Post-transplant lymphoproliferative disorder (PTLD)

This page is about post-transplant lymphoproliferative disorders (PTLD). PTLDs are lymphomas that can develop in people who are taking treatment to dampen their immune system after a transplant.

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What is post-transplant lymphoproliferative disorder (PTLD)?

Post-transplant lymphoproliferative disorders (PTLDs) are lymphomas that can develop after a transplant. ‘Lymphoproliferative’ means relating to proliferation (rapid growth) of lymphocytes.

PTLD can develop in people who are taking medicines to dampen their immune system in order to prevent rejection after an organ transplant or an allogeneic (donor) stem cell transplant. However, PTLD is rare. Most people who have had transplants do not develop PTLD.
There are four main types of PTLD, ranging from pre-cancerous disorders to more aggressive lymphomas:

1. In early PTLD, lymphocytes and other immune cells divide more often than usual and may build up in lymph nodes. The cells themselves are not cancerous and the lymph nodes still look normal under a microscope. There are three types of early PTLD, called ‘plasmacytic hyperplasia’, ‘infectious mononucleosis-like PTLD’, and ‘florid follicular hyperplasia’. Early PTLD often gets better if drugs that suppress the immune system are reduced or stopped.

2. In polymorphic PTLD a mixture of abnormal B cells and T cells develop. Some of the cells might be cancerous. They can build up in lymph nodes and sites outside lymph nodes (extranodal sites). The affected lymph nodes look abnormal under a microscope.

3. Monomorphic PTLD is the most common type of PTLD. In monomorphic PTLD, the abnormal cells are cancerous. They are all the same type of cell. Monomorphic PTLD usually develops from B cells but it can develop from T cells or NK cells. Monomorphic PTLD is classified based on the type of lymphoma it looks like under a microscope. The most common type is diffuse large B-cell lymphoma (DLBCL) but sometimes Burkitt lymphoma and other, rarer lymphomas such as peripheral T-cell lymphoma not otherwise specified (PTCL-NOS) can occur.

4. Classical Hodgkin lymphoma PTLD is rare. It can develop as a late complication of transplantation. Under a microscope, cancerous cells called Reed-Sternberg cells are present. These are characteristic of Hodgkin lymphoma.

What causes PTLD?

Many cases of PTLD are related to infection with a virus called Epstein–Barr virus (EBV). This is sometimes called ‘EBV-positive PTLD’.

EBV is a very common virus: about 9 in 10 adults have been infected with it. EBV infects B lymphocytes. It may not cause any symptoms at all and many people don’t know they’ve had it. Sometimes, it can cause glandular fever. After you’ve been exposed to it, EBV stays in your body but it is normally kept under control by your immune system. If EBV isn’t kept under control, it might cause some of your lymphocytes to transform (change) into cancerous cells.
If you have had EBV in the past, it might flare up when your immune system is suppressed (lowered) after your transplant. If you have not had EBV before, a transplant may introduce EBV-infected cells from your donor. Your doctors try to avoid this but because there are lots of factors to consider when matching a recipient and a donor, it is not always possible.

Some cases of PTLD are not related to EBV (EBV-negative PTLD). They tend to occur months or years after transplant, when the risk of lymphoma is usually lower than it is in the early months after transplant. The causes of these lymphomas are not clear. EBV-negative PTLD is more common in people who have had solid organ transplants than stem cell transplants.

**Who might get PTLD?**

**PTLD is rare. Most people who have transplants do not develop PTLD.**

For solid organ transplants, your chances of developing PTLD depend partly on the type of transplant you’ve had and whether or not you’ve had EBV infection in the past. You are more likely to develop PTLD if you have not had EBV, because the donor tissue could introduce it into your body. In general, your chances of developing PTLD after a solid organ transplant are:

- kidney transplant: around 1 to 3 in 100 people
- pancreas transplant: around 1 to 5 in 100 people
- liver transplant: around 1 to 6 in 100 people
- heart transplant: around 2 to 8 in 100 people
- lung transplant: around 3 to 10 in 100 people
- gut transplant or transplant of multiple organs: less than 10 in 100 people.

The risk of getting PTLD after a donor stem cell transplant depends mainly on how well matched you and your donor are and what conditioning treatment you need. Most cases occur within the first 6 months after transplant. In general, your chances are:

- matched, related donor: 1 to 3 in 100 people
- umbilical-cord transplant: 4 to 5 in 100 people
- matched, unrelated donor: 4 to 10 in 100 people
- partially-matched donor (sometimes known as a ‘haploidentical donor’, usually a family member): up to 20 in 100 people.
The risk of developing PTLD is higher in children than adults. This is because children are less likely than adults to have had EBV, which may be introduced in the donor tissue.

Your chances of developing PTLD are highest during the first few months after a transplant, when you are on a stronger dose of immunosuppressive medicine. However, it can sometimes develop later, even several years after your transplant.

Your transplant team will talk to you about your individual risk and any signs or symptoms you should look out for. Ask them if you have any questions about PTLD.

**Symptoms of PTLD**

The most common symptom of PTLD is a painless lump or lumps, usually in the neck, armpit or groin. These are swollen lymph nodes (glands). You might have swollen lymph nodes deep within the body, where they can’t be felt from the outside. PTLD can also develop outside lymph nodes, where it might cause local symptoms.

You might also have more general symptoms, such as fever, fatigue, weight loss and night sweats, or feel generally unwell. In people who have had a transplant, these general symptoms might be mistaken for other infections, symptoms of transplant rejection or a reaction to medication.

