

Soft Tissue Sarcoma at a Dialysis Access Site in a Transplant Recipient

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Abstract

Soft tissue sarcomas typically present as soft, painless masses on an extremity. Here, we present a patient with metastatic soft tissue sarcomas at his dialysis access site. This association with dialysis access has not been documented previously.

A 62-year-old man presented with a nonhealing wound on his left upper extremity after excision of a pseudoaneurysmal arteriovenous fistula. The patient had received a second kidney transplant that was functioning well. Immunosuppression included tacrolimus, mycophenolate mofetil, and prednisone. He was induced with thymoglobulin twice.

A biopsy was performed showing a high-grade pleomorphic sarcoma. A magnetic resonance image of his left upper extremity showed an 11 × 5.5 × 3 cm mass abutting the biceps and brachialis muscles. Also, we discovered several lesions in the axilla and the left side of the neck, which were suspicious for metastases. A positron emission tomography-computed tomography scan confirmed a left upper extremity soft tissue mass, with marked fluorodeoxyglucose uptake, in abnormally enlarged axillary, and supraclavicular lymph nodes of the left thorax, consistent with metastases. The patient underwent chemotherapy and radiation therapy.

Soft tissue sarcomas are rare. A high index of suspicion is needed to make a diagnosis. This is the first reported case of a soft tissue sarcoma discovered at a dialysis access site. As with all malignancies, early diagnosis is key to patient

survival. Thorough physical examinations and increased vigilance by physicians caring for immunosuppressed patients is invaluable.

Key words: Cancer, Immunosuppression, Metastatic, Kidney transplant, Wound

Introduction

Cancer is now the third leading cause of death in kidney transplant recipients.¹ Recent evidence suggests that in the next 2 decades, it will surpass cardiovascular disease as the most-common cause of death.² van de Wetering demonstrated a shorter median for patient survival after the diagnosis of cancer (2.1 vs 8.3 y; $P < .001$).³

Solid organ transplant recipients have elevated cancer risk owing to immunosuppression and oncogenic viral infections. Among kidney recipients, kidney cancer risk was elevated and bimodal in onset time. This increased risk of cancer was confirmed by a large Canadian study as well; however, in this study, sarcoma was not mentioned.⁴ The incidence of malignancy has been estimated at 20% after 20 years of chronic immunosuppression.⁵ Soft tissue sarcomas (STS) are rare neoplasms comprising less than 1% of all adult malignancies. In the United States, in 2007, there were approximately 9220 new cases. Up to one-third of these tumors occur on the lower extremities, while 14% occur on the upper extremities.⁶

To the examiner, an STS typically presents as a painless mass that may not appear potentially malignant. Occasionally, the mass is excised before any preoperative work-up, and it is not until the pathology returns that a diagnosis of sarcoma is made. Unfortunately, sarcomas are highly malignant and improper management can prove devastating.

The majority of STS are localized at the time of presentation.⁷ Of the 10% of patients who do have

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metastatic disease, the most-common sites of metastases are the lung, followed by lymph nodes and bone.^{7,8} Lymph node metastases are rare (3% of cases) and generally seen in patients with epithelioid sarcomas (up to 15%).⁹

We present a patient with an STS at his previous dialysis access site that had metastasized to regional lymph nodes at the time of presentation. The patient was on maintenance immunosuppression for a functioning kidney allograft. The purpose of this case report is to discuss diagnosing and managing an STS in the transplant patient and treating the metastatic disease.

Case Report

The patient is a 62-year-old male smoker who presented with a nonhealing wound on his left upper extremity after excision of an arteriovenous fistula (Figure 1). A review of his medical history did not reveal any concomitant viral infection including human immunodeficiency virus. His family history was negative for any malignancy. The results of the patient's purified protein derivative test and chest radiograph were negative and clinically, there was no evidence of *Mycobacterium tuberculosis* infection. At the time of presentation with a nonhealing wound, the patient had a functioning kidney graft. His maintenance immunotherapy regimen was prednisone, tacrolimus, and mycophenolate mofetil.

After a failed kidney transplant 2 years earlier, he had an arteriovenous fistula placed for hemodialysis. The patient subsequently developed an infected pseudoaneurysm in this fistula and it was excised. In the interval between developing the infected pseudoaneurysm and creation of the fistula, a second kidney transplant was performed that was functioning well. He received thymoglobulin induction for both transplants.

