Chronic Myelogenous Leukaemia

You have just been diagnosed with chronic myelogenous leukaemia (CML).

'Leukaemia' means it is a blood disorder characterised by an elevated white blood cell count.

'Myelogenous' refers to the bone marrow, that is the soft tissue located inside your bones which is responsible for the production of all types of blood cells. Some chromosome anomaly in the stem cells of the bone marrow (or blasts, which produce all blood cells) is responsible for this overproduction.

'Chronic' means that the onset of the disease is gradual and the disease progresses slowly at first.

Medecin's notes :

Chronic myelogenous leukaemia is one of the 'myeloproliferative' syndromes. Its main feature is the sustained overproduction of white blood cells (or leucocytes) by the bone marrow. Some of those white blood cells are abnormal; they are immature, i.e. they pass into the blood before their growth is over.

The disease has to do with an anomaly occurring in the fusion of two stem-cell chromosomes in the bone marrow, leading to the formation of a small abnormal chromosome called the Philadelphia chromosome (after the American city where the two researchers who discovered it worked in the 60s). This anomaly stems from a chromosome 9 gene (called ABL) mistakenly rearranging with a chromosome 22 gene (called BCR). The end product is the BCR-ABL gene which is present only in the disease-specific cells. This gene abnormally produces an enzyme called tyrosine kinase which is responsible for the overproduction of white blood cells.

The Philadelphia chromosome is a genetic defect acquired by abnormal cells, which means that the disease is not hereditary. Its causes are unknown sofar. However CML has been observed to be more common among Hiroshima and Nagasaki nuclear explosion survivors, which has led to suspect ionising radiations as likely causes of the disease, but this has never been truly demonstrated.

Chronic myelogenous leukaemia is relatively rare and only 600 people are diagnosed with it each year in France. It is slightly more common among men than among women and its frequency rises with age. The average age at diagnosis is 53 years.

Diagnosis

Chronic myelogenous leukaemia is a slowly-growing disease at first, with no specific symptom outside moderate fatigue and an enlarged spleen. It is most often discovered by chance, during a blood test showing a higher white blood cell count.

The diagnosis is then confirmed with several investigations:

- a full blood count
- a bone marrow biopsy (myelogram). It is performed under local anaesthesia and consists in inserting a hollow needle into a bone, usually either the breastbone or the hipbone. A small quantity of bone marrow is then removed to make a karyotype, i.e. a study of the chromosomes, and to look for the Philadelphia chromosome. The sample is also used to assess the amount of abnormal white cells in the bone marrow.
- molecular studies of the blood to screen for the BCR-ABL gene, to assess the number of carrier-cells carry it (that is the BCR-ABL load) and thereby to determine the number of leukaemic cells.

The diagnosis is then made when both the Philadelphia chromosome and the BCR-ABL gene are found. These different investigations also allow to stage the disease.

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Chronic Myelogenous Leukaemia (suite)

Main adverse effects

CML treatments may cause adverse effects. Most frequent are leg cramps and oedema (superficial swelling) of the face, especially of the eyelids. These swellings occur mostly as the treatment is started. There are frequent reports of weight gain and stomach troubles (nausea, vomiting or diarrhoea). These adverse effects are not necessarily present and their severity varies from one patient to another.

Your treatment may induce adverse effects and carry risks. Your doctor will keep you informed and tell you what symptoms to watch out for before you start on the suggested treatment.

Participating in a clinical trial

The best way to contribute to the improvement of disease management is to treat patients in the context of clinical trial. If your doctor suggests this could apply to you, he will explain its purpose, protocol, expected benefits, potential risks and will give you an information leaflet.
Participating in a trial of course means you will first have to give your written informed consent.

Useful contacts:

- **Secretarial / appointment:**
- **Nursing consultation:**
- **Consulting psychologist:**
- **Social worker:**
- **In an emergency:**

Evolution

There are three stages to chronic myelogenous leukaemia:

- **Chronic phase.**
  The disease is usually diagnosed at this stage. During this phase the evolution is then slow and there are hardly any symptoms. There are still few abnormal white blood cells in the bone marrow and the blood. This phase lasts about four years without any treatment.
- **The accelerated phase.**
  It is characterised by a higher rate of abnormal white blood cells in both the bone marrow and the blood, and by a higher BCR-ABL load or the apparition of new chromosome anomalies. Symptoms, though non-specific, are more frequent, like fatigue, loss of appetite, unexplained fever. If untreated then the disease will evolve towards the acute phase over a few months.
- **Blastic phase.**
  The disease has evolved from chronic to acute. The bone marrow is invaded by abnormal white blood cells and stops working as it should. The disease is then very serious.

Management

The treatment of chronic myelogenous leukaemia rests on tyrosine kinase inhibitors. These drugs block the abnormal enzyme, thereby allowing the white blood cell count to drop gradually back to a normal range. Meanwhile the BCR-ABL load in the blood drops and the Philadelphia chromosome finally becomes undetectable in the bone marrow.
Response to this chronic phase treatment is usually good. However should it prove inefficient or not efficient enough another tyrosine kinase inhibitor can be substituted for the first one. Today several such drugs are available.
The treatment must be taken unfailingly on a daily basis.

Follow-up

Treated patients whose white blood count is back to normal must see their haematologist every three to four months to check their overall health condition. Various blood tests are then performed, especially to measure the BCR-ABL load. Sometimes it is necessary to know how much of the drug is present in the blood to ensure the right dosage is prescribed.

Thanks to the drugs currently available people treated for chronic myelogenous leukaemia can have an almost normal life.

Patients association → Fédération Leucémie Espoir
Site Internet : www.leucemie-espoir.org

Association Laurette Fugain
www.laurettefugain.org