NATIONAL CENTRE FOR HUMAN RETROVIROLOGY

Your guide to

Adult T-cell Leukaemia /Lymphoma (ATL)

Information for patients, relatives and carers

What is ATL?

Adult T-cell leukaemia/lymphoma (ATL) is a rare type of blood cancer that can develop in people infected with the human T- lymphotropic virus type I (HTLV-I). It occurs in a type of white blood cell called a T-cell or T-lymphocyte, which is responsible for recognising and fighting infection. ATL is one of the types of non-Hodgkin lymphoma (NHL) but only occurs in individuals with HTLV-1 infection.

ATL cells increase in number in the blood or in a lymph node (gland). They can spread to other glands, organs such as the liver or spleen, the skin and the bone marrow. ATL can take the form of either lymphoma or leukaemia, or have features of both. Lymphoma means the lymph nodes are enlarged due to the increase in abnormal T-lymphocytes.

Leukaemia, literally meaning “white blood”, describes the increased numbers of abnormal white blood cells in the blood and the bone marrow. This excessive growth of white blood cells can interfere with the function of the bone marrow, which produces new blood cells, leading to reduced production of other blood cells. This can put the patient at a higher risk of infection, anaemia and/or easy bruising/bleeding.

Who gets ATL?

Most patients who develop ATL live in, or are descendants of those who come from the areas where HTLV-I infection is most common. These areas include Japan, the Caribbean, Romania, West Africa, the Middle East and South America.

Persons carrying HTLV-1 infection have a three to five per cent chance of developing ATL during their lifetime. However the risk is mostly in those who were first infected at birth or during early childhood.

The average age at which ATL occurs is 55 years.

Environmental factors including diet, air quality, radiation or toxic chemicals do not play a role in the development of ATL.

What are the types of ATL?

There are four main types of ATL:

- **Acute ATL**

Symptoms can include tiredness, fevers and sweats (often at night), itchy skin, weight loss, confusion and frequent infections or a rash. Some patients notice enlarged glands, which will feel like firm swellings in the neck, armpits and/or groins. Acute ATL is diagnosed if the blood tests show a high white blood cell count and typical ATL cells seen down the microscope, often with enlarged lymph node (glands) seen on CT or PETCT scans.

- **ATL lymphoma**

Symptoms are similar to those for acute ATL (please see above). However, in ATL lymphoma, the ATL cells are only present in the glands (lymph nodes) or other organs, usually liver, spleen or tonsils, but not the blood, so swellings in the glands is often the most obvious symptom.

- **Chronic ATL**

Symptoms may include tiredness, weight loss and itchy skin but many patients may have no symptoms (asymptomatic). Chronic ATL is therefore often discovered following a routine blood test or when tests are done for another reason and a raised white blood cell count is found.

- **Smouldering ATL**

Symptoms include skin rashes or itchy skin only, with no evidence of any leukaemia.

How is ATL diagnosed?

ATL is usually diagnosed by:

- Finding a raised white blood cell count due to increased numbers of lymphocytes
- Finding of enlarged lymph nodes on CT or PETCT imaging. Lymph nodes may need to be tested (biopsy) to confirm the diagnosis
- Seeing the typical ATL cells (known as 'flower cells') under the microscope
- Showing that these lymphocytes belong to a particular subset called CD4 CD25
- Demonstrating HTLV-I infection

What happens if I am diagnosed with ATL?

Before treatment is started further tests to see the spread of the disease are performed. These usually include:

- **CT** (computerised tomography) or **PET/CT** (positron emission tomography) scan of the body (from the neck to the groin) to look for enlarged glands, liver or spleen. CT scan is a type of three-dimensional X-ray and will provide detailed cross-sectional pictures of your body. A PET/CT is similar to a CT scan but also uses a mildly radioactive drug to identify areas where cells are more active than others
- **Bone marrow biopsy** (sample) to look for ATL cells
- **A lumbar puncture**, to check whether the brain or spinal cord has been affected by obtaining a sample of the fluid that circulates round the brain and spinal cord

How is ATL treated?

Smouldering and Chronic ATL may need to be treated if you have symptoms, or if the lymphocyte count is increasing rapidly. If treatment is needed we now know that antiviral therapy is best. Sometimes these types are treated even if you are feeling well to reduce the risk of the disease becoming more aggressive in the future.

ATL lymphoma and acute ATL always require treatment. Lymphoma subtypes always require a combination of chemotherapy (anti-cancer treatment) and antiviral therapy may be added in during chemotherapy or at the end of treatment (maintenance). Antiviral therapy is sometimes used as the main therapy for acute ATL providing the lymph nodes are not too enlarged.

Chemotherapy drugs kill cancerous cells and are usually most effective when given in combination. One combination used in treatment of ATL in the UK is called CHOP (cyclophosphamide, vincristine, doxorubicin and prednisolone). However, other combinations are also available and may be used. To prevent ATL from spreading to the brain chemotherapy may be given via lumbar puncture. Details on the individual drugs and side effects can be found on the Macmillan cancer support website (www.macmillan.org.uk).

Side-effects of chemotherapy may include nausea and vomiting, diarrhoea or constipation, and increased risk of infection. However, supportive medications are given to prevent or manage these side-effects.

