Waldenstrom Macroglobulinaemia

- The titles in this series are intended to provide general information about the topics they describe.
- In many cases the treatment of individual patients will differ from that described.
- At all times patients should rely on the advice of their specialist who is the only person with full information about their diagnosis and medical history.

Waldenstrom macroglobulinaemia (WM) is a disorder which has features in common with an indolent non-Hodgkin lymphoma and with multiple myeloma. The pace of progression of the condition more closely resembles the indolent non-Hodgkin lymphoma. Leukaemia & Lymphoma Research booklets are available on Multiple Myeloma and non-Hodgkin Lymphoma.

What is Waldenstrom macroglobulinaemia?

Waldenstrom macroglobulinaemia is a chronic disease similar to myeloma but without the bone damage seen in myeloma. It arises from a particular type of white cell called a lymphocyte. The affected lymphocytes produce an excess amount of an antibody. This type of antibody is known as IgM; the M stands for Macroglobulin, hence the term macro-globulinaemia.

A Swedish doctor called Jan Waldenstrom discovered the condition in 1944.

The cells producing the IgM antibody tend to accumulate within the bone marrow, lymph nodes (glands) and the spleen. However most patients are found to have the disease because of symptoms caused by the excess of antibody in the blood.

What causes it?

The condition is rare, with an incidence of about 5 cases per million per year in the UK.

It is rather more common in men than women and most often occurs in people in their early sixties and older. The cause is unknown but it is certainly not infectious and is not hereditary.

What are the signs & symptoms?

The condition typically develops slowly with complaints of tiredness, weakness and possibly weight loss. The problems can be separated into those which are caused directly by the presence in the bone marrow and spleen of abnormal
lymphocytes (the tumour cells) and those which are caused indirectly by the antibody (the macroglobulin) in the blood.

The growth of tumour cells often causes the spleen to become enlarged and occasionally there is enlargement of the lymph nodes (‘glands’) in the neck, armpits or in the groin. As the condition progresses, which is usually over some years, problems with blood cell production may occur including reduced numbers of red cells causing tiredness and breathlessness, a low white blood count which causes a risk of infection, and a low platelet count which carries the risk of bruising or bleeding.

The abnormal antibody production causes a condition known as hyperviscosity in which the blood is literally too thick and cannot flow properly. The poor circulation as a result of this hyperviscosity can cause headache, confusion, sleepiness and vision problems. Occasionally the antibody can damage individual nerves which leads to weakness in parts of the body. The antibody also sometimes damages the kidneys.

**How is it diagnosed?**

A blood sample may show an increased number of small lymphocytes, although this is not always the case. It is usually necessary to confirm the diagnosis by taking a bone marrow sample.

This involves obtaining a small amount of marrow from inside the bone with a needle and a tissue sample to show if the structure of the bone marrow cavity is normal or changed. The first is known as a bone marrow aspirate, the second as a bone marrow trephine. The samples are usually obtained from the back of the hip bone, although the breast bone (sternum) may be used instead for bone marrow aspirates (but not for trephines). The procedure causes some discomfort but does not take very long. The procedure is usually carried out with sedation as well as local anaesthetic.

The blood and bone marrow cells are examined under the microscope. Cells typical of Waldenstrom macro-globulinaemia can then be seen in the specimen but final confirmation may require special laboratory investigations. Examination of the bone marrow sample will also give important information about the extent to which the marrow is affected.

The blood is also examined for the presence and amount of the abnormal protein. The levels of this protein can subsequently be used to monitor the progress of the disease.

**How is it treated?**

Some patients may have stable (non-progressing) disease which will not need treatment. If the original diagnosis was made because of tiredness and lethargy, removal of some of the antibody from the blood may improve the patient’s condition. This is done using a machine in a process called plasmapheresis.

If the symptoms are all due to hyperviscosity, drug treatment...
(chemotherapy) may be used after initial plasmapheresis to prevent protein levels from rising again. If the tumour cells are numerous enough to need treatment this can usually be done quite safely as an outpatient also with chemotherapy. The most common drug used to be chlorambucil but several newer drugs have shown great promise. A highly targeted drug called rituximab has been shown to benefit some patients.

Treatment is not aimed at curing the disease but at controlling the symptoms and making the patient comfortable. The age of the patient usually rules out bone marrow transplantation as a treatment option.

More aggressive treatment does not appear to improve the response in this disease. However Waldenstrom macro-globulinaemia is so rare that there have been very few studies comparing different treatments.

**What is the prognosis?**

See above.