Figure 1. Left Arm Lesion at 2 Months



The patient returned to the hospital 6 months later with fever and leukocytosis. There was an abnormal scab overlying his previous fistula excision site, and a biopsy was taken. Pathology showed a high-grade pleomorphic sarcoma (see Figures 2-5).

A magnetic resonance image of his left upper extremity showed an 11 × 5.5 × 3 cm mass abutting the biceps and brachialis muscles (Figure 6). Several enlarged and enhancing lesions in the axilla and the left side of the neck were suspicious for metastases.

A positron emission tomography-computed tomography scan was performed that confirmed a left upper extremity soft tissue mass with marked fluorodeoxyglucose uptake and strongly positive fluorodeoxyglucose uptake within abnormally enlarged axillary and supraclavicular lymph nodes on the left side of the thorax. Additional bilateral small lung nodules, less than 5 mm and too small for resolution for fluorodeoxyglucose activity, were noted (Figures 7 and 8). His treatment plan included local external beam radiation (5000 cGy) to the left

Figure 2. H&E Stain at ×60

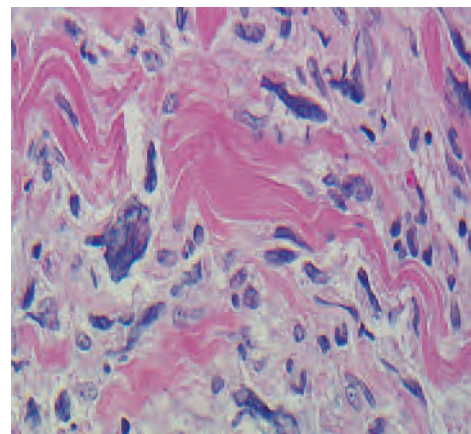


Figure 3. H&E Stain with Pleomorphic Cells

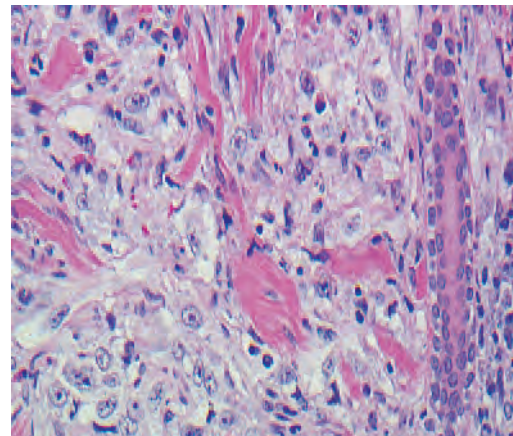
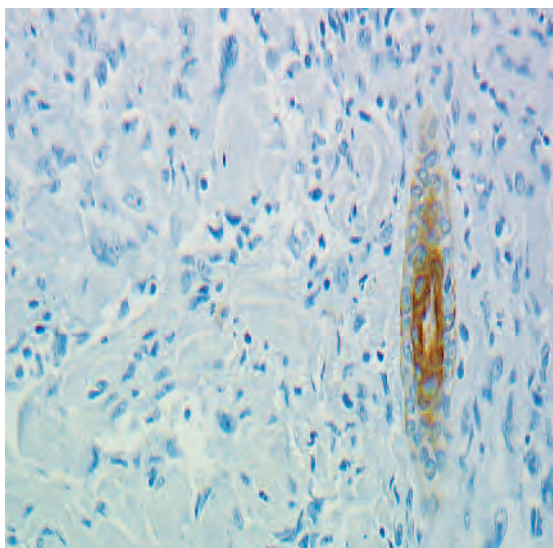
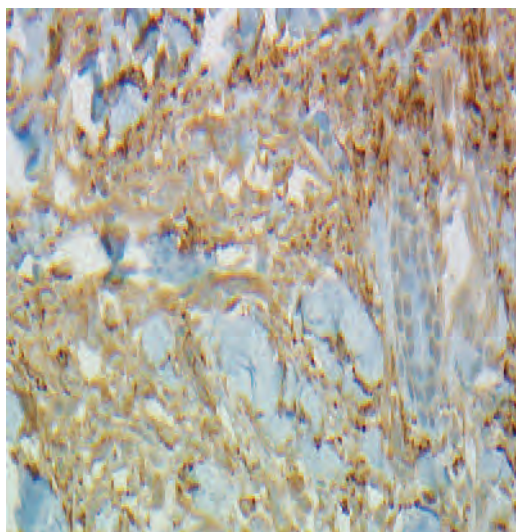
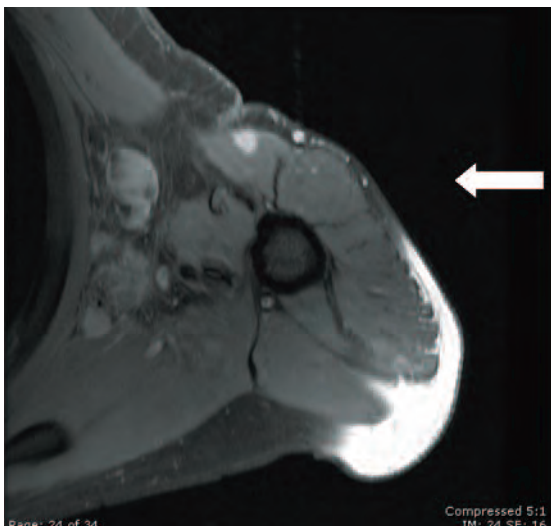


