

## **UT Medical Center Sarcoma Outcomes Study (1997-2007)**

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### **Introduction**

Pleomorphic, clear cell, and angio, are only a small representation of a broader class of tumors categorized as sarcoma. The goal of this manuscript is to review the nationally published literature on sarcoma and compare our outcomes at the University of Tennessee Medical Center (UTMC). These soft tissue and bony cancers have captivated clinicians for years. Each must be individually approached for a “best fit” treatment plan.

Jemal et al. estimated 10,660 new diagnoses of soft tissue sarcomas in 2009. These were distributed between men and women with a slight male predominance at 5,780 and 4,880, respectively. (1) The term sarcoma, derived from Greek, literally means “fleshy.” These tumors account for approximately 1% of all cancer diagnoses. (2) Sarcomas all have origins from mesenchymal tissue, or in other words, structures of the musculoskeletal system. This variability in tissue of origin accounts for the over 50 sarcoma subtypes. For example, a liposarcoma’s benign counterpart is a lipoma, both being derived from adipose tissue. Figure 1 demonstrates an abbreviated list of progenitor tissue, its benign tumor, and its malignant counter part.

One challenge in treating these tumors is the site of origin. Sarcomas are musculoskeletal in origin, and may occur anywhere in the body. The extremity is the most common site of presentation accounting for up to 60% of all sarcomas. Nineteen percent will present in the trunk, 13% in the retroperitoneum, and another 8% occur in the head and neck. The site of origin also carries different incidence of subtypes. For example, the most common sarcoma of the extremity is the pleomorphic sarcoma, whereas, liposarcomas have the highest incidence of retroperitoneal sarcomas. (2)

Sarcomas are the sixth most commonly diagnosed malignancy in children. Collectively these tumors account for about 7% of all pediatric cancers, with an annual incidence of 8-9/million children younger than age 19. (3)

Rhabdomyosarcoma is the most common pediatric sarcoma. This differs compared to adults where pleomorphic sarcoma and liposarcoma are the most common sarcoma subtypes accounting for up to 45% of diagnoses over all. (2) Other sarcomas more common to the pediatric population include osteogenic sarcoma and synovial sarcoma.

To emphasize the multidisciplinary approach to these rare tumors, we offer a case presentation. Surgery offers the best chance for cure, but due to the variable presentations of sarcoma, surgery, chemotherapy, and radiation may all be in the treatment armamentarium.

#### **Case Presentation**

BS had been experiencing right calf pain and swelling for several months. He had been seen by physicians in his community and the pain was attributed to a fall he had experienced and a Baker's cyst. Prior to evaluation at UTMC, BS had developed significantly increasing pain and right leg swelling. With pain persisting, he was evaluated with MRI at an outside facility. His outside working diagnosis was then hematoma and BS was subsequently referred to UT vascular surgery. CT angiogram was performed which demonstrated a large soft tissue mass in the popliteal fossa (the space behind the knee). There was an associated deep vein thrombosis secondary to mass effect, but no hematoma. Surgical oncology was consulted for further treatment and recommendation. After full history and physical exam, a core biopsy was performed at bedside. Pathology confirmed a "low" grade myxoid liposarcoma. Imaging revealed a 7.7 x 20 x 8.4 cm mass that compressed critical neurovascular structures and rested against bone. (Figure 2) Resection at this point would have resulted in positive margins, a high risk of limb or functional loss, and no improvement in overall survival.

BS was presented at our multidisciplinary tumor board. Staging studies revealed no evidence of metastatic disease and a neoadjuvant chemotherapeutic and radiation approach was taken. Our patient received 2 cycles of Adriamycin and Mesna followed by 5000 cGy of external beam radiation. Six weeks after completion of these therapies, staging studies showed some downsizing of the tumor and no evidence of metastatic disease.

