

Peripheral T-cell Lymphoma (PTCL)



OVERVIEW

Lymphoma is the 6th most common cancer in Australia in adult men and women. It can affect people of all ages and is the most common blood cancer. Lymphoma is a cancer of the immune system and affects lymphocytes which are a type of white blood cell. When lymphocytes gain DNA mutations they divide and grow uncontrollably resulting in lymphoma.

There are two main types of lymphocytes called B lymphocytes (B-cells) and T lymphocytes (T-cells). Lymphomas caused by B-cells are more common and account for around 85% of lymphoma cases and lymphomas caused by T-cells account for around 15% of lymphoma cases. The first lymphoma to be discovered was called "Hodgkin lymphoma" (around 15% of all B-cell lymphomas), after Thomas Hodgkin, who described it. All subsequent lymphomas discovered were called "non-Hodgkin lymphoma" (around 90% of all lymphomas, both B-cell & T-cell lymphomas).

There are over 80 different subtypes of lymphoma, that are classified according to its clinical behaviour. "Aggressive" (high grade or fast growing) lymphomas are those that grow quickly, usually weeks to months and need treatment immediately. "Indolent" (low grade or slow growing) lymphomas usually develop over years and often are not treated straight away but are monitored. It is important to know your subtype of lymphoma. Lymphoma cells can travel to any part of the body and be found in lymph nodes, the bone marrow, the spleen, blood, bone, skin and almost any organ or tissue.

Peripheral T-cell lymphoma (PTCL) is a form of lymphoma accounting for around 10% of lymphoma cases and develop from mature-stage T-cells and natural killer (NK) cells. "Peripheral" does not refer to the extremities, but as a cancer that arises in the lymphoid tissue outside of the bone marrow such as lymph nodes, spleen, gastrointestinal tract, and skin. PTCL affects both men and women and can also affect people in childhood and young adolescent age groups.

PTCL is an aggressive lymphoma which means the abnormal T-cells are fast growing. Most commonly the first sign of PTCL is a painless lump that is rapidly growing in the neck, arm pit or groin that is caused by the swelling of the lymph nodes due to the presence of the lymphoma. For some patients, this swelling

may be painful if the lymph node is pressing on an area of the body causing pain. Other symptoms may include sweats, fever, unexplained weight loss, generalised all over body itch and people may also notice fatigue, loss of appetite, shortness of breath or pain.

There are more than 29 different subtypes of PTCL which may affect what treatment a person receives and how well they respond to this treatment. Each individual subtype of PTCL is therefore very rare and most are aggressive in nature with the exception of some forms of cutaneous T-cell lymphomas (CTCL). There are 4 main groups of PTCL; cutaneous, extranodal, nodal and leukaemic. The most common PTCL subtypes are as follows:

Peripheral T-Cell Lymphoma Not Otherwise Specified (PTCL-NOS) is the most common subtype of PTCL accounting for 35 percent of T-cell lymphomas and refers to a group of diseases that do not fit into any of the other PTCL subtype. The disease is aggressive and can be nodal and/or extranodal which may include the liver, bone marrow, intestinal tract and the skin. PTCL-NOS usually occurs in adults in their 50s and 60s and many tend to relapse (come back).

Angioimmunoblastic T-Cell Lymphoma (AITL) is one of the most common subtypes of PTCL, accounting for about 20% of all T-cell lymphomas. AITL is a fast-growing nodal lymphoma, which displays common symptoms including generalised lymphadenopathy (swollen or enlarged lymph nodes), fever, weight loss, skin rash, and some types of autoimmune disorders. Patients are mostly diagnosed from around 60 years of age and often with advanced disease.

Anaplastic Large Cell Lymphoma (ALCL) is a common subtype of PTCL accounting for 10% of PTCL lymphomas. ALCL has the presence of the protein, 'CD30 antigen' on the surface of lymphoma cells is the hallmark of the disease. ALCL can occur in two different forms, a systemic type, where it is found mainly in lymph nodes and a primary cutaneous type, where it occurs only in the skin.

There are two subtypes: ALK-negative and ALK-positive, depending on whether the lymphoma cells produce a protein called 'anaplastic large cell kinase' (ALK). Systemic ALK-positive ALCL is more likely to affect children and young adults (median

age 34), although there is a group who present later in life. People with systemic ALK-negative ALCL present at a later age (median age 58 years). Systemic ALCL is slightly more common in men than in women.

Cutaneous T-Cell Lymphoma (CTCL) is a rare extranodal form of T-cell lymphoma. The mutated T-cells migrate to the skin which often first presents as a rash which can be itchy. As the disease progresses the lesions form plaques and tumours which change shape as the disease progresses. The lymphoma can then spread to other parts of the body. These lymphomas are generally less aggressive and are treated differently than other types of PTCL. The most common subtype of CTCL is mycosis fungoides, accounting for 50% of cases. It is generally an indolent lymphoma that starts in the skin and can appear as patches (look like a rash), plaques that are often mistaken as eczema, psoriasis or dermatitis or tumours (raised bumps which may or may not ulcerate).

Sezary Syndrome is a rare subtype of CTCL that affects both the skin and peripheral blood. The most common symptoms are swollen lymph nodes and a red, very itchy rash that covers large portions of the body. Abnormal T-cells, called Sezary cells can be seen under a microscope and are present in the blood.

Adult T-Cell Leukaemia/Lymphoma (ATLL) is a rare and often aggressive T-cell lymphoma that can be found in the blood, lymph nodes, skin or other areas of the body. ATLL has been linked to infection by HTLV-1 (sexually transmitted or exposure of contaminated blood), although less than 5 per cent of people with HTLV-1 will develop ATLL.