Figure 4. Residual Eccrine Duct in the Lesion**Figure 5.** Pleomorphic Cells Stained by Fibrohistiocytic Marker**Figure 6.** MRI of Left Arm Mass

upper extremity as well as the axilla along with infusional doxorubicin.

Discussion

Soft tissue sarcomas are rare. They account for approximately 7% of new cancer cases in children and 1% of new cases in adults.¹⁰ Forty-three percent of STS cases occur on the extremities, with the lower extremity being the most-common site.¹¹ The most-significant risk factor identified for developing an STS is exposure to external beam radiation. Historically, patients who receive radiation treatment for cancers of the breast, testes, retina, ovary, or the lymphatic system are at an increased risk of developing an STS.¹² Typically, the interval between radiation exposure and diagnosing an STS is 10 years. The disease-specific survival is worse in patients with radiation-associated STS when compared with sporadic STS.¹³

Exposure to certain environmental toxins also can predispose a patient to developing an STS. These include vinyl chloride, arsenic, herbicides, and wood preservatives that contain chlorophenols.¹² Genetic associations exist between STS and Li-Fraumeni syndrome, hereditary leiomyomatosis, renal cell carcinoma syndrome, and hereditary retinoblastoma have been documented.¹⁴ In this patient, there was no family history of cancer.

Immunosuppression has been identified as a risk factor for a specific type of STS—Kaposi sarcoma. Typically, this is associated with patients infected with human immunodeficiency virus. There is also a well-established connection between transplants and Kaposi sarcoma.¹⁴ Unlike other sarcomas, there is a clear connection with concomitant infection with human herpes virus 8, which must occur to develop Kaposi sarcoma.

Another possible manifestation of an opportunistic infection that could present in an immunocompromised patient is mycobacterial pseudotumor. This rare manifestation of a mycobacterium *avium-intracellulare* infection presents as spindle cell lesions in the skin, soft tissue, and lymph nodes, and could potentially be confused with an STS.¹⁵

The incidence of all cancers (except breast and prostate) are increased in patients who have received solid organ transplants.¹⁶ Immunosuppression alone increases the chances of a patient developing a cancer by 3-fold.¹⁷ In one large study, 175 732 transplants

Figure 7. A PET-CT Scan with Marked Fluorodeoxyglucose Uptake in the Left Arm Mass