Six months after diagnosis, complex surgical resection was performed. Plastic surgery was involved in the event to assist if the surgical defect could not be closed primarily. The tumor was excised with preservation of all neurovascular structures. (Figures 3-5)

At 15 months BS has no evidence of local or systemic recurrence. He experienced some minor wound breakdown postoperatively, but no major complication. BS has developed a contracture at the knee, but, he is ambulatory with a cane and stable. In all, six medical teams have contributed to BS's care: vascular surgery, surgical oncology, plastic surgery, medical oncology,

and radiation oncology. Ancillary services have included skilled oncology nurses and physical therapists.

### **Treatment**

As seen in our case example, many modalities may be used in the treatment of a sarcoma. Surgery is a mainstay of therapy and the only single modality that may result in cure. In all 50% of sarcomas will recur with the majority of patients succumbing to their disease after recurrence. Chemotherapy may be used in conjunction with other therapies or at the discovery of systemic metastasis, where as radiation may be used to treat local recurrence or in the adjuvant or neoadjuvant setting as was used in our patient BS.

### **Prognosis**

As stated above, roughly 50% of patients diagnosed with sarcoma will succumb to their disease. (4) In the past, radical amputations or debilitating surgeries were standard of care. As we have progressed in the treatment of these rare tumors, a multimodal limb sparing treatment has become the accepted treatment. Only 10% of patients with extremity sarcomas go on to receive amputation. Rosenberg et al demonstrated that the combination of surgery and radiation compared to amputation were similar in overall survival for patients with extremity sarcomas. (5) Factors influencing recurrence and survival include the stage at presentation, size and histological grade of the tumor, and the ability to resect with free margins.

## **Materials and Methods**

University of Tennessee Medical Center Cancer Institute's Tumor Registry was queried for all cases of soft tissue sarcoma compiled from 1997-2007. Patients seeking second opinion but not receiving any medical treatment, and bony sarcomas were excluded from review. All patients were staged clinically and pathologically according to the AJCC staging system. (6,7) UTMC outcomes are compared to the National Cancer Data Base (NCDB) Registry.

## **Results**

Sixty-four patients with soft tissue sarcoma were treated at UTMC from 1997 - 2007. Ages of patients treated in this time period ranged from 18 - 86 years of age with a median age of 59. (Figure 6) Sixty-six percent of patients treated at our institution were male, which is slightly higher than the national average of 54% male. The most commonly treated sarcoma subtype overall was pleomorphic sarcoma, followed by leiomyosarcoma, and non-subtyped sarcoma. Figure 7 demonstrates the seven most common subtypes treated in our series. Nationally, the most common subtypes are pleomorphic sarcoma (40%) followed by liposarcoma (25%). (8)

At our institution, the most common primary site was the extremity (47%) followed by trunkal sarcomas (45%). (Figure 8) This is noticeably disparate when to the literature where roughly 60% of sarcomas occur in the extremities, followed by 19% in the trunk, 13% in the retroperitoneum, and 8% in the head and neck. (4) If we examine the grade of sarcomas alone presenting at UTMC,

we see the most common histological grade was three of four (52%). Figure 9 depicts the range of tumor size distribution. While surgery remains the mainstay of treatment for sarcoma, a multimodal approach may be necessary. This may be in part due to stage at presentation. In our series there is a roughly equal distribution of stage at presentation. (Figure 10) Surgery was the only treatment modality in 41% of our patients. This was followed by 36% of patients who had a combination of surgery and radiation. Figure 11 demonstrates the variety of treatment modalities utilized in treating sarcomas at our institution from 1997 - 2007.

At our institution the overall median survival for all patients was 36 mo. (Range: 1-91 months). As would be expected, patients presenting with an earlier stage had improved prognosis compared to those presenting with advanced disease. Figure 12 demonstrates a survival rate of UTMC patients compared to National Cancer Data Base patients.

