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CASE REPORT | LIVER

Synovial Cell Sarcoma in an Adolescent Liver Transplant Recipient

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ABSTRACT

Solid organ transplant recipients are at increased risk of malignancy. Pediatric transplant recipients particularly have a potentially higher risk given the young age of immunosuppression initiation. Posttransplant malignancies are the main cause of death in 5%–16% of liver transplantation patients. The frequency of de novo malignancies in pediatric liver transplant recipients has been reported to be 13%. Synovial sarcoma is a malignant mesenchymal neoplasm that has not been previously reported after liver transplantation. We report the case of an adolescent liver transplant recipient who was diagnosed with synovial sarcoma 14 years after liver transplantation.

INTRODUCTION

Malignancy is a well-recognized complication in solid organ transplant recipients, with a 2–4 fold increase in risk.[1] This risk is due to exposure to chronic, lifelong immunosuppression.[1,2] Pediatric transplant recipients have a higher risk of malignancy given the young age of immunosuppression initiation and may often require re-transplantation which results in additional immunosuppressive therapy.[3] Pediatric solid organ transplant recipients can have 30 times greater cancer incidence compared with the general population.[3] Posttransplant malignancies are the cause of death in 5%–16% of liver transplantation patients. De novo malignancy frequency in pediatric liver transplant (LTX) recipients is 13%, with posttransplant lymphoproliferative disease most frequently diagnosed (53%) and mean time to diagnosis of 35 months.[4] Synovial sarcoma is a malignant mesenchymal neoplasm that occurs predominantly in older children/young adults and can occur at almost any anatomic site.[5] It accounts for 5%–10% of all childhood/adult soft-tissue sarcomas.[5,6] Although soft-tissue sarcomas have previously been described in the post-LTX population, synovial sarcoma has not been previously reported after LTX.[1,3] We report the first case of an adolescent male diagnosed with synovial sarcoma 14 years after LTX.

CASE REPORT

A 15-year-old white male with a history of biliary atresia, polysplenia syndrome, and primary ciliary dyskinesia, who underwent LTX at 1 year of age, presented with intermittent right ankle pain and tenderness for 3 years. He was seen by multiple providers, had unrevealing ankle radiographs, and was treated with physical therapy on at least 2 occasions. Due to the persistence of the pain, a noncontrast magnetic resonance imaging (MRI) was performed, which demonstrated what was thought to represent a benign ganglion cyst. After 2 attempts at the aspiration of the ganglion cyst which were unsuccessful, he was referred to a local orthopedic surgeon. He underwent excision of the ganglion cyst measuring $2.7 \times 2 \times 1.2$ cm. Histopathologic examination revealed a spindle cell neoplasm with positive immunohistochemical staining for transducin-like enhancer of split 1 (TLE1), a protein specific to synovial sarcoma (Figure 1). This was confirmed by the presence of the chromosomal translocation t(X;18)(p11;q11) (Figure 2). Several margins were positive for the tumor. The patient was referred to Pediatric Orthopedic Oncology at our institution for further management. A chest computed tomography scan was negative for pulmonary metastasis, and therefore, management required only

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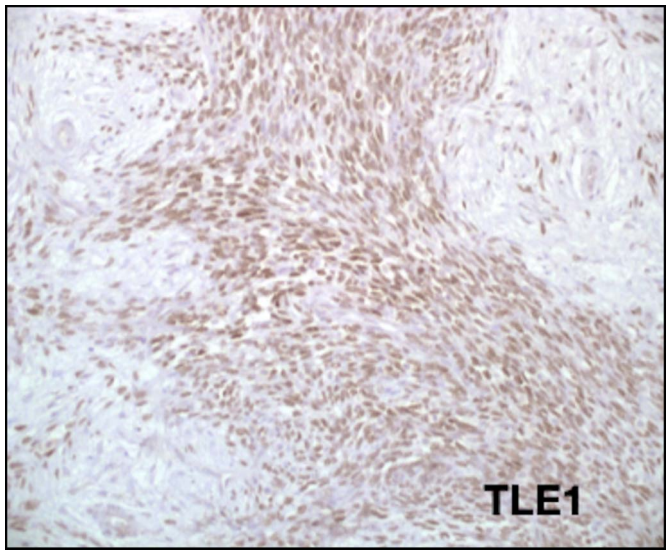

Figure 1. Positive immunohistochemical staining for transducin-like enhancer of split 1 (TLE1) of the tumor.

local control measures. After discussion of this case at the Solid Tumor Board, 2 therapeutic options were offered: limb salvage with tumor bed resection, free-flap coverage, and whole-foot radiation, or below the knee amputation. Given that whole-foot radiation would likely result in irreversible nerve damage and paralysis, the patient and his family decided to proceed with amputation. Pathology specimens from the amputated limb did not reveal residual tumor, and right inguinal sentinel lymph node biopsies were negative for metastasis.