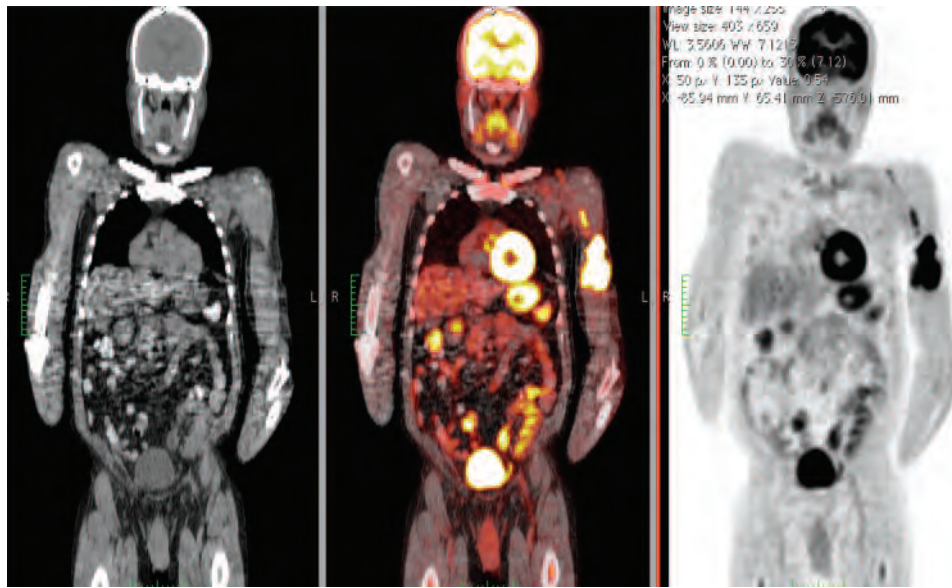
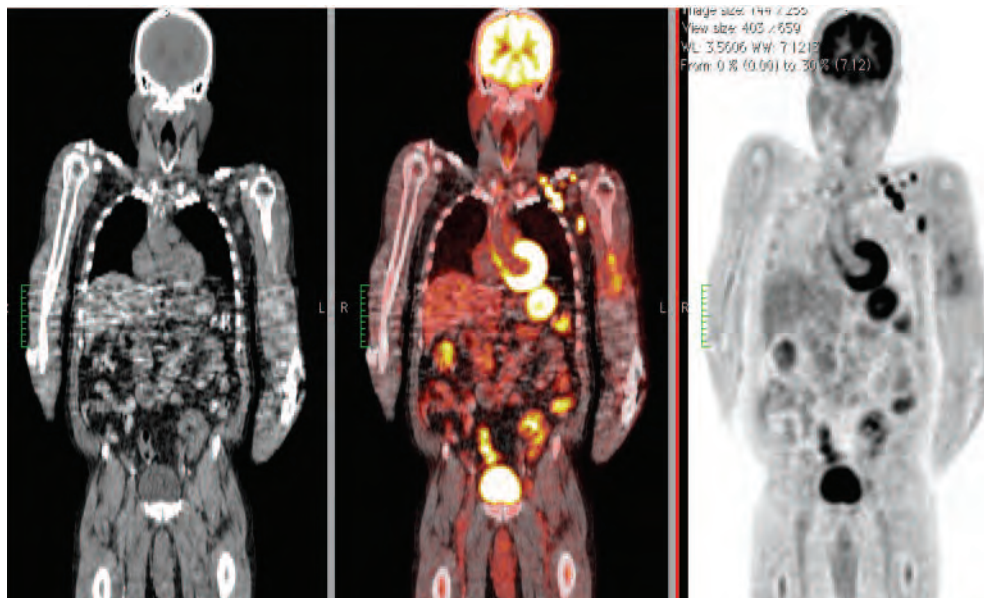


Figure 8. A PET-CT Scan with Positive Axillary and Supraclavicular Lymph Nodes



were analyzed. Transplant recipients were linked to 10 656 malignancy diagnoses during follow-up, corresponding to an overall doubling of cancer risk compared with the general population. Their study cohort was composed of kidney, liver, heart, and lung recipients.¹⁸ It has been hypothesized that the cause for this increase in malignancy is due to impairment of the immune system's tumor surveillance as a result of immunosuppression.

In the case of this patient, there was no history of previous radiation or environmental factors that could predispose him to an STS. The patient did not have any known genetic mutation or tumor

syndrome. The sarcoma he developed was not Kaposi sarcoma; and thus, has no association with human herpes virus 8. Although he was a smoker and tobacco abuse is associated with developing many different cancers; STS, per se, is not directly associated with smoking. The tumor pathology was consistent with an STS (and not the spindle cell lesions of mycobacterial pseudotumor), and the patient did not manifest other symptoms of this infection.

The patient was on maintenance immunosuppression at the time he presented with the STS and therefore, was at increased risk of developing a

malignancy, although this malignancy has not been previously associated with a transplant or immunosuppression. Malignancies including posttransplant lymphoproliferative disorder and other lymphomas, as well as solid tumors, have been reported after thymoglobulin administration combined with multiple immunosuppressive agents. Recipients of older-aged donations (older than 65 y), with exposure to calcineurin inhibitors and previous use of thymoglobulin, are at greater risk.¹⁹

This patient's presentation of a high-grade sarcoma was atypical. It is common for a surgeon to excise a mass found by a patient on self-examination only to find out after the pathology report returns that the mass was malignant. However, in this case, there was never an appreciable mass noted by the physician or the patient, and the STS was only discovered after the patient had returned to the hospital several months later with what appeared to be a nonhealing wound secondary to a wound infection. At this time, the mass was biopsied (because its nonhealing nature was suspicious for cancer). This is the first report of a sarcoma arising at a dialysis access site.

