant soft tissue Tumors of the foot represent a unique subset of all soft tissue tumors, showing variance in type, location, age, prognosis, and treatment from tumors in the rest of the musculoskeletal system. The main objective was to describe the prevalence, demography and anatomical distribution of the malignant soft tissue tumors of the foot and subsequently, analyze the significance of operation, chemotherapy, and radiotherapy for local control and survival rate in patients with foot malignant tumors.

Methods: The malignant soft-tissue foot tumors surgically treated by the author during a 6-years period (2010-2016) were retrospectively studied for their presenting symptomatology, treatment modalities and outcomes. The follow-up was considered for at least 5 years survival benchmark.

Results: Only three of our patients under went amputation as a primary surgical plan. Others went under limb-salvage surgeries. Operation type had no significant effect on overall survival in our case series. The results of this study support the use of wide surgical excision and limb salvage surgery if obtainable, which is similar to previous reports.

Conclusion: Our study focused exclusively on the presentation, treatments and outcomes of malignant soft-tissue tumors of the foot. By focusing solely on malignant soft-tissue tumors of the foot we hoped to better characterize the presentation, treatment and outcomes of this rare clinical entity.

Keywords: Soft Tissue Neoplasms, Amputation, Survival Rate, Prognosis, Foot

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Introduction

Soft tissue Tumors of the foot represent a unique subset of all soft tissue tumors, showing variance in type, location, age, prognosis, and treatment, from tumors in the rest of the musculoskeletal system [(1)]. Soft-tissue sarcomas, as rare tumors of mesenchymal origin, target lower more frequently than the upper extremities [(2)]. Other rare malignancies with localization at the foot are tumors of skin, such as melanoma, giant cell tumors of the tendon-sheath, vascular sarcomas, and carcinoma metastases [(3)]. The foot has a particular anatomy with multiple small muscular compartments, terminal neurovascular branches, and a delicate soft tissue cover including a uniquely structured sole that cannot be replaced by adequate tissue in case of loss [(4)]. Owing to multidisciplinary advances in excision, reconstruction and adjuvant therapy, limb salvage procedure has become the technique of choice for lower extremity malignant tumors, particularly with adjuvant radiotherapy [(5)]. Primary amputations have been increasingly replaced by limb-salvage techniques, preserving extremity and function as much as possible [(6,7)]. The usefulness of radiotherapy for local control of tumors has been well demonstrated in patients with foot malignant tumors [(8)].

Owing to the rarity of these tumors, the particular clinic pathologic features, therapeutic approach, and outcomes in this setting are not well established. The current study high-lights the clinical features of malignant tumors of the foot, and presents the clinical outcomes of treatment for the patients treated at the authors' institution. The main objective was to describe the prevalence,

demography and anatomical distribution of the malignant tumors of the foot and subsequently, analyze the significance of operation, chemotherapy, and radiotherapy for local control and survival rate in patients with such malignant tumors.

Methods

The malignant soft tissue tumors of foot treated at "Shafa" and "Pars" hospitals in Tehran from 2010 to 2016 were studied.

The Patients were eligible for inclusion if they had histological confirmed soft-tissue malignant tumors located in the foot had been treated surgically and had been followed for at least five years postoperatively. The following information from each patient's medical record were extracted: age at presentation, sex, disease status at presentation (primary, locally recurrent or metastatic), prior treatment, medical history, histological diagnosis, lesion characteristics (e.g., tumor size and location), details of treatment (pre- or postoperative chemotherapy or radiation therapy, resected structures, surgical margins, reconstructive technique and complications) and condition at follow-up.

The exclusion criteria were insufficient data, including the lack of medical record data, imaging studies, or histological slides, all of which contributed to a vague or inadequate identification of a tumor. The present study did not include patients with pseudotumoral lesions, tumors treated with thermal ablation, or patients with metastatic lesions located in the foot. All malignant skin tumors were excluded from the study except malignant melanomas because the staging and treatment of melanomas are different from skin tumors and resemble those of sarcomas. All patients gave their informed consent at admission to be included in scientific studies. The investigation was approved by our institutional review board.