Enteropathy-Type T-Cell Lymphoma is a very rare and aggressive extranodal PTCL subtype. The lymphoma generally develops in the intestines (small intestine or colon). Symptoms can include abdominal pain, weight loss, diarrhoea or obstruction (on diagnosis). There are two forms, one type has been known to be preceded by celiac disease.

Nasal NK/T-Cell Lymphoma (NKTCL) is an aggressive, rare subtype which develops from NK cells (similar features to T-cells) and has been associated with Epstein-Barr virus. NKTCL frequently occurs in the nasal and upper airway passages but can also involve other organs (extranodal) including the gastrointestinal tract, and skin.

Hepatosplenic Gamma Delta T-Cell Lymphoma is an extremely rare extranodal lymphoma. It is an aggressive, systemic lymphoma that can infiltrate the liver, spleen, blood, and bone marrow. It is difficult to diagnose, often requiring a biopsy of the liver or spleen and most often occurs in young adults and most common in males.

**Note: For further information about most of these subtypes, refer to their individual fact sheet.*

DIAGNOSIS AND STAGING

A biopsy is always required for a diagnosis of PTCL. A biopsy is a surgical procedure to remove part of or all of an affected lymph node or other abnormal tissue to look at it under the microscope. The biopsy can be done under local or general anaesthetic depending on what part of the body is being biopsied.

Once a diagnosis of PTCL is made there are further tests that need to be performed to see where else in the body the lymphoma may be and is referred as staging (I-IV). Because PTCL is a blood cancer, the lymphoma can travel all over the body, so it is important that a check of the entire body is done looking for the lymphoma. Staging tests may include:

- Positron emission tomography (PET) /CT scan
- Computed tomography (CT) scan
- Bone marrow biopsy
- Lumbar puncture
- Further blood tests

Patients may also undergo a number of baseline tests prior to any treatment commencing to check their organ function and these baseline tests may include a heart scan and blood tests.

**Note: from here on, we will only be discussing the treatment for aggressive PTCL.*

TREATMENT OPTIONS

PTCL is generally an aggressive lymphoma and treatment is started soon after diagnosis. For most subtypes of PTCL, a combination of chemotherapy medicines are used to treat patients, with some also receiving radiotherapy. These may include:

- CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone)
- CHOEP (CHOP with the addition of etoposide)
- Chemotherapy followed by autologous stem cell transplant (some high risk)

For some people, the initial treatment is effective and the PTCL does not return after treatment, however for some people where the lymphoma returns (relapses) or in the rare cases does not respond to initial treatment (refractory), there are other treatments that can be successful.

- High dose chemotherapy & autologous stem cell

FACT SHEET

- transplantation (own stem cells; majority)
- High dose chemotherapy & allogeneic stem cell transplantation (donor stem cells; minority)
- Combination chemotherapy
- Biological medicines – such as romidepsin, brentuximab or pralatrexate
- Radiotherapy
- Clinical trial

TREATMENTS UNDER INVESTIGATION

Many new individual and combination medicines are currently being tested in clinical trials around the world for both newly diagnosed and relapsed/refractory PTCL including:

- Romidepsin (Istodax™)
- Pralatrexate (FOLOTYN™)
- Brentuximab Vedotin (Adcetris)
- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo™)
- Durvalumab (IMFINZI™)
- Lenalidomide (Revlimid™)
- Vorinostat (Zolinza™)
- Belinostat (Beleodaq™)
- Alemtuzumab
- Bortezomib (Velcade™)
- Carfilzomib (Kyprolis™)
- Temsirolimus
- Deoxycoformycin (Nipent™)
- Tipifarnib (Zarnestra™)
- 5-Azacitidine (Vidaza™)

CLINICAL TRIALS

Clinical trials are essential in identifying effective medicines and determining optimal doses of these medicines for people diagnosed with lymphoma. People who are interested in participating in a clinical trial can find one using the following methods:

1. Speak to their specialist to see what options are available
2. Go to the ClinTrial Refer website www.clintrial.org.au to search available clinical trials
3. Download the ClinTrial Refer app from the Apple or Android stores for your smart phone or device. The ClinTrial Refer service was developed to connect patients, health professionals and clinical trial sites to improve access to clinical trials for patients in Australia.
4. Blood Cancer Research Western Australia: www.bloodcancerswa.org.au/trials
5. See 'Understanding Clinical Trials' fact sheet, www.lymphoma.org.au

FOLLOW UP

Once treatment is completed, people with lymphoma need to be followed up by their specialist with regular appointments to monitor:

- Evaluate the effectiveness of the treatment
- Ongoing treatment side effects
- Recovery from treatment
- Signs of lymphoma relapsing
- Potential late effects caused by treatment that can occur months or years later, that can be based on the duration and frequency of treatment, age, gender and overall health of each person

RESOURCES AND SUPPORT

Lymphoma Australia offers a wide variety of resources and support for people with lymphoma and their carers. Please visit our website www.lymphoma.org.au for further information.

Cutaneous Lymphoma Foundation (USA), promote awareness and education for those affected. For more information please visit their website www.clfoundation.org

SOME QUESTIONS TO ASK YOUR DOCTOR

- What subtype of PTCL do I have?
- Is there any additional testing that can be done to give you greater insight into how to treat my type of lymphoma?
- What are the treatment options for my type of PTCL?
- Are there any treatment options that are better for my type of lymphoma but are yet to be funded by the PBS in Australia?
- Are there any clinical trials currently available to me?
- If you think my PTCL has relapsed, will you do another tissue biopsy to confirm this?

This resource was last reviewed and updated August 2019