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Case Report

Unilateral Leg Edema as the First Manifestation of Testicular Seminoma in a Kidney Transplant Patient

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Abstract

De novo malignancies are more common post-solid organ transplantation, especially post-transplant lymphoproliferative disorders. We present the unusual case of a kidney transplant patient who developed unilateral lower extremity edema secondary to a pelvic mass initially thought to be post-transplant lymphoma but turned out to be metastatic seminoma from a testicular primary. Testicular germ cell tumours are rare cancers affecting young adults. However, they are 3 times more frequent and more aggressive in renal transplant recipients and can present a diagnostic challenge.

Keywords: Leg Edema; Renal Transplant; Malignancy; Pelvic Mass; Seminoma

Introduction

De novo malignancies are common in the setting of immunosuppression and transplantation with post-transplant lymphoproliferative disorder (PTLD) being the most common of the tumours [1-3]. Testicular germ cell tumours, 50% of which are seminomas, are rare cancers affecting young adults between 14 and 44 years of age [4]. However, these cancers occur 3 times more frequently and more aggressively in renal transplant recipients compared to the general population and can have unusual clinical presentation making it a diagnostic challenge [3]. We present a case of metastatic seminoma in a renal transplant patient presenting unusually with right lower extremity swelling and a retroperitoneal pelvic mass initially suspected to be PTLD.

Case Presentation

A 60-year-old Caucasian man was admitted to the hospital for workup of gradually increasing painless right lower limb swelling associated with off and on painful scrotal swelling for the past two months. The review of systems was otherwise unremarkable. His past medical history was significant for hypertension, hyperlipidaemia, and end stage kidney disease secondary to polycystic kidney disease for which he had received a living related kidney transplantation from his cousin (4 antigen mismatch; CMV donor & recipient were negative; Thymoglobulin induction; maintenance immunosuppression with Tacrolimus and Prednisone 5 mg daily) in the right iliac fossa 10 years prior to this admission, followed by bilateral native nephrectomies. He was hospitalized 2 months prior to this admission for elevated serum creatinine level from a baseline of 1.3-1.4 mg/dL to 3 mg/dL and increase in random urine protein/creatinine ratio from a baseline of ~ 1g/g creatinine to 3-6 g/g creatinine. He had admitted that he had not taken his maintenance immunosuppressive medication for 3 months due to losing his insurance. His donor specific antibody screen was positive for anti-HLA B45 with MFI 4000, and a percutaneous allograft biopsy had shown C4d negative chronic active antibody-mediated rejection with moderate glomerulitis and peritubular capillaritis, 20-30% interstitial fibrosis and tubular atrophy, and early transplant glomerulopathy. He was treated with IV Solumedrol 500 mg X3, Plasmapheresis X3 sessions, IVIg 1 g/kg X2 doses, and his maintenance immunosuppression was increased. On this admission he was found to have three plus pitting edema in his right lower limb and no edema in his left lower extremity. The rest of the physical exam was unremarkable. A Doppler ultrasound of the right lower extremity ruled out deep