## **Discussion**

Although the etiology of sarcomas is generally unknown, a few contributing factors are recognized. These include exposure to ionizing radiation, various environmental and chemical exposures, or genetic syndromes such as Li Frumeni Syndrome or Neurofibromatosis. The difficulty in treating these tumors is inherent in the multiple subtypes and general rarity of soft tissue sarcomas. Our series encompasses 10 years, over which time 64 patients were treated. Nineteen

percent of these tumors were already metastasized at the time of treatment. In general, UTMC had a generally lower survival rate as compared to the National Cancer Registry. In all likelihood this is due to sampling error and selection bias. Our series of 64 patients is likely more subject to variation compared to the NCDB database numbers of 14,723. Also, the NCDB data included all sarcomas as compared to UTMC data which includes only soft tissue sarcomas. A primary difference in the population treated at UTMC is seen in the distribution of sarcoma locations. UTMC has a much higher distribution of trunkal and retroperitoneal sarcomas as compared to the national database. It is recognized that extremity sarcomas have an improved prognosis compared to the sites of other sarcomas. (9) This difference of locations can be attributed to be a referral bias. The prognosis with high grade tumors is worse, but in particular for the non-extremity sarcomas. Often complete resection is limited in the retroperitoneum and radiation delivery is more difficult due to injury of surrounding normal tissues. (10) Factors associated with a poorer prognosis include age greater than 60, tumors larger than 5 cm, and high grade histology. (11) Predictors of long term survival is resectability with clear margins. Factors predicting overall survival are tumor grade, ability to perform complete resection with free margins, tumor size, and tumor subtype.

## Conclusion

Sarcomas are heterogeneous cancers that require individualized treatment plans and close follow-up. These needs are best served in a multi-specialty treatment plan and overseen by a multidisciplinary tumor board.

## Bibliography

- 1) A Jemal, R Siegel, E Ward, et al: Cancer Statistics 2009. CA Cancer J Clin 2009;59:225-249.
- 2) SW Weiss, JR Goldblum: General Considerations, in Enzinger and Weiss 's Soft Tissue Tumors, ed 5. St. Louis. Mosby – Year Book, Inc. 2008, pp 1-14.
- 3) LL Robinson: General principles of epidemiology of childhood cancer, in Pizzo PA, Poplack DG (Eds): Principles and practice of pediatric oncology, ed 2. Philadelphia, JB Lipincott Co, 1993
- 4) Enzinger FM, Weiss SW: Clinical evaluation and treatment of soft tissue tumors, 3<sup>rd</sup> ed. St. Louis: CV Mosby, 1995, pp 1-16.
- 5) Rosenberg SA, Tepper J, Glatstein E, et al: The treatment of soft-tissue sarcomas of the extremities: prospective randomized evaluations of (1) limb-sparing surgery plus radiation therapy compared with amputation and (2) the role of adjuvant chemotherapy. Ann Surg 196:305, 1982.

- 6) Greene, FL, Page DL, Fleming ID, et al: AJCC Cancer Staging Handbook  
From the AJCC Cancer Staging Manual, Sixth Edition. Philadelphia:  
Lippincott Raven Publishers, 2002, pp 221-228
- 7) Fleming ID, Cooper JS, Hensen DE, et al: AJCC Cancer Staging Handbook  
From the AJCC Cancer Staging Manual, Sixth Edition. Philadelphia:  
Lippincott Raven Publishers, 1998, pp 139-146
- 8) Gaynor JJ, Tan CC, Casper ES, et al: Refinement of clinicopathologic  
staging for localized soft tissue sarcoma of the extremity: a study of 423  
adults. *J Clin Oncol* 10 (8): 1317-29, 1992.
- 9) Jaques DP, Coit DG, Hadju si, et al: Management of primary and  
recurrent soft-tissue sarcoma of the retroperitoneum. *Ann Surg* 212:51,  
1990
- 10) Lewis JJ, Leung D, Woodruff JM, et al: Retroperitoneal soft-tissue  
sarcoma: analysis of 500 patients treated and followed at a single  
institution. *Ann Surg* 228 (3): 355-65, 1998
- 11) Vraa S, Keller J, Nielson OS et al: Prognostic factors in soft tissue  
sarcomas: the Aarhus experience. *Eur J Cancer* 34 (12): 1876-82, 1998.