Role of diffusion weighted imaging in diagnosis of post transplant lymphoproliferative disorders: Case reports and review of literature

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ABSTRACT

Post transplant lymphoproliferative disorder include a spectrum of conditions occurring in immunosuppressed post transplant recipients, lymphoma being the most ominous. ^{18}F-fludeoxyglucose positron emission tomography with computed tomography CT) is the current imaging gold standard for lymphoma imaging as it allows both morphological and functional assessment. CT and/or conventional magnetic resonance imaging (MRI) are used for morphological evaluation in transplant recipients. Integrating diffusion weighted imaging with apparent diffusion coefficient analysis in MRI protocol enhances its sensitivity and may prove invaluable in response assessment in transplant recipients.

Key words: ^{18}F-fludeoxyglucose positron emission tomography with computed tomography, diffusion weighted imaging, magnetic resonance imaging, post transplant lymphoproliferative disorders

Introduction

Post transplant lymphoproliferative disorders (PTLD) include myriad of lymphoproliferative manifestations occurring in transplant recipients ranging from innocuous flu like conditions (mononucleosis) to the development of aggressive widely disseminated malignancy (lymphoma).[1] PTLD is a rare, but potentially fatal complication seen in ~1% of transplant recipients (solid and stem cell).[1,2]

Risk factors for developing PTLD are multifactorial which includes Epstein–Barr virus (EBV) seronegativity, immunosuppression administered to recipients (intensity, amount, and duration), co-existing cytomegalo virus or hepatitis C infection, cadaveric donor and use of anti CD3 monoclonal antibody. The incidence of PTLD is higher in pediatric patients who are usually EBV seronegative.[1,3] The overall incidence of PTLD is least in renal transplant (nearly 13%) as compared to other solid organ transplant recipients (~15%).[4] PTLD most frequently involves extra nodal sites with reportedly highest incidence in gastro-intestinal tract and allograft. However, it can involve any organ including skin and brain.[1,5] Clinically, PTLD is a great masquerader, the diagnosis of which rests on a high index of clinical suspicion. It can manifests with a variety of nonspecific symptoms that may resemble any other post transplant complications including graft rejection and sepsis.[1,6]

Compared to lymphoma occurring in general population, PTLD lymphoma carries a dismal prognosis (nearly 30–60% mortality)[1,5,7] with an aggressive downhill course; hence, timely diagnosis is warranted. As majority

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of these cases are diagnosed on imaging, radiologists should be familiar with its morphological gamut. Further, timely diagnosis will expedite the management which in most cases consists of mere reduction of the degree of immunosuppresant only.

Case Reports

Case 1

A 36 years old male presented in emergency with complaints of fever, weight loss, and vague upper abdominal pain of 1-month duration. Renal allograft transplantation had been done 1-year back and he was kept on immunosuppresants (azathioprine, cyclosporine and prednisolone). Ultrasonography (USG) abdomen revealed multiple conglomerate as well discrete hypoechoic solid lesions in upper abdomen in mesentery and peripancreatic locations. Contrast enhanced computed tomography (CECT) abdomen showed multiple non-necrotic, non calcified lesions in central mesentery and upper retroperitoneum [Figure 1a]. Bowel and vascular encasement were present with no obstruction or luminal compromise. On magnetic resonance imaging (MRI), lesions were mildly hyperintense on T2-weighted image, however, marked diffusion restriction was present with corresponding hypointensity on apparent diffusion coefficient (ADC) images [Figure 1b-e]. Provisional diagnosis of PTLD related lymphoma was kept. USG guided biopsy revealed diffuse large B-cell lymphoma. Subsequently immunosuppressants doses were lowered and chemotherapy started. Follow-up MRI 2 months later revealed complete resolution of lesions.

Case 2

A 40 years old male renal transplant recipient came to emergency with vomiting and jaundice, 2 years post transplant, maintained on immunosuppression (cyclosporine and prednisolone). USG showed mild bilobar intrahepatic biliary dilatation and dilated common bile duct (CBD). CECT abdomen revealed circumferential nodular hypodense mural thickening involving second part of duodenum causing mild upstream dilatation of CBD and intrahepatic biliary radicles [Figure 2a]. MRI done 2 weeks later showed similar findings with mildly T2 hypointense mural thickening involving second part of duodenum showing markedly restricted diffusion and hypointensity on ADC images [Figure 2b-e]. Degree of proximal CBD dilatation and intrahepatic biliary dilatation had increased. Upper gastrointestinal (GI) endoscopy and biopsy revealed diffuse large B-cell lymphoma. Immunnosuppressants were stopped and patient was put on chemotherapy. However, the patient succumbed to his illness 15 days after initiation of chemotherapy due to fungal pneumonia.

