Primary myelofibrosis

You have just been diagnosed with primary myelofibrosis, also known as myeloid splenomegaly.

'Myelofibrosis' refers to bone marrow fibrosis, that is to say the bone marrow has become invaded by fibrous tissue. 'Primary' means there is no known cause for this disease so far.

'Splenomegaly' means that the spleen, the organ in the left part of the abdomen, has enlarged. 'Myeloid' refers to the bone marrow, i.e. the tissue inside your bones where all blood cells are produced. The origin of the disease is in the bone marrow.

Medecin's notes :

Primary myelofibrosis is one of a group of chronic conditions known as myeloproliferative syndromes which are characterised by the overproduction of one or more types of blood cells by the bone marrow. In the case of your condition this overproduction leads to two main consequences:

- Gradual bone marrow fibrosis, which disrupts normal blood cell production
- Spleen enlargement. Fibrosis modifies the environment of bone marrow cells so that some migrate into the blood and settle in the spleen to find an environment more favourable to their development, which causes the spleen to swell.

The early stage of the disease is usually symptom-free, but the following signs may gradually appear:

- Overall signs due to disease progress, such as fever, weight loss, sweats (especially in the evening and at night), fatigue and bone pain.
- Troubles, mostly digestive ones, due to spleen swelling (discomfort or pain after eating, constipation). When it is much enlarged and presses on other organs, the spleen may be responsible for abdominal fullness and breathlessness on exertion, and more rarely for leg swelling.
- Anaemia, that is to say a lower red blood cell count and haemoglobin level, inducing fatigue, pallor, breathlessness and palpitations on exertion.

Primary myelofibrosis is a rare disease: each year only three to seven new cases per million inhabitants are diagnosed, i.e. 200 to 400 new cases for the whole of France. It usually affects the over 50-year-olds, with an average diagnostic age of 60 to 65. The disease is acquired, which means that it is neither hereditary nor contagious. Its cause is unknown as yet, except when it is secondary to a similar disease, such as Vaquez disease (overproduction of red blood cells by the bone marrow) or basic thrombocytopenia (increased platelet production).

Diagnosis

Primary myelofibrosis is most often suspected in case of anaemia or of an enlarged spleen combined with abnormal blood test results (full blood count). As it is almost always enlarged the spleen can be felt though the abdominal wall and it can be accurately measured with a US or a CT scan.
In three quarters of cases the full blood count shows anaemia (haemoglobin ≤ 12g/dl), with misshaped red blood cells (tear- or pear-shaped). An abnormally small amount of bone marrow cells may also be observed among white blood cells (myelocytes, erythroblasts) which are 'immature' white and red blood cells.
The diagnosis of the disease requires a biopsy of the bone marrow (or osteomedullary biopsy). This investigation is performed under local anaesthesia and consists in inserting a hollow needle into the iliac bone, i.e. the bulging part of the pelvis, so as to remove a sample of bone marrow. This is then examined under a microscope to look for the disease's specific features, mostly fibrosis associated with cell and blood vessel anomalies.

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Primary myelofibrosis (suite)

Blood cells produced in the bone marrow

Three types of blood cells are produced in the bone marrow:

- Red blood cells or erythrocytes carry haemoglobin-bound oxygen to the body's tissues. The haemoglobin rate best testifies to the number of red blood cells. It normally ranges between 12 and 16g/dl of blood in females and 13 to 17g/dl in males.
- White blood cells or leucocytes are necessary to fight infections. A normal white blood cell count ranges from 4 to 10 X 10^9, that is to say 400X10^9/l.
- Platelets allow blood to clot and prevent bleeding. Their range is from 150 to 400 X 109/l, that is to say 150000 to 400000/mm^3.

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:**

The diagnosis is further supported by the karyotype (chromosome study) made from the blood cells, as well as by screening for a genetic marker called JAK2, which is present in half of the patients. Neither the genetic modifications nor the JAK2 mutation are hereditary; they both appear with the disease.

Further blood tests enable to assess the functioning of other organs (such as the kidneys or the spleen).

The early signs of the disease (anaemia, white blood cell count, karyotype, overall signs…) enable to make the prognosis and to tentatively predict the progression of the disease. In most cases the latter is both chronic and over a long period of time. As years go by splenomegaly and anemia usually worsen; however a minority of patients may have a more acute form of the disease.

Treatments

Today there is no treatment likely to cure primary myelofibrosis. The treatment aims to lessen the symptoms and preserve quality of life, which is why, if there are no symptoms or complications, no treatment is usually prescribed and many patients do not need to be treated for a number of years.

When necessary treatment rests on chemotherapy, most often via the oral route, using a DNA-synthesis-inhibiting cytostatic agent. Its aim is to reduce the overproduction of the cells responsible for the disease. Meanwhile other treatments may be prescribed to replenish blood cells and counter anaemia; they may include corticosteroids, androgens, erythropoiesis stimulators or still angiogenesis inhibitors. When anaemia is severe or does not respond to these treatments, blood transfusions are required.

Research is active and new medications are being developed in ongoing clinical trials; they target the mechanisms responsible for the development of the disease, which are becoming better understood.

When the spleen becomes voluminous and troublesome, it may be surgically removed (splenectomy). However, this decision must be taken carefully as this surgery is delicate and may lead to serious complications, so that it should be performed only by a highly skilled medico-surgical team.

Hematopoietic stem cell transplantation is the only current treatment leading to a cure, but requires finding a perfectly matching donor. It is a constraining treatment which could induce serious complications and is only offered to young patients with a progressing form of the disease. This explains why transplantation concerns only a minority of patients. However lighter protocols have allowed to postpone the age limit.

Follow-up

The progress of primary myelofibrosis is chronic and gradual, with variations from one patient to another. It depends on several factors such as age, anaemia, overall signs, and other biological characteristics. Follow-up mainly relies on consultations with a hematologist at regular intervals and on blood tests.

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