Evaluation: The foot was subdivided into the forefoot and hind foot at the level of Lisfranc. Radiography, computed tomography (CT) and magnetic resonance imaging (MRI) were used to diagnose and examine all body systems. The greatest diameter of each tumor was identified by magnetic resonance imaging (MRI) analysis_ T2-weighed fat-saturated images_ and was categorized into two groups, less and more than 5cm. Histologic typing of foot tumor was based on the World Health Organization (WHO) histologic typing of musculoskeletal tumors [(9)].

Treatment: A standardized treatment protocol was followed for all patients. Types of surgical procedures included marginal excision, wide excision, and amputation. We decided to avoid primary amputation as long as possible. Limb salvage was attempted whenever possible.

Radiotherapy & Chemotherapy: Neoadjuvant and adjuvant chemotherapy was given in 10 patients at the discretion of the staff medical oncologists (Table 1). Radiotherapy was mostly applied to cases with tumors larger than 5 cm.

Chemotherapy, used in the neoadjuvant, adjuvant, or palliative setting, consisted of multi-agent regimens containing, in most cases, cysplatin, doxorubicin, Methotrexate, Etoposide, Paclitaxel, and Gemcitabine. Mostly, the tumors located in the hind foot received radiotherapy and chemotherapy, postoperatively.

Overall survival (OAS) was defined as the time from surgery to 5 years follow-up visit. Local recurrence-free survival and metastasis-free survival were defined as the time from surgery to recurrence and metastasis at the latest follow-up visit, respectively.

Statistical analysis: The effect of each prognostic variable was analyzed using SPSS statistics version 17.0 software (SPSS Inc., Chicago, IL, USA). For all statistical analyses, P values < 0.05 were considered significant.

Results

Patients in current study included six female (mean age=30) and nine male cases (mean age=31) (Table1). Descriptive statistics of patients are presented (Table 2). Two patients received preoperative chemotherapy.

Table 1: Patient Demographics of current case series					
Sex	Number	Age			
		Minimum	Maximum	Mean	Std. Deviation
Female	6	19	46	30.50	10.368
Male	9	2	63	31.00	19.481
All	15	2	63	31.00	15.982

Table 2: Histology, site, and size of tumors in current case series			
Tumors Characteristics		Frequency	Percent
Histology	DFSP	1	6.7
	Epithelioid Sarcoma	2	13.3
	Ewing/PNET	1	6.7
	Fibro Sarcoma	1	6.7
	Leiomyosarcoma	1	6.7
	Malignant Melanoma	2	13.3
	MFH	1	6.7
	MPNST	1	6.7
	Rhabdomyosarcoma	1	6.7
	Synovial Sarcoma	4	26.7
Site	Forefoot	6	40.0
	Hind foot	9	60.0
Size	<5 cm	5	33.3
	>5 cm	10	66.7

The histological diagnosis was synovial sarcoma in 4, malignant melanoma in 2, DFSP (n=1), Epithelioid sarcoma in 2, and Ewing/PNET, Fibrosarcoma, Leiomyosarcoma, MFH, MPNST, and Rhabdomyosarcoma 1 of each. The tumors were located in hind foot in 9 and forefoot in 6. Five cases presented with tumor size less than 5 cm (33%) and ten with more than 5 cm (67%) (Table 3).

Three patients underwent ray-amputation (20%) and twelve cases underwent excision: Three marginal excisions (20%), and nine wide excisions (60%) (Table 4). Two patients received preoperative chemotherapy (patients' number 7 and 11) and 66.7% of the patients received postoperative chemotherapy. Chemotherapy, used in the neoadjuvant, adjuvant, or palliative setting, consisted of multiagent regimens containing, in most cases, cysplatin, doxorubicin, methotrexate, etoposide, paclitaxel, and gemcitabine. Of the 15 patients, 46.7% received radiotherapy for loco regional disease control. No operative mortality or major morbidity related to treatment occurred [10] (Table 5). Postoperatively, all cases received primary closure except the case with DFSP which underwent rotational flap. The treatment of patients is summarized in Table 4. The 5-year overall survival, local recurrence survival and metastasis free survival of soft tissue sarcomas were 87, 80 and 87%, respectively. Three cases presented with skin complications.