Discussion

PTLD of abdomen can present with nonspecific symptoms like pyrexia of unknown origin, weight loss, irritability, lymphadenopathy, or more specific symptoms which may vary from indolent pharyngitis and diarrhea to acute abdomen due to obstruction, GI bleed or perforation due to its higher tendency for ulceration as compared to lymphoma occurring in immunocompetent individuals.[8-10]

PTLD related lymphoma most commonly involves gastrointestinal tract (GIT), followed by the central nervous system and kidneys.[10] Distal small intestine is the most common hollow viscera to be involved, followed by proximal colon, stomach, duodenum, and esophagus. For GIT associated PTLD, pan endoscopy remains useful tool for the initial diagnosis, management, and treatment.[3] CECT is the most widespread imaging modality in diagnosing lymphoma due to its relative low cost and easy availability. Diagnosis of PTLD on CECT rests on morphological evaluation with the lesions being solid and either hypo or nonenhancing. Failure to provide functional information coupled with inability to distinguish residual disease from fibrosis remains its lacunae.[2,10-12] ^{18}F-fludeoxyglucose positron emission tomography with computed tomography (^{18}F-FDG PET/CT) is currently the imaging gold standard for lymphoma evaluation with lesions being FDG avid. It provides the dual advantage of providing both morphological and functional information, thus proving invaluable in diagnosing, staging, and response assessment. Sensitivity and specificity of PET/CT in initial staging approaches 100% regardless of lymphoma grade. Moreover, quantifying standardized uptake value helps in assessing metabolic activity in tumor and may help *in vitro* diagnosing the aggressiveness of lymphoma. However, high radiation exposure and costs remain its limitations.[11-15]

Conventional MRI sequences, much like CT helps in morphological assessment only. However, due to its superior spatial resolution and radiation free modality, it scores over CT, hence benefitting in evaluating extra-nodal disease. Due to compromised renal function in postrenal transplant recipients, iodinated nonionic contrast usage is discouraged; hence MRI is preferred over CECT for morphological assessment if available.[13]

Lymphoma is hypointense on T1-weighted, mildly hyperintense on T2 weighted sequences and shows minimal enhancement if any on postcontrast images. Diffusion weighted imaging (DWI) is increasingly being used in lymphoma evaluation on which it shows restricted diffusion due to hypercellularity.[11] Calculation of ADC

