A Pictorial Review of Spectrum of Radiologic Finding in PTLD

Poster No.: R-0045
Congress: RANZCR-AOCR 2012
Type: Educational Exhibit
Authors: Y.-T. Huang\textsuperscript{1}, C. Yu\textsuperscript{2}, Y.-T. Huang\textsuperscript{2}, A. Ravi Kumar\textsuperscript{1};\textsuperscript{1}Herston/AU, \textsuperscript{2}Woolloongabba/AU
Keywords: Oncology, Nuclear medicine, PET-CT, Molecular imaging, Transplantation, Cancer
DOI: 10.1594/ranzcraocr2012/R-0045

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Learning Objectives

To illustrate the spectrum of imaging findings in patients with post transplant lymphoproliferative disorder (PTLD). Like lymphoma, PTLD can present with varied findings and requires clinical and pathologic correlation. Multi-modality imaging is required for staging and follow-up of PTLD. In particular, Positron Emission Tomography (PET) with F18-Fluorodeoxyglucose (FDG) is now a mainstay in the imaging of PTLD.

Background

POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)

- PTLD is a heterogeneous disorder that ranges from abnormal lymphoid hyperplasia to disease resembling frank lymphoma. It is a serious complication of both solid organ and allogeneic bone marrow transplantation [1-5]. It is a specific pathological entity in response to immunosuppression. This feature distinguishes PTLD from lymphoma [1-6].

Epidemiology

- There is a 10% incidence post solid organ transplantation, with high morbidity and mortality up to 60% [1-3]. PTLD is the most common post-transplant malignancy in children and the second most common one in adults [3].

Pathogenesis

- Most cases of PTLD (85%) are related to Epstein-Barr virus (EBV) infection and immunosuppression [1-3]. Normally in immune-competent individuals, EBV stimulated B-cell proliferation are controlled by T-cell mediated immune response [1-3]. In immunosuppression, depressed function of EBV specific T-cells results in uncontrolled proliferation of EBV infected B-cells [1-3].
- In some patients, PTLD is secondary to T-cell and natural killer cell response [1-3]. EBV-negative cases are also known. These cases are not fully explained by the EBV-infection theory [1-3].

Clinical Manifestations
- The majority of PTLD occurs within one year of transplantation[1-3]. Clinical presentation is often non-specific and difficult to differentiate from infection or allograft rejection[1-3].
- PTLD preferentially affects the transplanted organ, thus allograft dysfunction should alert clinicians to the possibility of PTLD[1-5]. Compared to lymphoma, PTLD is more common in extra-nodal sites particularly the gastrointestinal (GI) system [1-4].

**Medical Imaging in PTLD**

- Medical imaging has an important role to establish PTLD as a tentative diagnosis, to guide biopsy, stage disease and assess therapy response [1-5]. While imaging findings may overlap with lymphoma, the main differentiating feature is the high incidence of extra-nodal involvement [1-5]. Application of multi-modality imaging is pivotal as each has strengths and improves diagnostic specificity.

**Ultrasound Imaging (US)**

- Ultrasound is routinely used for assessment of the allograft organ [7]. Therefore, it is often the first imaging modality to suggest the diagnosis of PTLD. In children, it has high sensitivity and is particularly valuable in evaluation of disease without need for repeated radiation exposure [5-8].

**Computed Tomography (CT)**

- CT often detects more disease than radiography or US and helps with staging, guiding tissue biopsy and follow-up [1-8]. However, CT even with contrast has limitation in lesion characterization and identification of bony involvement [4-12].

**Magnetic Resonance Imaging (MRI)**

- MRI is particularly useful in Central Nervous System (CNS) and skeletal involvement of PTLD [1,13].

**F 18 FDG-PET/CT**

- FDG-PET/CT is now considered to be the mainstay imaging investigation for PTLD [9-12]. PTLD (similar to most subtypes of lymphoma) shows high avidity for FDG [9-12]. PET/CT has the potential to identify additional site of PTLD involvement, especially extra-nodal deposits [1-3, 9-12].
• The ability to differentiate between residual disease and post-therapy changes is the most advantageous attribute of PET/CT over other conventional imaging modality [1-3, 9-12].
• "False positive" FDG uptake in infectious/inflammatory lesions can be avoided by correlation with radiologic features and clinical symptoms [3, 9-12].

Diagnosis and Histological Classification

• Distinguishing between subtypes of PTLD is important for treatment planning. This distinction can not be reliably made on the basis of imaging features alone [7].
• There are four major pathological category of PTLD (Table 1). The main subtypes are monomorphic and polymorphic of which the latter may respond to immunomodulator therapy alone [4].

Management

• Treatments are often based on PTLD pathological subtype, disease burden as well as patient's clinical state and transplant organ function [1-6].
• Management of PTLD generally consists of reduction of immunosuppression which leads to restoration of cytotoxic T-lymphocyte function[1-6]. A partial or complete response may result; however, monoclonal antibody and chemotherapy are often required [1-8].