Unplanned partial excision of an STS does not affect long-term outcome if the patient undergoes a wide margin free excision of the tumor.²⁰ If a mass is excised without clean margins initially, it is still possible to return to the original excision site to achieve clean margins.

Atalay and associates suggest that it may be feasible to treat patients with lymph node metastases on presentation with wide local excision and radical lymph node dissection to achieve complete tumor resection.²¹ Unfortunately, this patient presented with axillary and supraclavicular lymph node metastases, and wide local excision of the primary tumor was not advisable.

The patient's chemotherapy and radiation were delayed significantly because of social issues. This allowed the tumor to grow locally as well (Figure 6). The lung metastasis on the computed tomography scan of the chest and on positron emission tomography-computed tomography made this case of an STS stage IV disease, based on the American Joint Committee on Cancer staging system (Figure 9). If possible, primary treatment of a pulmonary metastasis from an STS is primary resection. The reported median survival for patients who do not undergo resection has been reported to

be 15 months; this increases to 33 months after primary resection.²² In this patient's case, the lesions were multiple and bilateral and not amenable to resection, giving him a poor prognosis.

To investigate the history of sarcoma in other institutions, a UNOS query was performed²³ that revealed 19 patients who had a sarcoma after a kidney transplant between January 1, 2000 and September 30, 2011 (Table 1). There were 9 whites, 6 African Americans, 3 Latin Americans, and 1 Asian. There were 14 men (age range, 29-75 y). The primary causes of death included 3 cases of Kaposi sarcoma, 3 cases of Ewing sarcoma, 2 cases of leiomyosarcoma, and 11 sarcoma cases that were not defined further. Fifteen of the 19 patients were on mycophenolate maintenance. Thirteen of the 19 patients were

Figure 9. CT of the Chest with Axillary and Supraclavicular Lymphadenopathy on the Left

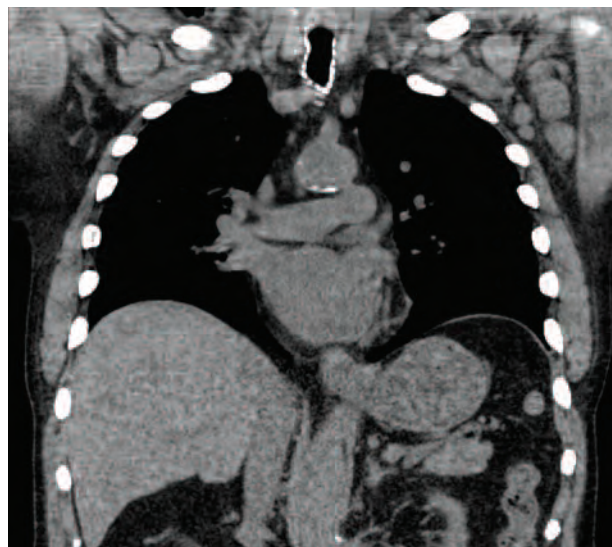


Table 1. Information of sarcoma patients (2000-2011) received from UNOS (n=19)

Age (y), median (range)	58 (29-75)
Sex	
Male	15
Female	4
Race	
White	9
African American	6
Latin American	3
Asian	1
Primary cause of death	
Kaposi sarcoma	3
Ewing sarcoma	3
Leiomyosarcoma	2
Not delineated sarcomas	11
Immunosuppressive maintenance	
Steroid	13
Mycophenolate	15
Induced with thymoglobulin	8

maintained on steroids. Eight of the 19 patients had been induced with thymoglobulin. None of the patients reported soft tissue sarcoma in a chronic wound or dialysis access site.

Conclusions

Soft tissue sarcomas are rare and can be missed easily by the clinician. A high index of suspicion is required for diagnosis. A thorough search of the literature was done using PubMed and Medscape databases looking for similar case presentations. Using the terms "sarcoma and transplantation," "cancer and dialysis access," "sarcoma and dialysis access," and "sarcoma and renal failure," no similar case could be found in the literature. This is the first reported case of an STS discovered at a dialysis access site.

As with all malignancies, early diagnosis is key to patient survival. This can prove difficult in an STS if no mass is noted on examination. Thorough physical examinations and increased vigilance by all physicians caring for immunosuppressed patients is invaluable for patient outcomes.

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