Although all fifteen patients presented with nonmetastatic disease, two of them subsequently developed pulmonary metastases, both of them died of disease,

later. Both of them had recurrence requiring amputation but died subsequent to pulmonary metastasis. Two patients had regional lymphatic metastasis (Figure 1).

Table 3: Operative approaches, chemotherapy and radiotherapy data of case series			
Treatment		**Frequency**	**Percent**
Operation	Marginal Excision	3	20.0
	Ray Amputation	3	20.0
	Wide Excision	9	53.3
Chemotherapy	No	5	33.3
	Yes	10	66.7
Radiotherapy	No	8	53.3
	Yes	7	46.7

Table 4: Postoperative complications and survival rate			
Complications & Survival		**Frequency**	**Percent**
Local Recurrence	No	12	80.0
	Yes	3	20.0
Metastasis	No	13	86.7
	Yes	2	13.3
Skin Complications	No	12	80.0
	Yes	3	20.0
Regional Lymph Node	No	13	86.7
	Yes	2	13.3
Overall Survival	No	2	13.3
	Yes	13	86.7

Discussion

We presented fifteen cases with malignant soft-tissue foot tumors, thirteen sarcomas and two malignant melanomas. All cases were surgically managed. Given the rarity of tumors presenting in the foot and the unique anatomy and function, diagnosis and surgical treatment of malignant tumors are challenging in every consideration.

Soft-tissue tumors of the foot present a challenge to achieve limb salvage with acceptable functional and oncologic outcomes [11]. However, only three of our patients underwent amputation as a primary surgical plan. The rest had limb-salvage surgeries. Among thirteen limb-salvage cases, only two resulted in amputation surgery both died later. Despite what may seem in some cases to be a lengthy program of treatment, with the potential for complications and a poor outcome, we have shown that good results can be achieved, with preservation of the limb by a combined approach. We had only two treatment failures, requiring amputation, and this compares well with other published series, which have lower rates of reconstruction [4]. The fact that amputation as a curative treatment strategy for sarcomas in the extremities has no survival benefit [3].

All of our cases were managed with planned surgical excisions. In the foot, unplanned surgical excision of soft tissue tumors occurs frequently, with patients undergoing a unplanned surgery at increased risk of recurrence [12]. Properly performed limb salvage surgery procedures and amputations are generally expected to give similar oncological outcomes [6]. However, surgical treatment of foot and malignancies is often hindered by morphological and epidemiological factors [10].

Table 5: The list of all patients included in research

No.	Sex	Age	Tumors Characteristics	Site	Size	Margin	Chemotherapy	Radiotherapy	Recurrence	Metastasis
1	M	27	DFSP[1]	Fore foot	>5 cm	Wide	No	No	No	No
2	F	23	EpiSA[2]	Fore foot	<5 cm	Marginal	Yes	Yes	Yes	Yes
3	M	16	EwiP[3]	Hind foot	>5 cm	Wide	Yes	Yes	No	No
4	M	22	FibroSA[4]	Fore foot	>5 cm	Wide	No	No	No	No
5	F	19	Sy.SA[5]	Hind foot	>5 cm	Wide	Yes	Yes	No	No
6	F	44	MPNST	Hind foot	>5 cm	Wide	Yes	Yes	No	Yes
7	M	2	EpiSA	Fore foot	<5 cm	Amputation	Yes	Yes	No	No
8	M	49	Sy.SA	Hind foot	>5 cm	Marginal	No	No	Yes	No
9	M	63	LeiomyoSA[6]	Fore foot	>5 cm	Wide	No	No	No	No
10	M	33	Melanoma[7]	Hind foot	<5 cm	Amputation	No	No	No	No
11	F	15	Sy.SA	Fore foot	>5 cm	Marginal	Yes	No	No	No
12	M	29	EpiSA	Hind foot	<5 cm	Amputation	Yes	No	Yes	No
13	F	7	RhabdomyoSA[8]	Hind foot	>5 cm	Wide	Yes	Yes	No	No
14	M	17	Sy.SA	Hind foot	>5 cm	Wide	Yes	Yes	No	No
15	F	52	MFH[9]	Hind foot	<5 cm	Wide	Yes	Yes	No	No

