Letters to the Editor

Massive cardiac disease in a patient with Waldenström's macroglobulinaemia

Waldenström’s macroglobulinaemia is characterised by the proliferation of malignant plasmacytoid lymphocytes secreting a monoclonal paraprotein of the IgM class. The disease usually presents with malaise, anaemia, haemorrhage, neurological and visual disturbance. One third of patients develop the hyperviscosity syndrome.1 Pulmonary masses have been described2-4 but cardiac disease has not been reported.

We describe a patient with Waldenström’s macroglobulinaemia who presented with resistant heart failure due to massive cardiac disease despite being in remission biochemically.

An 81 year old man presented with sudden onset of breathlessness. Two years previously Waldenström’s macroglobulinaemia had been diagnosed on the basis of anaemia (haemoglobin 8.2 g/dl), an IgM monoclonal (50 g/l), and 80% plasmacytoid lymphocytes in a bone marrow aspirate. He had been treated with oral cyclophosphamide 50 mg twice daily with a good haematological and immunological response (haemoglobin 12 g/dl; IgM monoclonal 15 g/l).

Examination showed that he had a left sided pleural effusion and signs of congestive heart failure with raised jugular venous pressure and hepatomegaly. He had a haemoglobin concentration of 13.1 g/dl; serum immunoglobulins showed an IgM monoclonal (12 g/l), with normal concentrations of IgG and IgA. Chest x-ray picture confirmed the presence of the left pleural effusion and no pulmonary infiltrates. The pleural fluid contained 40 g/l of protein with no demonstrable monoclonal. There were no abnormal plasmacytoid cells on examination of the pleural fluid and in a pleural biopsy specimen. All pleural fluid and tissue cultures yielded negative results.

His heart failure was treated with frusemide and the cyclophosphamide was continued. He improved initially but six weeks later deteriorated and complained of increasing breathlessness. Repeated laboratory investigations showed no change in haemoglobin and the IgM was 9 g/l. An echocardiogram was normal with no evidence of a pericardial effusion. The heart failure remained resistant to increasing doses of diuretics and angiotensin converting enzyme inhibitors and he died five months after the first episode of breathlessness.

The findings at necropsy confirmed that the immediate cause of death was heart failure. Right sided cardiac failure was evidenced by leg oedema, liver congestion, and ascites; and left sided cardiac failure by severe pulmonary congestion and oedema. A 1300 ml left sided pleural effusion was present, but no tumour deposits were present in the pleura.

The heart was greatly enlarged, weighing 880 g. The pericardium was thickened and infiltrated by multiple white tumour nodules, forming an unyielding capsule around the heart. A large tumour deposit projected from the infiltrated wall of the right atrium into its chamber, causing extensive obstruction of the tricuspid valve (figure). Tumour infiltrated the tricuspid valve ring and extended into the myocardium of the superior half of the right ventricle. A further large tumour deposit was located in the intraventricular and intra-atrial septum. These tumour deposits caused decreased compliance of the myocardium, tricuspid valve obstruction, and pericardial constriction.

Histological examination of the heart showed that the myocardium was infiltrated by plasmacytoid cells. Staining with immunoperoxidase PAP, using conventional controls, showed that most of these cells contained granular cytoplasmic IgM alone. Apart from local infiltration of mediastinal structures adjacent to the pericardium, no tumour deposits were demonstrable in lymph nodes, liver, spleen, bone marrow, lung, pleura or any other tissues.

Congestive heart failure has been reported in 4% of cases of Waldenström’s macroglobulinaemia and has usually been attributed to an expanded plasma volume and increased blood viscosity.1 In our patient the low monoclonal IgM concentration indicated that the disease was in remission and that hyperviscosity was not responsible for the heart failure. Cardiac infiltration with amyloid deposition has been described in cases of Waldenström’s macroglobulinaemia,2 but amyloid was not demonstrable in this patient. We did not consider direct cardiac disease as a cause for the heart failure because it is not a recognised complication of the disease. In addition, there was no evidence of disease radiologically or on echocardiography. Nevertheless, massive cardiac disease caused by tumour was present at necropsy and was the cause of the

