Isolated Muscular NK/T Cell Lymphoma: A Rare Presentation of Post-Transplant Lymphoproliferative Disorders

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Abstract

Posttransplant lymphoproliferative disorders (PTLDs) represent a spectrum of malignancies occurring in transplant recipients under immunosuppression, often linked with Epstein–Barr Virus infection. PTLD has a varied presentation, and isolated muscular involvement is infrequent. Here, we present the case of a 47-year-old female renal transplant recipient presenting with acute left knee joint swelling, initially suggestive of an infective or inflammatory etiology. Biopsy revealed high-grade non-Hodgkin lymphoma of natural killer/T-cell lymphoma. F-18 Fluorodeoxyglucose positron emission tomography–computed tomography scan revealed metabolically active soft tissue mass lesions isolated to thigh muscles. The patient was on a modified chemotherapy regimen tailored to accommodate renal function. This case underscores the necessity for heightened vigilance in diagnosing PTLD, particularly considering its atypical presentations.

Keywords: *Immunosuppression, muscular lymphoma, natural killer/T-cell lymphoma, non-Hodgkin lymphoma, posttransplant lymphoproliferative disorders*

Introduction

Posttransplant lymphoproliferative disorders (PTLD) are a spectrum of benign to potential life-threatening malignancies arising in transplant recipients under immunosuppression. They are often associated with Epstein–Barr Virus (EBV) infection.[1] The incidence of non-Hodgkin lymphoma (NHL) subset is substantially higher than in the general population, particularly within a year of transplantation (early PTLD). Late PTLDs (>1 year) are often EBV seronegative.[2] The highest incidence is seen in small intestine transplant recipients (up to 32%). Meanwhile, the pancreas, heart, lung, and liver recipients are at intermediate risk (3%–12%), with the lowest incidence in renal transplant recipients (1%–2%). The early PTLD is usually polymorphic, diffuse large B cell or other B cell lymphoma. Burkitt's lymphoma is more common in late-onset PTLD.[3] Histology includes early lesions, monomorphic PTLD, polymorphic PTLD, and classic Hodgkin lymphoma.[4] The treatment includes immunosuppression reduction, resection, radiotherapy, and rituximab with or without chemotherapy.[5]

Case Report

A 34-year-old female had renal failure with contrast-induced nephropathy. She received a renal allograft from her cytomegalovirus seropositive father in 2011. She was on maintenance immunosuppressive therapy (prednisolone, tacrolimus, and azathioprine) for 13 years. She presented with a progressive left knee pain and swelling associated with fever, night sweats, chills, and weight loss for 4 months. She was febrile with left knee joint swelling, edema, warmth, and restricted joint movements. A hematological workup revealed anemia (hemoglobin: 8.4 g/dL) and leukocytosis - 24,000/mm^3, with neutrophilia (95% neutrophils). Magnetic resonance imaging (MRI) of the left knee revealed synovial thickening and inflammation along periarticular soft tissue. Synovial fluid analysis from knee effusion showed leukocytosis with neutrophil predominance (total leukocyte count 20,000/mm^3 with 90% neutrophils). The patient was started on antibiotics without any clinical response. Synovial biopsy comprised pleomorphic cells with bizarrely shaped nuclei and irregular nuclear contours. A high nucleocytoplasmic ratio and scant cytoplasm were noted. The tumor cells were positive for vimentin,

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LCA, CD3, and MUM-1, weakly positive for CD56 with a Ki67 index >80%. They were negative for CD20, and bcl2 confirmed natural killer/T-cell lymphoma (NKTL). F-18 Fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) was done for pretreatment staging. The scan demonstrated metabolically active soft tissue mass lesions (SUV_{max}: 37.4) involving the distal 1/3rd of the anterior compartment of the left thigh, proximal 1/3rd of tibialis posterior, soleus, and peroneus longus muscles. There was no evidence of any other metabolically active lesion in the body, thus confirming isolated disease [Figure 1]. The patient received three cycles of modified cyclophosphamide, vincristine, and prednisone regimen, meticulously tailored to accommodate the patient's renal function, with etoposide capped at 50 mg.

Discussion

PTLD is a heterogeneous disease of benign and malignant entities. The EBV-specific cytotoxic T-cell response is suppressed in transplant recipients on immunosuppression. EBV infection occurs from the latent viral reactivation or primary EBV infection in EBV-seronegative patients receiving an EBV-seropositive donor organ. It results in unchecked EBV-infected B cell growth and, subsequently, PTLD. The incidence of PTLD is higher in pediatric patients.[6] Risk factors include organ transplants, T-cell-depleting agents for induction, and pretransplant immunosuppression. Clinical manifestations include fever, weight loss, lymphadenopathy, central nervous system, gastrointestinal, and pulmonary features. The most common sites are lymph nodes, liver, lung, kidney, bone marrow, gastrointestinal tract, spleen, and central nervous system.[7] FDG PET/CT has performed excellently in managing the PTLD. In a meta-analysis (five studies, 1276 patients), the pooled sensitivity and specificity were found to be 0.90 (95% confidence interval [CI]: 0.85–0.93) and 0.90 (95% CI: 0.86–0.93). The diagnostic odds ratio was 83 (95% CI: 46–149), with receiver operating characteristic (ROC) showing an area uder the ROC curve of 0.96 (95% CI: 0.94–0.97).[8]