Images for this section:

Table 1
Imaging Findings OR Procedure Details

REVIEW OF IMAGING FEATURES WITH ILLUSTRATIVE CASES

A series of adult and paediatric cases are presented here to illustrate the key imaging features of PTLD. Although PTLD is often a systemic disease, this section has been divided in abdominal, chest, CNS, head and neck and cutaneous to better focus on the specific radiologic findings.

ABDOMINAL

*Gastrointestinal Tract*

**Table 2. Imaging Features of Gastrointestinal PTLD Involvement**
Localised circumferential bowel wall wall thickening with dilatation of involved loops

*Ulceration / Perforation*

Eccentric non-obstructive polypoid mass involving bowel segment

*Extramural extension*

*Short segment intussusceptions*

*Skip lesions*

Figure 1 - Small bowel

Figure 2 - Small bowel and Gastric

Figure 3 - Caecum
Table 3. Imaging Features of Solid Organ PTLD Involvement

**Nodules** - single or multiple, usually low attenuation on CT / hypoechoic on US

**Diffuse infiltration** - Ill-defined mass(es) of heterogeneous enhancement on CT with or without **organomegaly**

**Solid organ with adjacent lymphadenopathy**

**Encasing mass** at liver or renal hilum with **obstruction to outflow tract** (bile or urine) respectively

Figure 5 - Hepato-renal (native kidneys)

Figure 6 - Spleen

Figure 7 - Renal (transplanted kidney)

Table 4. Imaging Features of Intra-abdominal Nodal PTLD Involvement

**Discrete, homogenous enlarged lymph node**

**Conglomerate of enlarged nodes**

**Bulky soft-tissue mass with central necrosis**
THORACIC

Table 5. Imaging Features of Thoracic PTLD Involvement

**Nodules** - single or multiple discrete homogenous or centrally cavitating lesions (55% of patients). Often mistaken as infection - requires histological confirmation to differentiate from infection

**Diffuse infiltration** with patchy airspace consolidation

**Mediastinal lymphadenopathy or mass** (45% of patients)

**Pleural effusion**

**Thymic enlargement**

Figure 10 - Pulmonary nodule and lymphadenopathy

Figure 11 - Diffuse pulmonary infiltration

CENTRAL NERVOUS SYSTEM

Table 6. Imaging Features of CNS PTLD Involvement

**Lesion necrosis** is more common

**Subcortial white matter or basal ganlion**
Signal characteristics similar to opportunistic infection and lymphoma in HIV:
Multiple lesions with heterogeneous or ring enhancement

Delayed biopsy site haemorrhage and haemorrhage at other sites has been reported in small series of cases

Figure 12 - Multi-focal

Figure 13 - Haemorrhagic

HEAD AND NECK

Table 7. Imaging features of Head and Neck PTLD Involvement
Waldeyer ring focal mass with central low attenuation (necrosis), often mistaken for abscess

Extensive submucosal extension into parapharyngeal space is a distinguishing feature from those of lymphoma (exophytic solid mass growing into the airway lumen)

Cervical Lymphadenopathy, often necrotic

Bulky mass with bone/orbit involvement

Figure 14 - Nasopharynx

CUTANEOUS

- Rare occurrence
- Important to distinguish from other cutaneous malignancy

Figure 15 - Cutaneous PTLD
Images for this section:
Fig. 1: Small Bowel PTLD. Contrast-enhanced (CE) axial CT (A) of an 81-year-old lady post renal transplant. Gross dilatation of a segment of small bowel with marked bowel wall thickening is evident (A). Monomorphic PTLD is confirmed on histology. Fusion FDG-PET/CT scan (B) revealed high FDG avidity in involved segment in contrast to the physiologic uptake in other small bowel loops.