Figure  Heart, containing a large tumour deposit in the right atrium (A), extending through and partially obstructing tricuspid valve (arrows). Large tumour deposit is present in interventricular septum (bottom right).
heart failure. There is no doubt that this mass was due to the Waldenstrom’s macroglobulinaemia as IgM was detected on histological examination of the tumour. Discrete soft tissue masses are most uncommon in Waldenstrom’s macroglobulinaemia, but pulmonary tumours have been described. They are usually accompanied by other signs of the disease such as lymphadenopathy, hepatomegaly, splenomegaly and increased serum IgM concentrations. Cardiac disease caused by tumour has not previously been reported. Our patient was unusual in that he had no bone marrow or extramedullary lymphoid tissue metastases at the time of death despite massive tumour load in the heart. In addition, the disease was in remission biochemically as shown by the persistently low monoclonal IgM. This may have been an atypical form of the disease in which IgM was synthesised by the tumour but not secreted into the circulation.

To our knowledge, cardiac disease with tumour metastases in the cardiac tissue has not been described previously in a patient with Waldenstrom’s macroglobulinaemia. This possibility should be considered as an alternative to hyperviscosity or amyloidosis as a cause for heart failure in Waldenstrom’s macroglobulinaemia.

**Unchanged concentrations of plasma fibronectin in Alzheimer’s disease**

In Alzheimer’s disease the capacity to remove intracellular and intercellular debris is considered to be impaired. It is also claimed that abnormalities attributed to Alzheimer’s disease can often be observed in peripheral tissues including skin fibroblasts and the blood. It was therefore thought that an analysis of plasma in relation to repair and maintenance systems might be useful to develop simple tools for the diagnosis of Alzheimer’s disease.

In man the concentration of fibronectin in the plasma increases exponentially with age. Such changes in plasma fibronectin concentrations are usually associated with the changes in its rates of synthesis, changed proteolytic breakdown, and inefficient scavenging systems. Some age related diseases, such as diabetes and atherosclerosis, show prematurely increased concentrations of plasma fibronectin. There is, however, no report on the concentrations of fibronectin in the plasma of patients with Alzheimer’s disease. We therefore estimated plasma fibronectin concentrations in such patients.

Plasma samples from seven patients with Alzheimer’s disease (six women and one man, aged between 55 and 81 years) were kindly provided by Dr J VJi, TNO Institute for Experimental Gerontology, Rijswijk, The Netherlands. The clinical diagnosis of the disease in these patients was made by Dr P Eikelboom (Valerius Clinic, Amsterdam) and was found to be in accordance with the diagnostic criteria for “possible senile dementia of Alzheimer’s type”, as described by McKhann et al. The number of years for which these patients have now been under observation is between seven and 14.

Plasma fibronectin concentration (mg/l) was determined in these samples by a double antibody sandwich ELISA technique, using rabbit anti-human fibronectin antibody as the catching antibody and the same conjugated to horseradish peroxidase as the secondary antibody. For comparison, plasma fibronectin concentrations were also determined in a section of the normal Danish population. For this, venous blood samples from more than 90 apparently healthy volunteers aged between 20 and 82 years were taken in dipotassium edetic acid and using standard methods. Concentrations of fibronectin in plasma were determined as described above. All estimates were made simultaneously in multiple replicates and repeated twice at different times. In an apparently normal section of the population, an age related exponential increase (from 200 mg/l at 20 years of age to more than 600 mg/l at 80 years) was observed, which is similar to previous estimates. The increase observed was significant (2 p < 0-01), and the extent of the increase was slightly less in men than in women. Patients with Alzheimer’s disease had unchanged concentrations of plasma fibronectin compared with their age and sex matched normal counterparts. Many other biochemical processes, such as calcium homeostasis, DNA and protein synthesis and DNA repair, seem to be changed in Alzheimer’s disease, and these changes can be identified in the peripheral tissues of patients with Alzheimer’s disease does not occur generally throughout the body.

**References**