NKTL is a rare EBV-associated PTLD, comprising <2% of all T-cell lymphomas. It primarily affects the nose and upper aerodigestive tract in 80% of cases, with less frequently involving the skin, gastrointestinal tract, testis, and salivary gland. Rarely, it presents with a leukemic phase.[9] Muscular involvement is seldom reported.[10] Localized NKTL is curable; however, advanced stages carry a poor prognosis.[11] The cornerstone of PTLD is restoring the host's immunity. Treatment for advanced NKTL involves a combination of radiation therapy and multidrug chemotherapy.[12] The 5-year survival rate is only 30% for high-grade lymphomas.[13]

NKTL with musculoskeletal symptoms and isolated muscular involvement in postrenal transplant PTLD is a rare clinical scenario. The lesion simulated an inflammatory/infective pathology during clinical assessment and MRI. NK/T cell is a rare subtype with a poor prognosis. This case shows the importance of a multidisciplinary team approach, vigilant long-term clinical observation, and individualized management in this vulnerable patient population.

Conclusion

We report a rare case of PTLD presenting as isolated muscular NK/T-cell NHL occurring more than a decade after renal transplantation. The clinical and laboratory findings suggested an acute infection or inflammatory pathophysiology. However, subsequent histopathological examination and F-18 FDG PET/CT imaging confirmed the malignancy and delineated its extent. The aggressive

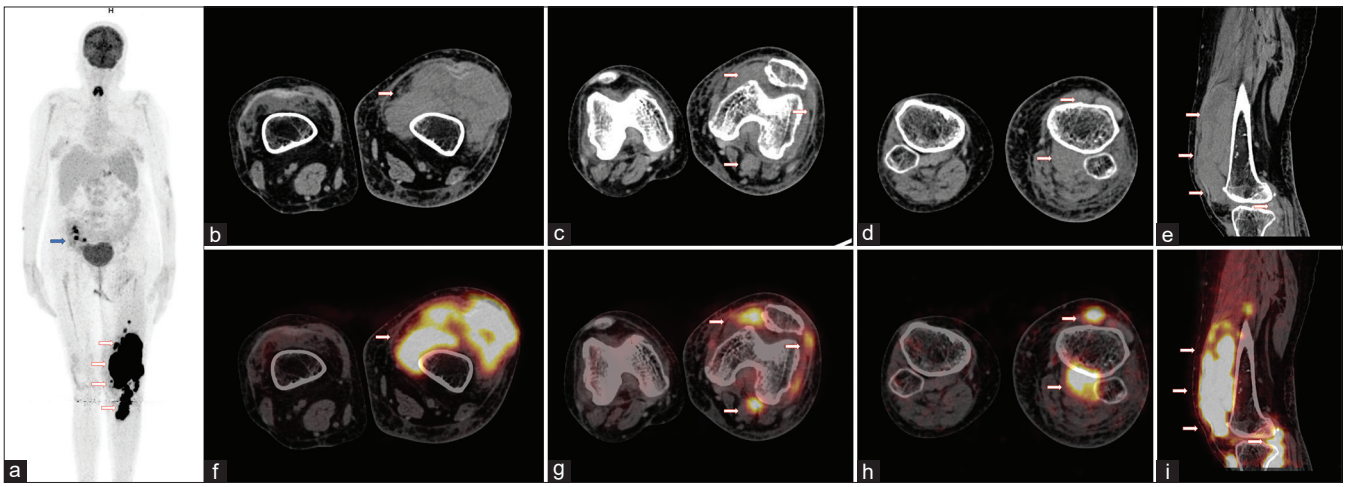

Figure 1: (a) Maximum intensity projection of F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) shows a large FDG-avid lesion in the left lower limb (white arrows). A note is made on the transplanted kidney in the right iliac fossa (blue arrow). Axial CT image (b-d) and corresponding fused FDG PET/CT images (f-h) at the level of the lower thigh, knee joint, and upper leg reveal a large FDG-avid mass in the anterior compartment of the left thigh (white arrows). Fat planes with the vasti, rectus femoris, and sartorius muscles are indistinct. FDG-avid lesions are noted in the interpatellar fat pad, left patellar retinaculum, popliteal fossa, and gastrocnemius muscle. The lesion is closely abutting bones with no changes. Sagittal CT (e) and FDG PET/CT (i) show the muscular involvement of the anterior compartment of the left thigh and muscle adjacent to knee joints

nature of the malignant variant, further complicated by the patient's postrenal transplant immunosuppressed state, posed significant challenges in management. This report contributes to the current literature by shedding light on the complexities inherent in diagnosing and managing PTLD in the backdrop of immunosuppression following solid organ transplantation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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