vein thrombosis. A magnetic resonance imaging and angiography (MRI, MRA & MRV) of abdomen and pelvis revealed a 10.9 x 6.2 x 4.9 cm right pelvic mass encasing the right external and internal iliac arteries and veins with severe compression of the iliac and renal transplant veins. A second mass, predominantly in retrocaval position, measuring 4.1 x 4.4 x 2.4 cm was also discovered. There was extensive lymphadenopathy, most significantly in the retro-crural space, aortocaval space, and posterolateral to the right psoas muscle. Other MRI findings included a 2.9 x 1.9 cm right adrenal mass without signal loss on opposed phase images consistent with metastatic involvement, a mildly enlarged spleen measuring 14.1 cm, and bilateral hydroceles, greater on the right than on the left. The MRI findings strongly suggested PTLD and tacrolimus dose was significantly reduced while a low dose sirolimus was initiated along with continued prednisone at 5 mg daily. A CT scan of the chest, abdomen and pelvis with & without contrast showed a 2.1 cm round mass in the upper lobe of the left lung reflecting either primary tumour or a distant metastasis, numerous enlarged retroperitoneal lymph nodes, an ill-defined hypo-attenuating pelvic mass measuring 8.7 X 6.5 X 4.2 Cm encasing the right common, right internal and external iliac arteries and veins, and an occlusive thrombosis of the transplant renal vein (Figures 1 & 2). Patient was started on heparin for the management of the renal vein thrombosis. A CT-guided needle core biopsy of the retroperitoneal mass showed a poorly differentiated malignant neoplasm with neoplastic cells exhibiting rare weak staining with CD30, raising concern for anaplastic large cell lymphoma, however, T-cell markers and ALK1 were negative. There was also no staining with CD20, excluding a B cell lymphoma, and EBER ISH did not reveal evidence of Epstein-Barr virus considering PTLD in our differential diagnosis. The results were inconclusive based on the small sample size and a repeat biopsy was required for final diagnosis. A subsequent FDG PET/CT scan confirmed a widespread malignant process (Figure 3). Two differentials became more plausible: 1) Lymphoma, given the involvement of multiple retroperitoneal lymph nodes, iliac lymph nodal mass, splenomegaly and an enlarged (7 cm) hyper metabolic right testis, or 2) Primary right testicular malignancy with nodal, adrenal, penile (an area of increased uptake in the root of penis), and pulmonary metastasis. The testicular enlargement with increased FDG uptake was assumed to be either due to a lymphomatous testicular involvement or a primary testicular malignancy. Another significant finding on PET scan was a focus of increased FDG uptake along the medial margin of the anterior pole of the transplanted kidney suggestive of either a metastasis in an adjacent lymph node or a hyper metabolic focus within the transplant tissue.

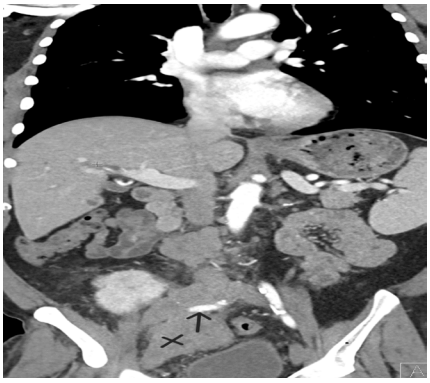

Figure 1: CT with contrast showing Pelvic mass (x) encasing the External iliac artery (arrow).

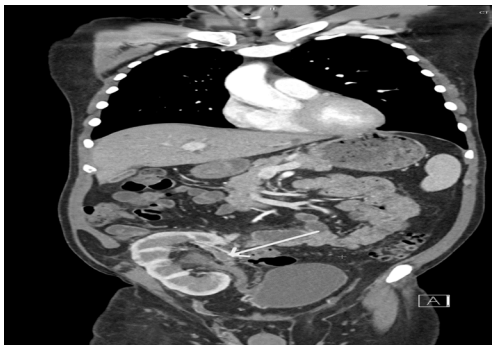

Figure 2: CT with contrast showing Transplant Renal Vein Thrombosis (arrow).

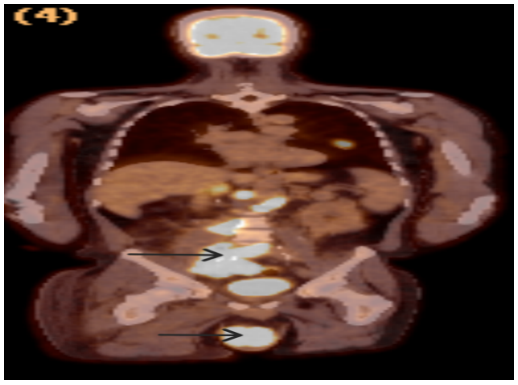

Figure 3: PET CT showing intense FDG uptake by pelvic mass (upper arrow) and Scrotal mass (lower arrow).