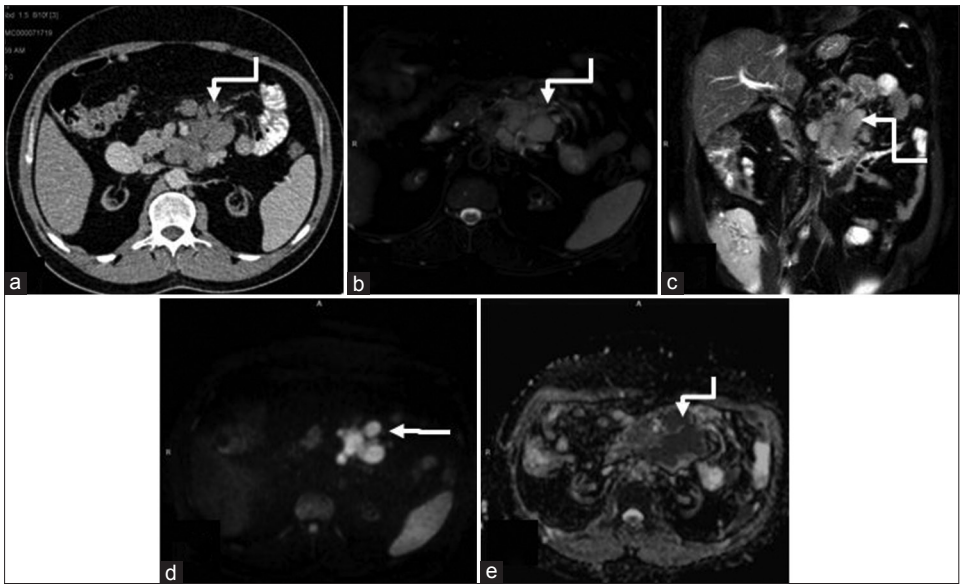

Figure 1: (a) Contrast enhanced computed tomography abdomen showing homogeneously hypodense conglomerate and discrete circumscribed lesions (arrow) in mesentery and peripancreatic locations. Axial (b) and coronal. (c) T2-weighted fat suppressed images showing mild T2 hyperintensity (arrow) with restricted diffusion on DWI (d) and ADC hypointensity (e)

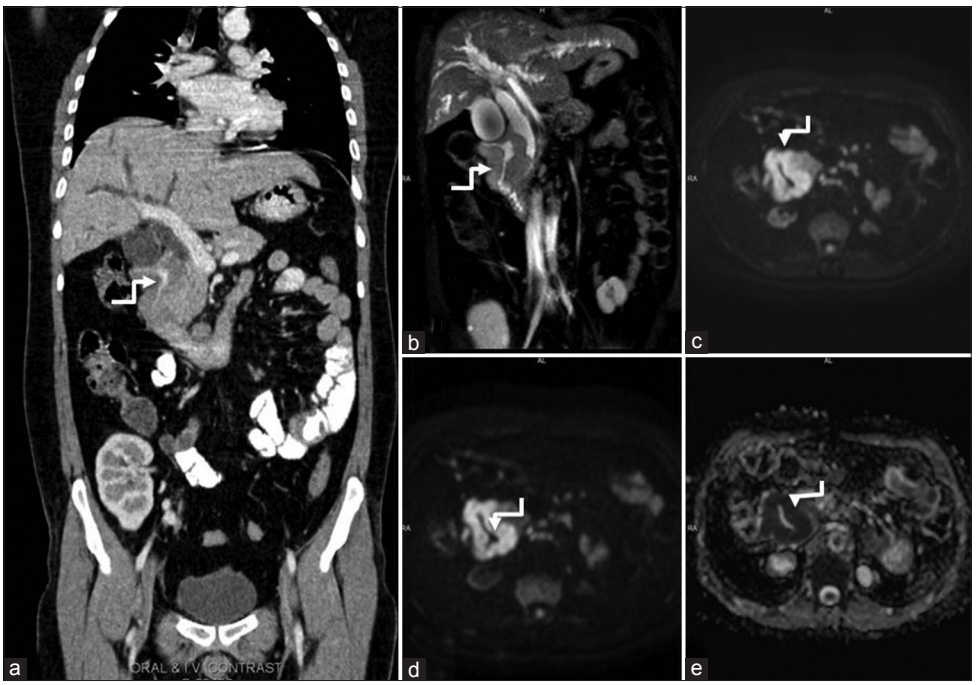

Figure 2: (a) Contrast enhanced computed tomography abdomen coronal reformat showing circumferential infiltrative nodular hypodense mural thickening involving second part of duodenum (arrow) with mild upstream dilatation of intrahepatic biliary radicals and common bile duct. (b) Coronal T2-weighted image showing mild T2 hyperintense duodenal mural thickening (arrow) with marked diffusion restriction on diffusion weighted imaging (c and d) and hypointensity on corresponding ADC images (e)

value provide quantitative information which adds to the functional assessment of disease, thus, helping in staging, grading, and response assessment following treatment.[11]

By adding whole body diffusion weighted imaging with background suppression (DWIBS) in lymphoma assessment protocol, MRI is comparable to FDG-PET/CT as it also provides one stop shop for diagnosis, staging and therapeutic response assessment. Furthermore, inverted gray scale DWIBS images are alike PET images with added advantage of increased lesion conspicuity and no radiation exposure.[10,11]

To the best of our knowledge, no study in literature until date has described the incremental utility of DWI in management of PTLD. Due to increased accuracy in

lymphoma detection we recommend incorporation of DWI in while performing MRI in PTLD which not only guide tissue sampling of these lesions but can also be very useful to evaluate treatment response in terms of ADC calculation.

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Conflicts of interest

There are no conflicts of interest.

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