Fig. 2: Small Bowel and Gastric PTLD. CE-CT in coronal (A) and axial (B and C) views of a 17-year-old girl post liver transplant shows small bowel PTLD with multiple small bowel loops with circumferential wall thickening in the central abdomen. Gastric wall thickening is also evident in the fundus and antrum. Endoscopically, gastric and duodenal ulcers were present and biopsy confirmed PTLD.
Fig. 3: Large Bowel PTLD. CE-CT (A and B) performed in a 20-year-old girl post renal transplant for reflux nephropathy shows an eccentric mass with central low attenuation involving the caecum (white arrow). This lesion compresses the terminal ileum. Following confirmation of caecal PTLD, FDG-PET was performed to stage disease. Maximal Intensity projection (MIP) image (C) demonstrates isolated disease in the caecum (black arrow) lying superior to the transplanted kidney (Asterisk).
Fig. 4: Gastric PTLD. 59-year-old man ten years after renal transplant presented with weight loss and epigastric pain. Staging MIP(A) and corresponding CT, PET and fusion images at the level of the stomach (B) shows intense FDG-uptake. Tracer uptake elsewhere is physiologic, noting the renal allograft in the right pelvis. Post chemotherapy, the follow-up PET/CT MIP image(C) confirms complete metabolic response.
Fig. 5: Hepato-renal PTLD. 10-year-old boy with liver transplant underwent CT as part of his diagnostic evaluation for abdominal pain. CE-CT scan showing several low attenuating nodules in the native kidneys (A) and transplanted liver parenchyma (B) that was proven to be PTLD. Incidental CT findings of ileo-ileal intussusception(C and D, arrows) secondary to enlarged mesenteric lymph nodes.
Fig. 6: Spleen PTLD. 57 year-old man with renal transplant for polycystic kidney and liver disease presented for investigation of abdominal pain. US scan (A) shows numerous hypoechoic splenic nodules with splenomegaly. CE-CT (B) confirmed splenic involvement but no other abdominal disease or ascites. Reduction of immunosuppression followed by chemotherapy resulted in resolution of PTLD in spleen as seen in the follow-up US (C) and CT (D) scans.
Fig. 7: Renal PTLD. 66-year-old man post kidney transplant 15 years ago presented with acute renal impairment. US scan (A) found a hydronephrotic renal allograft and subsequently decompressed via a nephrostomy. Fluoroscopy (B) at time of nephrostomy reveals an external compression to the proximal transplanted ureter with incomplete obstruction. Further investigation with multiphase CE-CT (C and D) shows an ill-defined uniformly enhancing mass (arrow) centrally in the kidney, narrowing the infundibulae.
Fig. 8: Retroperitoneal nodal PTLD. Coronal CT (A) of a 69-year-old lady shows conglomerate retroperitoneal nodes. She presented with renal impairment twelve years following liver transplant. Staging FDG-PET (B) demonstrates intense FDG uptake in the biopsy proven retroperitoneal PTLD. Post-therapy, while residual nodal tissue were evident on CT (not shown), minimal FDG-uptake on PET (C) was interpreted as post-therapy inflammatory change. Patient was still in remission at 1 year follow-up.

Fig. 9: Mesenteric PTLD. 3-year-old girl 15 months post liver transplant presented with jaundice, weight loss and abdominal distension. CE-CT in axial and coronal planes
(A and B) illustrates a bulky heterogeneous mesenteric soft tissue mass with central low attenuation, suggestive of necrosis. It is encasing the superior mesenteric artery branches. Laparoscopic biopsy revealed PTLD.
Fig. 10: Pulmonary and nodal PTLD. CE-CT (A and B) of a 37-year-old man 14 years post renal transplant found to have 7cm diameter left supraclavicular nodal mass causing tracheal deviation. A solitary right middle lobe pulmonary nodule was evident. Further assessment with Gallium-67 Citrate Single Photon Emission Computed Tomography (SPECT) scan (C) shows focal intense uptake in the nodule, compatible with pulmonary PTLD.

Fig. 11: Pulmonary PTLD. 66-year-old renal transplant recipient presented with dry cough and lethargy. Chest x-ray (A) shows bilateral mixed interstitial and airspace opacities. Patient was treated for infection but had persistent changes on radiograph. Further CT (B) shows emphysema with extensive consolidation as well as nodules. It was nearly 1 month following presentation that a diagnosis of PTLD was made via a biopsy of a right axillary node.
Fig. 12: Multi-focal CNS PTLD. 52-year-old woman with heart-lung transplant was admitted with left upper limb paresis and seizures. 3D T1 Gadolinium-enhanced MRI shows multiple ring-enhancing lesions, the largest centered on the right motor cortex with adjacent oedema. Other lesions include thalami crossing midline and left temporal and parietal lobes.
**Fig. 13:** Haemorrhagic CNS PTLD. Same patient in figure 12 following cerebral biopsy confirming PTLD had further MRI. Non-enhanced axial T1 shows high signal in the biopsied right parietal lesion, consistent with expected minor haemorrhage. However, T1 hyperintensity was also evident in the midline thalamic lesion. Other lesions (not shown) also show similar MR signal. Delayed haemorrhage post biopsy or spontaneous haemorrhage in other lesions has been described in the literature to be a feature of CNS PTLD.[1,13]
**Fig. 14:** Nasopharyngeal PTLD. CE-CT (A and B) of a 17-year-old man post renal transplant shows asymmetric left nasopharynx soft tissue mass with central necrosis and effacement of the fossa of Rosenmuller. Bilateral large level II necrotic lymph nodes were evident. Biopsy of necrotic cervical nodes revealed PTLD.
Fig. 15: Cutaneous PTLD. 73-year-old man with heart transplant present with multiple erythematous nodules on his torso and extremities. Punch biopsy revealed uncommon cutaneous PTLD. MIP PET (A) demonstrates widespread superficial FDG-avid lesions.
These lesions correspond to the subcutaneous nodules clearly defined on the axial CT, PET and PET/CT images (B, C and D).
Conclusion

PTLD is an aggressive and rapidly progressive disease where prompt diagnosis and treatment is essential. Multi-modality imaging plays a pivotal role in suggesting the diagnosis, staging the disease and follow-up post therapy. Imaging specialists need to be familiar with the spectrum of imaging findings in PTLD.

Personal Information

References