A repeat biopsy of the retroperitoneal mass confirmed metastatic germ cell tumour, most consistent with seminoma. Histologically, discohesive large tumour cells with prominent

nucleoli, clear to pink cytoplasm and indistinct cell borders along with lesion cells in a fibrous background admixed with small lymphocytes and foci of necrosis were present. Large cells demonstrated membranous CD117 and D2-40 staining, but were negative for PAX5, ALK1, GATA3, P63, CD138, and CD61. A radical right orchiectomy confirmed the diagnosis: a 7.2 cm classic seminoma with focal tumour necrosis and haemorrhage, invading the epididymis, but negative for lymphovascular or spermatic cord invasion. The tumour was positive for CD117 and D2-40, and negative for CD30 and CD45, with CD45 highlighting occasional groups of intertemporal lymphocytes. SALL4 and OCT3/4 immunisations were strongly positive for neoplastic cells. The pre- and post-orchiectomy tumour markers B-HCG (167 preop vs 252 postop), AFP (2.1 preop vs 2.4 postop), and LDH (1417 preop [5.8 x upper limit of normal] vs 1475 postop [6.1 x upper limit of normal]) were all elevated. A definitive diagnosis of metastatic seminoma was established, and the patient was discharged with an outpatient referral to the oncology specialist for further management.

Discussion

The tendency to develop malignancies after kidney transplantation can amount to two to three times the general population with post-transplant lymphoproliferative disorders (PTLD) being the most frequently encountered tumours [1]. Common risk factors include immunosuppression, heightened immunosuppressive therapies for multiple rejections over the years, viral infections, male gender, white race, and increasing age of the recipient [2]. Among the genitourinary neoplasms seen in renal transplant patients, prostate cancer and renal cell carcinomas are the most common and are often detected earlier through screening leading to better outcomes. However, testicular cancers, though three-fold more common in renal transplant recipients, are still rarely encountered [3] and therefore, carry a risk of being overlooked due to lack of routine screening [4]. Classical seminomas, constituting about fifty percent of testicular germ cell type, are rare tumours usually affecting mostly young Caucasian males in their third and fourth decades of life and are an uncommon occurrence after the age of 60. Testicular seminomas usually present as a palpable hard testicular mass screened with a scrotal ultrasound followed by radical orchiectomy for definitive diagnosis [5]. However, in the immunosuppressed and transplant recipients, testicular cancers present at a more advanced stage and often have unusual presentations implying metastatic disease [6,7]. Unusual symptomatology includes, but is not limited to, unilateral lower limb swelling, groin pain, scrotal swelling, dyspnoea, cachexia, and peripheral neuropathy. On physical examination, testicular cancer presenting as a painful scrotal swelling could sometimes be mistaken as epididymo-orchitis, thus delaying definitive diagnosis [4,7]. On the other hand, testicular lymphomas, although rarer than seminomas, are more common in men over 60 years. PTLD (lymphomas occurring after transplantation), although usually presenting as nodal masses or extra-nodal disease, can uncommonly present as testicular lymphoma [8]. The clinical overlap between testicular seminomas and post-transplant lymphoproliferative disorder presents a diagnostic challenge as both follow completely different management algorithms. Our patient presenting with unilateral lower extremity swelling as the main sign of metastatic testicular seminoma underwent a detailed workup of an abdominopelvic disease process. As PTLD was highly suspected, a biopsy of the retroperitoneal mass was performed on the patient, which showed a metastatic germ cell tumour. There are no special screening guidelines for post-transplant malignancies, particularly testicular cancers, in place for transplant recipients and these patients follow the same screening recommendations as that of the public. Therefore, it is important to give due attention to every abnormal physical examination finding given the potential for developing de novo malignancies after renal transplantation. Additionally, routine testicular self-examination should be done by patients who have undergone renal transplantation with immediate physician consultation if any abnormality is noticed.

Conclusion

Classical seminoma, although rare after the fourth decade of life, could present in immunosuppressed patients and transplant recipients and has a more aggressive clinical course in this population. Any suspicious physical examination finding should be thoroughly investigated as the disease progresses rapidly. Clinicians should be wary of the propensity of renal transplant recipients to develop de novo malignancies and should screen appropriately depending on the risk factors present in an individual and the symptomatology.

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