*If you have had a transplant, look out for any changes in your health. Contact your medical team if you are worried about your health.*

Diagnosing PTLD early gives the best chance of successful treatment. You might have regular blood tests to check the level of EBV in your blood. A high level of EBV might mean you are at risk of PTLD. If this is the case, your medical team might recommend having treatment to prevent PTLD developing. This might involve reducing the dose of your immunosuppressive treatment, or other treatments such as rituximab or T-cell therapy.

PTLD is diagnosed using a biopsy. You might also need other tests, including blood tests, scans, and possibly a bone marrow biopsy, to make sure your medical team has all the information they need to decide on the best treatment for you.
Treatment for PTLD

If you develop PTLD, your transplant team should work closely with your lymphoma team to decide on the best treatment for you. The treatment you need depends on what type of PTLD you have and how widespread it is. Other factors, like your age, general fitness and any other illnesses you have, are also considered.

Treatment of PTLD has improved dramatically in the last few decades. Be wary of looking at out-of-date websites or older research papers, as these might not reflect current treatment pathways. Most cases of PTLD can be treated successfully, especially if they are diagnosed early. People who are at risk of developing PTLD are usually monitored closely to make sure it is picked up early.

The most common treatments for PTLD are:

- a reduction in the dose of your immunosuppressives
- rituximab
- chemotherapy
- surgery or radiotherapy
- T-cell therapy
- other treatments.

Reduction in the dose of your immunosuppressive drugs

The first step in treating PTLD is to reduce your immunosuppressive treatment to the lowest possible dose. This has to be done carefully to prevent your body rejecting your transplant. Depending on how aggressive your PTLD is, your dose of immunosuppressants might be reduced gradually over several weeks or months.

You are monitored closely to make sure you’re not rejecting your transplant and to find out if your PTLD is responding to the reduction in immunosuppressive treatment.

If you have early PTLD, reducing your immunosuppressive drugs might be the only treatment you need. If you do not respond completely to a reduction in immunosuppressant dose, you might need additional treatment.
Rituximab

Rituximab is an antibody therapy that helps your immune system recognise and destroy B cells. You might have treatment with rituximab if:

- you have early PTLD that doesn’t completely respond to a reduction in your dose of immunosuppressive drugs
- you have a more aggressive form of PTLD.

Rituximab only works against types of PTLD that have developed from B cells.

Depending on the type of PTLD you have and how well you respond to treatment, you might have rituximab on its own or it might be combined with chemotherapy.

Chemotherapy

You might need chemotherapy if:

- you have not responded completely to a reduction in immunosuppressive treatment or rituximab therapy
- you have a specific type of PTLD such as T-cell lymphoma, Burkitt lymphoma or Hodgkin lymphoma
- you have PTLD affecting your central nervous system (CNS lymphoma).

The chemotherapy regimen (combination of drugs) you need depends on the type of PTLD you have. If you have a B-cell lymphoma, it is often given together with rituximab. This is called ‘chemo-immunotherapy’.

Surgery or radiotherapy

Surgery or radiotherapy are not often used to treat PTLD. You might have radiotherapy, or surgery to remove affected lymph nodes, if you have PTLD that is only affecting one part of your body. Sometimes they are used to control symptoms (for example pain or breathlessness) by reducing the size of the lymphoma.

Radiotherapy is sometimes used after chemotherapy to treat Hodgkin lymphoma.

T-cell therapy

T-cell therapy aims to get rid of EBV from your blood. It involves having treatment with specific T cells that react to EBV and stimulate your own immune system to destroy it. The T cells usually come from donated blood. You have them through a drip into your vein, similar to a blood transfusion.
T-cell therapy might be used to prevent PTLD in people who are at high risk of developing it, or to treat people who have not responded to other treatment options.

**Other treatments**

Several **targeted drugs** are being studied to see if they are effective at treating PTLD. They include:

- cell signal blockers such as *ibrutinib* and *idelalisib*
- proteasome inhibitors such as *bortezomib*
- radioimmunotherapy such as 90Y-ibritumomab tiuxetan
- checkpoint inhibitors such as pembrolizumab and nivolumab
- antibody–drug conjugates such as *brentuximab vedotin*.

These might be available as part of a **clinical trial** (a scientific study that tests medical treatments on volunteers). This could be a clinical trial that includes only people with PTLD or people with the type of lymphoma you have.

If you are interested in taking part in a clinical trial, visit **Lymphoma TrialsLink**, our clinical trial information service, for more information. When you are ready, you may wish to search our **clinical trials database** to see if there is a trial that might be suitable for you.

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**Risks associated with PTLD**

If you have PTLD, you are monitored very carefully by your medical team to support you through your treatment for lymphoma. However, there are some risks you need to be aware of if you have lymphoma and you have also had a transplant. Ask your medical team if you’re not sure what to look out for or if you have any questions about PTLD.

**Increased risk of infection**

Treatment for lymphoma can reduce your white blood cell counts, leaving you more vulnerable to infections. If your immune system is already affected by immunosuppressive drugs, you have an even higher risk of serious infections.

If you have PTLD, you may be given **growth factors** called G-CSF to help restore your white blood cell counts after chemotherapy. You might also be given other drugs, such as antibiotics, to prevent infections.

**Contact your medical team immediately if you have any signs of infection.**
Risk of transplant rejection

If your immunosuppressive therapy needs to be reduced to treat PTLD, there is a risk that your body might reject your transplant. You are monitored carefully to try to prevent this. However, if it happens, you might need another transplant.

If possible, your team will try to wait at least 1 year after your treatment for PTLD before you have another transplant. This reduces the risk of PTLD coming back. If you need another transplant, the risk of developing PTLD again is low.

References

The full list of references for this page is available on our website. Alternatively, email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

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