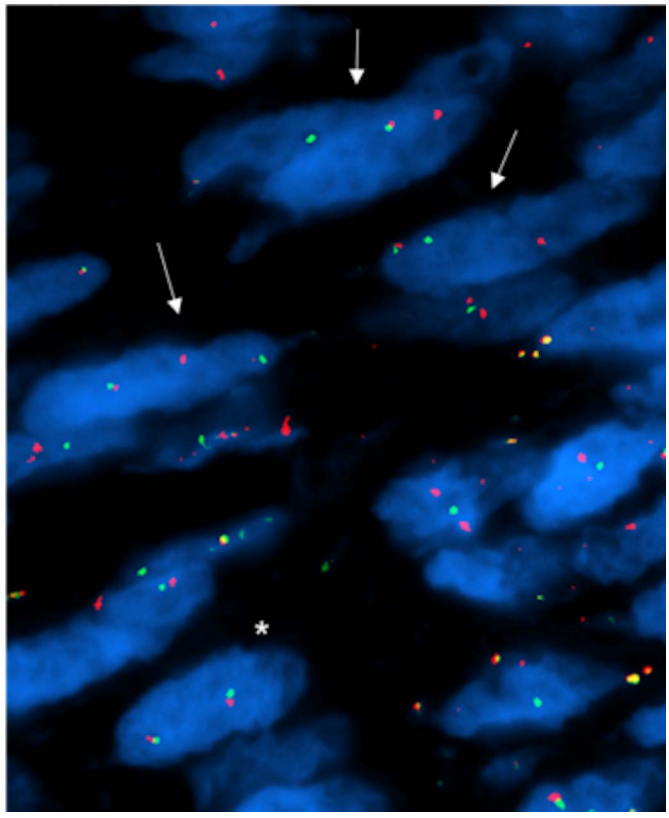

Figure 2. Interphase fluorescent in situ hybridization using a dual color showing a break apart translocation assay for the SS18 locus at 18q11, where the presence of an SS18 rearrangement is noted with a split signal pattern (red split from green—arrows). The asterisk indicates a normal signal pattern of 2 fusions in the lower left of the panel.

At the time of amputation, the patient also underwent a liver biopsy to reassess for immune tolerance. A liver biopsy performed 1 year before was normal. In the first 3 years after LTX, he was weaned off steroids by 7 months and his tacrolimus troughs initially ranged from 6 to 12 ng/mL, followed by a downtrend to 2–7 ng/mL during his third-year post-LTX. Afterward, he was on very minimal immunosuppression, with tacrolimus troughs ranging from undetectable to 3 ng/mL on a dose of 0.5 mg twice daily. His posttransplant course had been unremarkable without any episodes of rejection and only an episode of cholangitis 3 years post-LTX. His liver biopsy showed minimal periportal lymphocytes (within normal range) and no fibrosis. He was taken off tacrolimus, and he remains immunotolerant with normal liver enzymes.

DISCUSSION

Patients receiving solid organ transplants at a young age are at increased risk of malignancy, which is related to chronic immunosuppression in immune-naive patients at risk of oncogenic viruses.[3] A recent cohort study reported a 10-fold risk of cancer in pediatric LTX recipients compared with the general population, with an absolute cancer risk of 3–7 cases per 100 patients during a 10-year follow-up, with a cumulative incidence of 2% at 10 years posttransplant and 22% at 25 years posttransplant.[7] Pediatric patients most commonly had non-Hodgkin's lymphoma, and only one case of soft-tissue malignancy was described.[7] Another study reported a case of liver sarcoma in a pediatric LTX recipient.[4]

Our patient is the first described case in the literature of synovial sarcoma occurring in solid organ transplantation. Synovial sarcoma is the most common non-rhabdomyosarcoma soft-tissue sarcoma in childhood and adolescence. Although 30% occur in patients younger than 20 years, it is rare below the age of 10 years.[5] There is a slight male predilection. Up to 70% of cases present in the extremities (lower > upper), and it most commonly metastasizes to the lungs.[8] This tumor is slow growing and presents within deep soft tissues, and in more than 50% of cases, it is associated with pain/tenderness. Symptoms can last from a few years to as many as 20 years.[5] Whereas most lesions tend to be greater than 5 cm in diameter, distally located lesions tend to be smaller, which can be confused with benign pathologies, as in the case presented here.[5] Synovial sarcoma is considered a high-grade, aggressive sarcoma, with 5- and 10-year survival rates of approximately 60% and 50%, respectively.[5] Metastatic disease is more common in adults (up to 50%).[9] Risk stratification based on tumor characteristics puts patients into low-risk groups (age <25 years, tumor size <5 cm, and no histologic evidence of poorly differentiated tumor) with 88%

disease-free survival and high-risk groups (age ≥25 years, tumor size ≥5 cm, and poorly differentiated tumor) with 18% disease-free survival.[10]

Our patient presented with 3 years of symptoms, tumor location in the lower extremity, a lesion that was <5 cm, and no lung metastases, consistent with low-risk stratification. It is unclear whether the low-dose chronic immunosuppression post-LTX led to impairment in immune-mediated tumor surveillance. However, because the patient had normal liver tests for over 10 years and normal liver histology, immune tolerance of the liver allograft was likely, and he was safely weaned off all immunosuppression. The original MRI performed without contrast led to the erroneous description of an ankle cyst early on. In LTX recipients, musculoskeletal abnormalities such as pain or soft-tissue masses should warrant heightened surveillance. Practitioners should have a low threshold to pursue further imaging, such as MRI with contrast, as well as early referral to a pediatric orthopedic oncologist to exclude potential neoplasms.

DISCLOSURES

Author contributions: C. Jaramillo contributed to conception and design, acquisition, and analysis and interpretation of data; drafted the manuscript; critically revised the manuscript for important intellectual content; and gave final approval. A. Gilani contributed to acquisition editing of images/figures included in the manuscript as well as conception and design and analysis and interpretation of data, critically revised the manuscript for important intellectual content, and gave final approval. M. Haag contributed to acquisition editing of images/figures included in the manuscript, critically revised the manuscript for important intellectual content, and gave final approval. N. Donaldson contributed to analysis and interpretation of data, critically revised the manuscript for important intellectual content, and gave final approval. C. Mack contributed to conception and design and analysis and interpretation of data, critically revised the manuscript for important intellectual content, and gave final approval. C. Jaramillo is the article guarantor.

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