



MYELOMA CANADA

Complications of Multiple Myeloma

Chaim Shustik, M.D., FRCP(C)
Professor of Medicine, McGill University
Division of Hematology, Royal Victoria Hospital

Multiple myeloma is a cancer of plasma cells, cells which reside in the bone marrow and normally produce protective antibodies called immunoglobulins. Plasma cells are an important part of the immune system. Because the cancer develops from a single plasma cell which has become malignant, the malignant plasma cells are characterized as “monoclonal.” These cells produce an identical immunoglobulin which can be detected in the blood, and is identified as a “monoclonal” or M peak. This M peak can be measured and is monitored regularly as a marker of the disease and its response to treatment.

Bone Morbidity

Normally, there is an equilibrium or steady state between cells forming new bone (osteoblasts) and cells removing bone (osteoclasts). In multiple myeloma, increased activity of the bone-removing cells (the osteoclasts) is stimulated by substances released from both malignant plasma cells and neighbouring normal cells in the bone marrow (stromal cells). This imbalance results in generalized bone loss throughout the skeleton (similar to osteoporosis, the bone-thinning disease), as well as areas of discrete bone loss (lytic lesions), which can be seen in x-rays of the bones. As a result of weakening of the bone structure, painful fractures are among the most distressing complications of multiple myeloma. Fractures frequently occur in the spine and less commonly in the pelvis, arms or legs.

The standard treatment of multiple myeloma now includes the use of a bisphosphonate, a class of drug which blocks the activity of osteoclasts and decreases bone loss. These drugs, usually pamidronate or zoledronate, are given intravenously on a monthly basis to prevent the development of bony complications.

Newer orthopedic surgical procedures to restore compressed vertebrae include vertebral kyphoplasty. Kyphoplasty is a technique that uses balloon catheter technology to inject a bone cement in damaged vertebrae.

Excessive loss of bone may also result in the release of calcium into the blood. The complication of hypercalcemia (an increase in blood concentration of calcium) can be treated with bisphosphonates.

Anemia

Anemia is defined as a reduced level of red cells in the blood, usually measured as hemoglobin or hematocrit. Depending on the severity of the anemia, symptoms can include a decreased level of energy or fatigue, shortness of breath and other symptoms which impair a patient's quality of life. Anemia is often present in multiple myeloma and may be caused by the disease decreasing the production of red cells in the bone marrow, or by the drugs used to destroy the malignant cells. If necessary, blood transfusions may be required to raise the hemoglobin level quickly. An alternative for the sustained treatment of anemia is erythropoietin. Erythropoietin is a normal "growth factor" produced by the kidneys that stimulates the bone marrow to produce more red blood cells.

There are two forms of erythropoietin medications available in Canada: Epoetin alfa (Eprex*, r-HuEPO or human recombinant erythropoietin, EPO) and Darbepoetin alfa (Aranesp®). Both medications are given by injection under the skin. By increasing the hemoglobin level, erythropoietin can reduce fatigue and the need for transfusions.

Infections

Due to a reduction in the levels of normal immunoglobulins which protect against bacterial infections, multiple myeloma is associated with an impaired immune capacity. This can result in an increased susceptibility to infections caused by bacteria, including pneumonia and urinary infections. As well, the drugs used to treat multiple myeloma often lower the white blood cell count. If the white blood cell count drops severely, the risk of infection is increased

The usual sign of infection is fever. A temperature higher than 38°C requires prompt medical treatment. Other symptoms will be related to the site of infection (e.g., cough with sputum if pneumonia). Less commonly, viral infections such as shingles may develop. Bacterial infections may be treated with antibiotics.

Renal Insufficiency

The abnormal immunoglobulin produced by the malignant plasma cells in multiple myeloma may include only fragments of the immunoglobulin, called "light chains". Because of their small size, these light chains are removed by the kidney from the blood. In the process, the proteins may damage different structures in the kidney, resulting in decreased kidney function.

These light chains may also be deposited in the kidney as a protein-like material called "amyloid." Amyloid deposition can result in loss of many proteins in the urine, including albumin, resulting in a disorder called "nephrotic syndrome". The most obvious symptoms of nephrotic syndrome are fluid retention and swelling of the legs.

Successful treatment of myeloma reduces the production of the abnormal myeloma proteins and reduces the risk of kidney damage. If deterioration in kidney function is found, other treatable causes need to be considered, including kidney infection, dehydration and hypercalcemia. Kidney function is measured by the serum creatinine, and is part of routine testing in following patients with multiple myeloma. If kidney damage progresses, dialysis could become necessary.

High Calcium

As discussed above, elevated levels of blood calcium may result from excessive bone breakdown or resorption. Symptoms of high blood calcium include constipation, increased frequency of urination, weakness and changes in mental status including somnolence and confusion. There may be a sudden deterioration in kidney function associated with hypercalcemia, with prompt improvement following the treatment of hypercalcemia. The use of oral calcium supplements should be discussed with the physician.

Other Blood Complications

Because multiple myeloma is a disease of bone marrow and the treatment includes drugs that suppress normal marrow function, another blood cell that may be decreased is the platelet, a tiny cell involved in blood clotting. A lowering of the platelet count is referred to as "thrombocytopenia". Thrombocytopenia does not usually result in any symptoms, but if the platelet count is very low there is an increased risk of bleeding (e.g., from the gums after brushing) or pinpoint red spots ("petechiae") in the skin. Transfusion of platelets may be required temporarily.

Rarely, the level of M protein in the blood may be extremely elevated and interferes with the normal flow of blood through the skin and to different organs. The symptoms of this "hyperviscosity syndrome" are quite varied. Treatment of this complication may require the removal of the protein from the blood by a procedure termed "plasmapheresis" through a machine which separates the components of the blood and returns the normal blood cells to the circulation.

Dr. Chaim Shustik holds the Louis Lowenstein Chair in Hematology and Oncology at McGill University, and his clinical and research focus is upon the treatment of hematologic malignancies. He was chairman of the myeloma committee of the National Cancer Institute-Clinical Trials Group and principal investigator of a number of clinical trials in multiple myeloma. He has been on an advisory group for staging and prognosis in myeloma organized by the International Myeloma Foundation.

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