1. Desmoplastic Fibrom
2. Epithelioid Sarcoma
3. Ewing Sarcoma
4. Fibro sarcoma
5. Synovial Sarcoma
6. Leiomyosarcoma
7. Malignant Melanoma
8. Rhabdomyosarcoma
9. Malignant Fibrom Histiyo cytoma

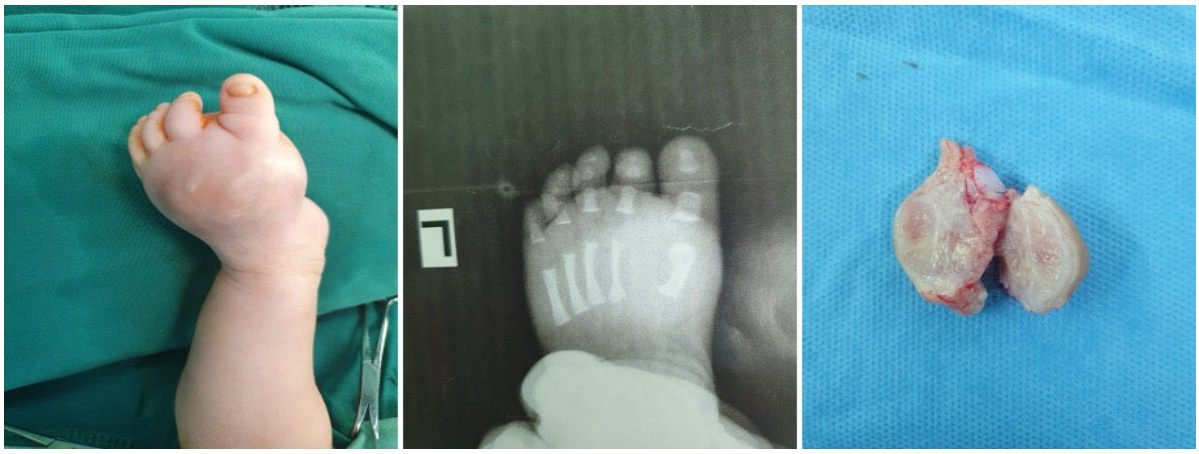

Figure 1: 2 years old boy with Epithelioid sarcoma of forefoot

The goal of surgical resection is to obtain wide margins and maintain a planti grade foot. Depending on the size and location of the tumor within the foot, these clinical goals may not be achieved practically, and amputation becomes necessary. Tumor size has been found in multiple studies to adversely affect outcomes, with tumors 5 cm or larger having poorer survival and recurrence outcomes. However, our result didn't reveal any significant effect of size on survivals. Because of the anatomical constraints of the foot, it may be difficult to achieve a wide margin without resorting to at least a partial amputation. The implementation of a radical surgical procedure in the distal region of the limb is often difficult due to a limited soft-tissue situation.

Limb-salvage surgery is preferable to amputation only if adequate margins and a durable, functional, and pain-free extremity can be achieved [1]. Approximately one fourth to one third of distal lower extremity sarcomas require some kind of amputation [13].

In our case series, there were just three cases with primary amputation; however, two other cases, one with marginal and the other with wide excisions, underwent amputation after tumor recurrence. Deep or subfascial localization is associated with a higher risk of local recurrence or distant metastasis when compared with superficial or epifascial localization [14]. The use of reconstructive surgery and adjuvant radiation since 1980s has been able to reduce the amputation rate to less than 20% [15]. The incidence of local recurrences under limb preservation therapy has decreased to 10–15% in recent years; this was 20% in our case series. A primary amputation must also be drawn early into consideration when satisfactory functional results cannot be expected from reconstructive techniques after extensive or disabling limb-salvage resections. In such cases, timely recovery and mobilization might be achieved earlier after primary amputation [3]. All the recurrences in our case series were from primary excision; however, two had received marginal excision.

Negative margins should be the goal of surgical therapy. Performance of the appropriate margins in soft-tissue sarcomas is often complicated by the extended growth of the tumor [3]. The results of this study support the use of wide surgical excision and limb salvage surgery when ever obtainable, which is similar to previous reports [16]. Operation type had no significant effect on overall survival in our case series. This is completely in agreement with previous studies [6, 17, 18]. Limb salvage surgery did not have an adverse effect on patient outcomes in regards to post-treatment complications and survival (disease-specific and overall).