Antiviral therapy for ATL consists of a combination of two drugs:

- Interferon-alpha (IFN-α) is a naturally occurring substance made by blood cells to fight infections. It is now widely used in treatment of ATL and given by injection under the skin (subcutaneous injection). Patients or relatives can learn to administer it.

- Zidovudine, which was the first drug used to treat HIV infection, is also effective in treating ATL when combined with IFN-alpha. Side-effects of antiviral therapy may include flu-like symptoms, tiredness, loss of appetite, nausea, an increased risk of infection, and depression. Paracetamol helps to relieve these side-effects which also usually become less noticeable over time.

ATL is prone to relapsing even after successful initial therapy and so an allogeneic stem cell transplant (sometimes called a bone marrow transplant) may be considered in order to prevent the ATL returning. Stem cell transplantation usually involves a prolonged hospital stay for many weeks and consists of initial chemotherapy and/or radiotherapy (X-ray treatment) to eradicate the patient's own blood producing cells (stem cells) and allow the new stem cells from the healthy donor to take their place (grafted). Further details on stem cell and bone marrow transplantation may be found on the Macmillan website (www.macmillan.org).

Stem cell transplantation offers a potential for cure but carries some risks and is not suitable for all patients. The patient must:

- Have a suitable donor
- Be fit enough to undergo chemotherapy, followed by a period of prolonged immune deficiency when there is a high risk of infections
- Have had a good initial response to first-line treatment

Maintenance therapy

After initial treatment with either chemotherapy or antiviral therapy, you may need to stay on a maintenance therapy in order to keep the ATL from returning. Types of maintenance therapy include low dose antivirals or low dose oral chemotherapy.

Other treatments are being investigated to improve the results of ATL therapy. They are normally given to patients who did not respond to first line treatments outlined above or in whom ATL has recurred after initially effective treatment.

These include:

- Monoclonal antibodies, which specifically target and destroy the cancerous cells while minimising damage to the body's normal cells. Alemtuzumab (Campath-1H), basiliximab (anti-CD25), brentuximab (anti CD30) and mogamulizumab (anti-CCR4) are monoclonal antibodies that have been used in ATL treatment with varying responses.
- Arsenic trioxide and lenalidomide – these are treatments that target pathways in the cancer cells or the environment of the cancer cells leading to their destruction.

Summary

ATL is a rare condition that remains difficult to treat. Until recently survival has been measured in months rather than years. However, antiviral therapy, either alone or together with chemotherapy, has significantly improved the survival rates and new drugs are being tested in clinical trials. Bone marrow transplantation offers a chance for cure but is high-risk and not suitable for all patients.

Further research, including clinical trials, is essential to make further progress in understanding and treating this disease. Please carefully consider this option if a research study is available to you.

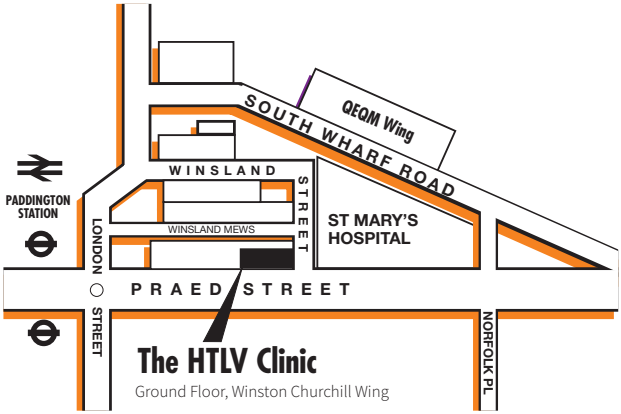
Where to find HTLV services in the UK

The National Centre for Human Retrcovirology is situated on the ground floor of the Winston Churchill Wing at St Mary's Hospital, London.

You are advised to travel, if possible, by public transport when visiting the clinic. Car parking is very limited and you may find it difficult to find a place to park near the hospital. Disabled parking is available on Winsland Street. The nearest tube station is Paddington (Bakerloo, District, Circle and Hammersmith & City lines), which is also a railway station. Buses that stop on Praed Street are numbers 7, 15, 23, 27 and 36.

If you or your family wish to know more about HTLV, ATL, HAM/TSP, or participate in research, please contact:

The National Centre for Human Retrovirology
Ground floor, Winston Churchill Wing
St Mary's Hospital, Praed Street, London W2 1NY
Tel: 020 3312 6604
Email: imperial.htlv@nhs.net
More information can be found at: www.htlv.eu



There are also HTLV Clinics in Birmingham, Manchester and York – see addresses and contact details below:

Manchester HTLV Clinic
Pennine Acute NHS Trust, Department of Infectious Diseases,
North Manchester General Hospital, Crumpsall, Manchester M8 5RB
Tel: 0161 720 2734

Birmingham HTLV Clinic
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital Birmingham, 3rd Floor East Block,
Main Drive, Edgbaston, Birmingham B15 2TH
Tel: 0121 371 6954

York HTLV Clinic
York Teaching Hospitals NHS Foundation Trust
Monkgate Health Centre, 31 Monkgate, York YO31 7WA
Tel: 01904 725423

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