FACT SHEET

Transformed Lymphoma

OVERVIEW

Lymphoma is the 5th most common cancer in Australia and is the most common blood cancer. Lymphoma is a cancer of the immune system and effects 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 are divided into groups, or categories, based on several classifications. The first lymphoma to be discovered was called "Hodgkin" lymphoma, after Thomas Hodgkin, who described it. All subsequent lymphomas discovered were called "non-Hodgkin lymphomas" (now over 60 different types). Lymphomas caused by B-cells are more common and account for around 85% of lymphoma cases (almost all are non-Hodgkin lymphomas) and lymphomas caused by T-cells account for around 15% of lymphoma cases (all T-cell lymphomas are non-Hodgkin lymphomas).

Lymphoma is also classified according to its clinical behaviour. "Aggressive" (or high-grade) lymphomas are those that grow very quickly-usually in weeks to months and need treatment immediately. "Indolent" (or low-grade, i.e. slow growing) lymphomas usually develop over years and often are not treated straight away but are monitored. 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.

TRANSFORMED LYMPHOMA

A transformed lymphoma is a lymphoma that was initially diagnosed as indolent (slow-growing) but has transformed into an aggressive (fast-growing) disease. Low-grade lymphomas are typically made up of small, slow-growing cells. If the proportion of larger, faster-growing lymphoma cells increases, the lymphoma begins to behave more like a faster-growing high-grade lymphoma such as diffuse large B-cell lymphoma. This process is known as 'transformation'. Although indolent B-cell lymphomas, such as follicular lymphoma, marginal zone lymphoma or chronic lymphocytic leukaemia (CLL), are most commonly associated with transforming to aggressive disease, slow-growing T-cell lymphomas can also progress to aggressive disease.
When we talk about transformed lymphoma we mean the switch from a slow-growing indolent disease with an indolent clinical history to a more aggressive appearance under the microscope and a more aggressive clinical history. It is important to make these distinctions because there are some people who have indolent follicular lymphoma and then they end up with quite aggressive disease but their biopsy still looks like follicular lymphoma. That is not a transformation, that is a more aggressive behaviour of a follicular lymphoma. Transformation is important because if your lymphoma 'transforms' into a more aggressive subtype, you will need a different type of treatment.

WHAT TYPES OF LYMPHOMA CAN TRANSFORM?

Transformation usually occurs in B-cell lymphomas but it can occur in T-cell lymphomas however this is much less common. It can happen with any low-grade non-Hodgkin lymphoma, but in particular:

- Follicular Lymphoma – most common transformation
- Marginal Zone Lymphomas (including MALT lymphomas)
- Lymphoplasmacytic lymphomas (including Waldenström's macroglobulinaemia)
- Small Lymphocytic Lymphoma / Chronic Lymphocytic Leukaemia (this transformation is called Richter syndrome)
- Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)

WHAT CAUSES THE TRANSFORMATION?

The genes in low-grade lymphoma cells can become damaged over time, this genetic damage causes the cells to begin to grow rapidly, more like the cells in a high-grade lymphoma. This doesn't mean that a person whose disease has transformed will only have aggressive cancer cells, rather the person's tumor will most likely include both indolent and aggressive cancer cells.

Not every low-grade lymphoma will transform; over half of follicular lymphomas will never transform for example. There is no definite way of telling in advance which lymphomas will transform into a faster-growing type. Being in a particular age group or being a male or female does not make the lymphoma more likely to transform. Nothing you do (or have done) can make transformation more or less likely to happen. It has not been shown that any of the treatments for low-grade lymphomas (eg.

chemotherapy drugs, antibody therapy or radiotherapy) increase or decrease the likelihood of a lymphoma transforming.

Transformation can happen at any time from when the low-grade lymphoma is first diagnosed onwards, but the risk is very low. Around 1-3% of follicular lymphomas will transform each year. The average time between the diagnosis of a low-grade lymphoma and its transformation is 3–6 years, but it has been known to happen many years later. It becomes more unusual after about 15 years.

HOW TO KNOW IF LYMPHOMA HAS TRANSFORMED

If you have a low-grade lymphoma and you develop new symptoms, your medical team will want to find out if your low-grade lymphoma has relapsed or if it has transformed.

Transformation might be detected if there is a change in your symptoms, such as:

- A rapid increase in the size of your lymph nodes
- Rapid swelling of your liver or your spleen
- Weight loss, sweats or fevers (these are known as 'B symptoms')

Transformation can also be detected when you have your blood test as there are certain chemicals measured and there can be changes such as high levels of lactate dehydrogenase (LDH) and high levels of calcium. It is important that a biopsy of a lymph node, bone marrow or another affected tissue is done to show large fast-growing lymphoma cells. Transformation can happen in some areas of your lymphoma but not in others, so you might have a PET/CT scan to find out where the most likely site of transformation is located.

TREATMENT OPTIONS FOR TRANSFORMED LYMPHOMA

Your treatment will depend on:

- What treatments you have had in the past for your low-grade lymphoma (if any)
- How well your lymphoma responded to past treatments
- Your general health

A transformed lymphoma needs to be treated in the same way as a high-grade lymphoma. Treatment usually consists of combination chemotherapy. Possible treatments include: R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) which is given over one day and repeated every 21 days to complete a cycle of treatment. There are other more intensive combination chemotherapy regimens (with or without rituximab) and there might be a possibility of an autologous stem cell transplant if the lymphoma responds sufficiently to the more intensive chemotherapy and your general health is good enough. If the transformed lymphoma is in just one place, it might be treated with radiotherapy (usually given after a course of chemotherapy).

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 http://www.clintrial.org.au/ to search available clinical trials

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.

FOLLOW UP

Once treatment is completed, people with lymphoma need to be followed up by their specialist to monitor and evaluate the effectiveness of the treatment, ongoing treatment side effects and to investigate any signs of the lymphoma relapsing. During this time, you will receive regular appointments with your specialist as well as blood tests and sometimes scans as required to monitor your progress. Some treatments received for lymphoma can cause effects later in time which can vary based on the duration and frequency of treatments, age, gender, and overall health of each patient. These potential late effects will be monitored for and treated if required during your follow up care with your specialist.

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.

SOME QUESTIONS TO ASK YOUR DOCTOR

- If you think my lymphoma has transformed, will you do another tissue biopsy to confirm this?
- What treatment options are available for my transformed lymphoma?
- Are there any treatment options that are better but are yet to be funded by the PBS in Australia?
- Are there any clinical trials currently available to me?