Multiple myeloma

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**Medecin’s notes:**

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**Clinical features and diagnosis**

The onset of multiple myeloma does not correspond to specific symptoms. Aches and pains in the bones, mostly in the vertebrae, are the most common. ‘Pathological’ fractures may occur and may affect long bones (the thighbone, the humerus), the ribs or vertebrae (compression of the spine, sometimes complicated with spinal cord compression). Multiple myeloma may also result in fatigue, anaemia, kidney failure and hypercalcemia. Infections, especially bacterial ones, are frequent and sometimes suggestive.

In about 20% of cases there is no physical sign of the disease and the latter is suspected in case of an abnormal blood test (this is asymptomatic multiple myeloma). The diagnosis of multiple myeloma is often considered after blood tests. The most common one is called serum protein electrophoresis to study blood protein. This investigation allows to see if some monoclonal immunoglobulin is present (as it forms a well-identified peak sometimes called a ‘monoclonal spike’). Further investigations are then required to identify this immunoglobulin accurately and to measure its rate. Electrophoresis may also be performed with urine as some of the monoclonal immunoglobulin is often detectable.

Multiple myeloma is a bone marrow disorder characterised by the multiplication of an abnormal plasmocyte within the bone marrow. Plasmocytes produce antibodies (a kind of protein also called immunoglobulin) which protect the body against infections. Some of these cells may become malignant and multiply into countless copies, so-called malignant plasmocyte clones which are all identical. All those cells then produce the same antibody, called monoclonal protein (M protein) or monoclonal immunoglobulin.

Abnormal plasmocytes invade the bone marrow, leading to various aftermath:

- A weakened immune system; the M protein is not a functional antibody and normal antibodies cannot develop normally due to the lower rate of normal plasmocytes usually ensuring their production. As a result the body is less apt to fight off infections.
- Fewer blood cells may be produced within the bone marrow as abnormal plasmocytes develop to the detriment of other cells. Therefore multiple myeloma may lead to anaemia (a lower red blood cell count).
- Abnormal plasmocytes activate cells which destroy bone and interfere with bone growth. This often accounts for bone aches and pains and the increased risk of ‘pathological fractures’ as they occur after minor trauma or after no trauma at all. Bone destruction may also lead to a higher blood calcium level (hypercalcemia), inducing other troubles.
- The monoclonal immunoglobulin produced by the abnormal plasmocytes circulates in the blood and may form deposits in the kidneys leading to impaired kidney function. Indeed kidney failure is a frequent complication of multiple myeloma.

In France about 3,500 people are diagnosed with multiple myeloma each year and about 12,000 people are under medical supervision. The disease affects men (54%) slightly more frequently than women and rather elderly people; the average age at diagnosis ranges from 70 years in males to 74 years in females. However about 65% of patients are below 65 when the disease is diagnosed. Today there is still no known reason for multiple myeloma, but it is neither contagious nor hereditary.
Multiple myeloma (suite)

Monoclonal dysglobulinaemia and multiple myeloma

Multiple myeloma may start after so-called monoclonal dysglobulinaemia of undetermined significance (also said to be benign or apparently benign). The monoclonal spike is moderate with no other clinical, radiological or biological sign. Monoclonal dysglobulinaemia does not require treatment and will remain stable in the vast majority of cases, with no progress of any kind. It may however evolve into multiple myeloma or some other blood disorder even if the chance is slight (about 1% a year).

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:

Patients association ➔ Association Française des malades du Myélome Multiple (AF3M)
Adresse : 86 ter Rue Hoche, 78 390 Bois d’Arcy. E-mail : myelomemultiple@aol.com

Meanwhile full body Xray pictures are taken to screen for possible bone damage.

Lastly in order to obtain foolproof evidence of the diagnosis a lumbar puncture (a myelogram) is performed. 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 examine the abnormal plasmocytes under a microscope and refine the prognosis with the study of the chromosomes and their genes.

Management

The diagnosis of multiple myeloma does not necessarily call for immediate treatment. Indeed as long as there are no symptoms studies have shown that treatment dose not bring any benefit as regards the progression of the disease. Routine medical supervision is enough with regular blood tests, urinalysis and Xrays.

The onset of symptoms requires a treatment tailored to different criteria such as the patient’s age and medical history and the features of the disease (whether kidney failure is present or not). Multiple myeloma treatment mainly relies on chemotherapy with such drugs as alkylating agents, corticosteroids, angiogenesis inhibitors and proetosome inhibitors mostly. Other drugs may be combined to protect bone mass (biphosphonates), prevent or treat anaemia (erythropoietin stimulants or ASE), prevent or treat infections and ease pain.

Various drug combinations and treatment courses are used. To put it simply:

- For the under-65s: treatment starts with induction chemotherapy over about four months to quickly alleviate the signs of the disease and allow to collect stem cells from the blood for later use. Then intensive treatment supported by a stem cell autograft is scheduled. The aim is to administer high doses of chemotherapy (alkylating agents) to destroy as many cancer cells as possible. The drawback of this treatment is the sharp drop of normal blood cells (so-called aplasia) which leaves the body defenceless against infections. In order to shorten aplasia and allow blood cells to be restored quickly an autograft is performed; before chemotherapy some of the patient’s stem cells are removed (stem cells produce all types of blood cells). They are collected by cytopheresis, a procedure which consists in passing a device through the blood in order to collect only stem cells which are then frozen. This procedure requires a several-week long hospital stay. The overall first line treatment course lasts six to eight months.

- For the over-65s: intensive chemotherapy combined with an autograft is seldom advised as too risky. Treatment consists in administering conventional chemotherapy over a longer period (twelve to eighteen months). These treatments usually lead to a plateau phase or a remission, i.e. an event-free period with a lower rate of the monoclonal immunoglobulin in the blood and/or urine so that drug treatment can be withdrawn. Regular medical supervision is then scheduled with blood tests, urinalysis and Xrays.

Unfortunately today treatments still offer no cure. After a lapse of time of various duration multiple myeloma tends to recur. A new treatment, different from the first one, will then be started.