Post-transplant Lymphoproliferative Disorders (PTLD)

What is PTLD?
Post-transplant lymphoproliferative disorders (PTLD) are a type of lymphoma that can be a result of both solid organ transplant (kidney, lung, heart, liver, lung) and allogeneic bone marrow or stem cell transplants (cells from a donor). PTLD is one of the most common post-transplant cancers. PTLD results from a rapid increase in lymphoid (immune) cells that can happen after transplant.

What causes PTLD?
In most cases, PTLD is thought to be caused by the Epstein-Barr virus (EBV) infection of B cells. EBV is a type of herpes virus that about 95% of adults are already infected with. Our immune system often keeps the virus in check and EBV often does not cause long-term health problems. However, after transplant, the virus may be reactivated or the patient may have a new EBV exposure. When coupled with taking immunosuppressive medications after transplant to prevent organ/graft rejection, the immune system cannot stop the B cells infected with EBV from growing out of control.

PTLD after bone marrow or stem cell transplant appears to be influenced by T cell depletion, which is often part of the transplant to help lower the chance of rejection. With T cell depletion, the rate of PTLD after BMT is around 1 in 200 patients. In patients who receive a solid organ transplant, the rate of PTLD varies amongst what type of organ is transplanted. There is a higher risk among those receiving heart, lung, intestinal, and multi-organ transplants (as high as 25%). In patients who have received a liver or kidney transplant, the rate is lower; around 1-5%. Children who receive transplants may also be at a higher risk for developing PTLD. This is related to the fact that the child is unlikely to have been previously exposed to EBV, and so may not have immunity to EBV that is present in the transplanted organ.

Types of PTLD
There are six main types of PTLD as classified in 2016 by the World Health Organization. The type of PTLD is important in identifying treatment plans.

- Plasmacytic hyperplastic PTLD – can often be reversed by lowering the dose of immunosuppressive medications.
- Infectious mononucleosis PTLD.
- Florid follicular hyperplasia PTLD.
- Polymorphic PTLD.
- Monomorphic PTLD – most common type, often a diffuse large B cell lymphoma.
- Classic Hodgkin-type lymphoma – least common.

Patients are most at risk for developing PTLD in the first few months after transplant when doses of immunosuppressive medications are at their highest. However, it can develop years after transplantation.

Symptoms of PTLD
Symptoms of PTLD include:

- Painless, swollen lymph nodes.
- Fever.
- Night sweats.
- Weight loss.
Fatigue.
General malaise.

It is important to talk to your transplant team about any new symptoms right away. If PTLD is suspected, you will likely need a biopsy. You may also need other scans and laboratory tests to determine the sub-type of PTLD.

**Treatment of PTLD**

PTLD treatment can be challenging. The goal is to cure PTLD while preserving the function of the transplanted organ. The first line of treatment is a reduction of the immunosuppressive medications the patient is taking. Additional therapies include the use of Rituxan (rituximab) and other chemotherapy (doxorubicin, cyclophosphamide, vincristine, prednisone) in combination with rituximab (called R-CHOP).

Occasionally, surgery and radiation may be used to treat PTLD. Antiviral medications, including ganciclovir and acyclovir, may be used to prevent EBV-related PTLD, but have not demonstrated much success in the treatment of PTLD. Other new therapies, including immunotherapy and targeted therapy, are being studied in clinical trials.

**Resources for More Information**

NORD PTLD: https://rarediseases.org/rare-diseases/posttransplant-lymphoproliferative-disorders/

Leukemia and Lymphoma Society PTLD Factsheet
http://www.lls.org/sites/default/files/National/USA/Pdf/Publications/FS33_PTLD_2018_FINAL.pdf

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