Background

- Individuals who receive solid organ transplants need to be maintained on immunosuppressive medications to prevent transplant rejection.
- This immunosuppressed state can predispose to infection-associated neoplastic complications.
- We present four cases of central nervous system Epstein–Barr virus (EBV)-related posttransplant lymphoproliferative disorder (PTLD) in individuals with solid organ transplants.

Methods/Materials

- The patients’ electronic medical records were thoroughly reviewed.
- Literature was searched and reviewed using appropriate key words.

Patient Summary

- **Patient A**: 62-year-old woman who received a kidney transplant 15 years previously. She presented with generalized weakness and falls. Magnetic resonance imaging (MRI) of her brain identified a left frontal lobe lesion.
- **Patient B**: 71-year-old woman who who is 15 years status-post renal transplant. She presented with progressive aphasia (word finding difficulty) and confusion. MRI of her brain revealed a left temporal lobe mass and a left frontal lobe mass.
- **Patient C**: 72-year-old man who is 16 years status-post renal transplant. He presented with right hand weakness and wrist drop. An MRI study of his brain identified a medial left frontal lobe lesion.
- **Patient D**: 70-year-old man who is 3 years status-post liver transplant. He presented with confusion. Imaging of his brain revealed a left frontal lobe lesion.

RESULTS

- **Patient B**
  - Brain Magnetic Resonance Imaging
  - Magnetic Resonance Imaging:
    - Imaging of the patient’s head identified (1) a left temporal lobe mass (●), 4.5 X 4.0 X 4.3 cm, with peripheral contrast enhancement and extensive surrounding edema and a 0.3 cm left-to-right shift across midline and (2) a superficial left frontal lobe lesion, 1.1 cm, enhancing with surrounding edema, not seen on an earlier imaging study, not shown.

- **Neuropathologic Evaluation**
  - Left: Resection specimen showing a “fish-flesh,” firm appearance peripherally and chalky, yellow-white necrosis centrally.
  - Right: Low power image of a portion of the resection specimen, hematoxylin and eosin stained, show viable neoplasm peripherally and necrosis centrally.
  - Immunohistochemical evaluation revealed that neoplastic cells showed strong membranous expression of CD20 and nuclear expression of MUM1 but lacked expression of CD10. By in situ hybridization Epstein-Barr virus expression was noted in most neoplastic cells.

  - Neoplastic cells were centered around blood vessels (arrows) with necrotic cells (pink areas) surrounding aggregates of viable cells.
  - Cytologically, neoplastic cells had moderately sized nuclei and scant but discernible cytoplasm.
  - Combined findings were consistent with designation as:
    - (1) Diffuse large B-cell lymphoma, non-germinal cell type, EBV-positive.
    - (2) Post-transplant lymphoproliferative disease (PTLD)

- **Summary of Cases**

<table>
<thead>
<tr>
<th>Case / Age (Yrs) / Sex</th>
<th>Transplanted Organ</th>
<th>Immunosuppression at Time of Lymphoma Diagnosis</th>
<th>Lymphoma Diagnosis: Years Post-Transplant / Location(s)</th>
<th>Lymphoma Treatment: Reduction of Immunosuppression</th>
<th>Lymphoma Treatment: Chemotherapy</th>
<th>Current Status</th>
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<tbody>
<tr>
<td>E</td>
<td>Woman</td>
<td>Kidney</td>
<td>Tacrolimus, mycophenolate, prednisone</td>
<td>15 Years Left frontal lobe</td>
<td>Currently on prednisone only</td>
<td>Oral Temozolomide</td>
</tr>
<tr>
<td>D</td>
<td>Man</td>
<td>Kidney</td>
<td>Tacrolimus, mycophenolate, prednisone</td>
<td>15 Years Left temporal and left frontal lobes</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>C</td>
<td>Woman</td>
<td>Kidney</td>
<td>Tacrolimus, mycophenolate, prednisone</td>
<td>16 Years Left frontal lobe</td>
<td>Currently on Temozolomide</td>
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</tr>
<tr>
<td>B</td>
<td>Man</td>
<td>Liver</td>
<td>CellCapt</td>
<td>3 Years Left frontal lobe and corpus callosum</td>
<td>No treatment; transferred to hospice care</td>
<td>Dexamethasone</td>
</tr>
</tbody>
</table>

- **Literature Review Summary**

- In solid organ transplant recipients, PTLD is the most commonly associated malignancy.
- The patient’s degree of T-cell immunosuppression in the context of an underlying, dormant EBV infection in the recipient or in the donor organ appears to be a critical risk factor for developing PTLD.
- PTLD can affect various sites with the CNS involved in 7-15% of cases, usually, as in these patients, with primary presentation in the brain rather than secondary involvement of the brain by a lymphoma arising in lymph nodes or an extranodal site.
- Primary central nervous system PTLD most commonly is associated with kidney transplants, often occurs years after transplantation, usually follows an aggressive course, and most commonly shows EBV expression in neoplastic cells.

Conclusions

- We present four cases of central nervous system Epstein-Barr virus (EBV)-related posttransplant lymphoproliferative disorder (PTLD) in individuals with solid organ transplants.
- In each case, biopsy of the patient’s brain lesion revealed an EBV-positive diffuse large B-cell lymphoma with no evidence of lymphoma elsewhere in their body, consistent with designation as primary central nervous system lymphoma.
- Combined findings are also consistent with designation of the lymphoma as an EBV-associated PTLD.
- Individuals who receive solid organ transplants need to be maintained on immunosuppressive medications to prevent transplant rejection.
- This immunosuppressed state can predispose to infection-associated neoplastic complications, as characterized by EBV driving the posttransplant lymphoproliferation that can transform to lymphoma.

References