The reconstruction of complex defects of the foot has experienced a steady improvement in recent decades [3]. Achievements in the therapy have been kept particularly for innovative surgical techniques and a better understanding of the specific tissue situation and functional requirements of the foot area. Although comparisons of the quality of life between limb salvage and amputation for sarcomas of the lower extremity show little difference [19], the presence of a soft-tissue sarcoma in foot is not an indication for amputation. Ozger et al. reported that they performed limb-salvage surgery in 88% of cases with an almost wide margin [20]. The rate in current study was 80% with acceptable overall survival (87%).

Both chemotherapy and radiotherapy have been shown to have a positive effect on survival [20]. Radiation therapy is often added to enhance local control of the disease. With this management, the local recurrence rate is reported to be below 10% [21] although we had 20% recurrence. Preoperative and postoperative chemotherapy is a standard treatment for soft-tissue sarcoma to increase survival in soft-tissue sarcomas [22]. When to use radiation therapy in conjunction with local surgical excision in the foot remains under debate. In a study by Talbert et al, this combination has been shown to reduce rates of recurrence [18]. Accordingly, postoperative radiotherapy in one of our patients with Ewing resulted in no recurrence. However, it was not clear whether radiation had provided a beneficial effect for those who underwent wide re-excision with negative margins. Since the number of patients in the current study

was relatively small, the lack of a statistically significant difference in local recurrence rates for radiated and nonradiated patients should not be interpreted with caution.

Tumor removal is often accompanied by major tissue defects. Furthermore, there might be an exposure of functional structures, such as bones, tendons, nerves, and blood vessels. The soft tissue coverage of the area is scant and subjected to high loads and repetitive shear stresses, and the bony and articular elements must provide durable support and flexibility and still withstand the stresses of weight bearing. For these reasons, limb-salvage surgery, although considered the treatment of choice for sarcomas in most anatomic locations, must be carefully weighed against other options [23]. The calcaneal fat pad and heel skin are probably the most important anatomical components of the weight-bearing foot. Except for one case, other fourteen cases of ours had primary closure. However, as a reconstructive option after tumor resection, local flaps represent a reliable tool and can cover a wide range of smaller defects. The case with DFSP received rotational flap. All of our patients were able to return to wearing normal shoes.

Thacker et al. reported that no factors including tumor grade, size (5 cm), site, planned vs. unplanned excisions, radiotherapy and amputation vs. limb salvage, had a significant impact on the local control of tumors [24]. Talbert et al reported that the size of the primary tumor correlated with total tumor-free survival, whereas no factors correlated with local control [18]. Our results agreed with the prior one. Although, small case series might not show a reliable statistical significance it was interesting that in the multivariate analysis of risk factors for local recurrence, covariates that emerged as an independent predictor were operation-type and/ the presence of metastasis at presentation. Our study focused exclusively on the presentation, treatments and outcomes of malignant soft-tissue tumors of the foot. By focusing solely on malignant soft-tissue tumors of the foot we hoped to better characterize the presentation, treatment and outcomes of this rare clinical entity.

Zeytoonjian et al. showed an overall death rate from all sarcomas of 26.6%, and from the foot [13]. The reasons for the improved survival in our series include the fact that small lesions in the foot are often noticed early because they interfere with function. A tumor which is small, noticed early, and in a distal part of the limb, which has a relatively limited blood supply, is less likely to metastasize and cause death [25].

Our study had its limitations. Because of the rare nature of this disease, the sample population is small. Moreover, the retrospective nature of the study limits the data analysis.

Conclusion

The goals of surgical treatment of malignant tumors in the distal lower extremity do not differ from those for any other part of the body; however, the unique anatomical and functional characteristics of the area require special consideration.

Given the improved survival of malignant tumors in this location, our treatment regimen would seem justified. Moreover, oncological outcomes should be interpreted in the light of the fact that this is a unique group of patients, some of whom with advanced disease refused amputation despite having been informed about increased oncological risks associated with limb salvage. The overall prognosis of the patients is unfavourable, and it is not at all certain whether an immediate radical amputation would improve the chances for survival.

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