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THE USE OF METHYLCOBALAMIN IN THE ACCOMPANYING THERAPY OF MULTIPLE MYELOMA

Ruziboyeva Oyjamol Narzullayevna*; Muyiddinov Zuhriddin Ziyadullayevich; Yigitov Akmal Uktamovich*****

*Assistant,
Department of Hematology,
Samarkand State Medical University,
Samarkand, UZBEKISTAN

**Assistant,
Department of Hematology,
Samarkand State Medical University,
Samarkand, UZBEKISTAN

***Head of the Department Hematology,
Samarkand Regional Multidisciplinary Medical Center,
Samarkand, UZBEKISTAN

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ABSTRACT

Multiple myeloma (MM) or plasma cell myeloma is a B-cell malignant tumor whose morphological substrate is plasma cells (PCs) that produce monoclonal immunoglobulin. Multiple myeloma is a malignant plasma cell tumor that produces monoclonal immunoglobulins that invade adjacent bone tissue and destroy it. Characteristic manifestations include lytic bone lesions causing pain and/or fractures, renal failure, hypercalcemia, anemia, and recurrent infections. Diagnosis usually requires detection of M-protein (sometimes present in urine rather than serum, but rarely absent entirely) and/or light chain proteinuria and excess plasma cells in the bone marrow. Specific treatment most often involves a combination of conventional chemotherapy, corticosteroids, and one or more new drugs such as proteasome inhibitors (e.g., bortezomib, carfilzomib, ixazomib), immunomodulatory drugs (e.g., lenalidomide, thalidomide, pomalidomide), or monoclonal antibodies (e.g., daratumumab, isatuximab, elotuzumab). It is also possible to prescribe melphalan in high doses, followed by transplantation of autologous peripheral blood stem cells.

KEYWORDS: *Conventional Chemotherapy, Corticosteroids, Hypercalcemia, Anemia, Monoclonal Immunoglobulins, Multiple Myeloma.*

INTRODUCTION

The pathogenetically decisive fact is long-term, chronic antigenic stimulation after viral infections or other chronic diseases, and prolonged exposure to toxic substances and radiation [2,

5]. As a result of a long series of genetic events, a pathological clone of B cells is formed, capable of differentiating to PC, but producing nonfunctional immunoglobulin.

The biological and clinical features of MM are associated with genetic aberrations, such as rearrangement of the immunoglobulin heavy chain (IGH) gene loci, as well as chromosomal deletions, mutations in somatic genes, and chromosomal hyperdiploidy involving an odd number of chromosomes. The presence of a significant number of various genetic disorders causes high variability in the course of the disease [2, 6-8].

Multiple myeloma is classified by stages and by risk factors.

Characterized by the development of diffuse osteoporosis or the appearance of individual osteolytic lesions, usually in the bones of the small pelvis, skull, vertebrae, ribs, femurs and humerus. These lesions are due to the replacement of normal bone tissue by a growing plasmacytic tumor, as well as exposure to cytokines that are secreted by malignant plasma cells, which causes osteoclast activation and osteoblast suppression. Osteolytic lesions are usually multiple in nature, in rare cases solitary intramedullary masses are formed. Increased bone loss may also be accompanied by hypercalcemia. Extraosseous solitary plasmacytomas are rare, but they can occur in all tissue types, especially in the upper respiratory tract.

Many patients have kidney failure at the time of diagnosis, or it develops during the course of the disease. Renal failure has many causes, most commonly due to light chain deposition in the distal nephron tubules (myeloma-associated kidney disease) or due to hypercalcemia. Also, patients often develop anemia due to kidney disease or suppression of erythropoiesis by tumor cells, but can also be caused by other unrelated causes, including iron deficiency or vitamin B12 deficiency.

Due to the lack of normal antibodies and due to other immune disorders, some patients have an increased susceptibility to bacterial infection. Against the background of the introduction of new therapies, especially the use of proteasome inhibitors bortezomib, ixazomib and carfilzomib and monoclonal antibodies such as daratumab, elotuzumab and isatuximab, viral infections, especially those caused by the herpes zoster virus, are increasingly emerging. Amyloidosis develops in 10% of patients with myeloma, most often in the presence of lambda-type M protein.

The most common manifestations are persistent bone pain (especially in the back or chest), kidney failure, and recurrent bacterial infections; however, in most cases, the diagnosis is made by routine laboratory tests that show elevated levels of total blood protein, proteinuria, or unexplained anemia or kidney failure. Pathological fractures are common (i.e., non-traumatic fractures or with minimal trauma), and spinal cord compression may occur due to vertebral involvement, resulting in paraplegia. It should be noted that the presence of anemia may be the primary or sole reason for the diagnostic search; in a small number of cases, manifestations characteristic of the syndrome of blood hyperviscosity are observed. Typical symptoms are peripheral neuropathy, carpal tunnel syndrome (especially with concomitant amyloidosis), abnormal bleeding, and signs of hypercalcemia (eg, polydipsia, dehydration). Renal failure may also develop. Lymphadenopathy and hepatosplenomegaly are uncommon.

An aspiration biopsy of the bone marrow is also performed, the biopsy reveals the presence of plasma cells located diffusely or in the form of clusters; the diagnosis of myeloma is established

when > 10% of this cell type is present. However, bone marrow involvement can be focal, so that <10% of plasma cells can be found in some specimens from patients with myeloma. Rarely, the number of plasma cells in the bone marrow may be normal. The morphology of plasma cells does not depend on the class of synthesized immunoglobulins. Chromosomal examination of the bone marrow (for example, using genetic methods such as FISH and immunohistochemistry) can detect specific karyotypic abnormalities of plasma cells, the presence of which is associated with differences in patient life expectancy.

Several criteria are usually required for diagnosis and differentiation from other malignancies (eg, metastatic cancer, lymphoma, leukemia) and unexplained monoclonal gammopathy:

- Clonal plasma cells in the bone marrow or plasmacytoma
- M-protein in plasma and/or urine
- Damage to internal organs (hypercalcemia, kidney failure, anemia, or bone damage)

In the absence of serum M-protein, the diagnosis of myeloma is based on the presence of Bence-Jones proteinuria > 200 mg/24 hours or abnormal serum levels of free light chains, osteolytic lesions (in the absence of reliable evidence of malignant metastasis or the presence of granulomatous disease), the presence of in the bone marrow of plasma cells located diffusely or in the form of clusters.

The disease is progressive and incurable, but recently median survival has increased to over 5 years as a result of advances in therapy. Poor prognostic factors at the time of diagnosis include low serum albumin, high beta-2-microglobulin, elevated LDH, and specific cytogenetic abnormalities in tumor cells. The prognosis of patients with pre-existing renal failure is also poor if the renal function does not improve with treatment (which is almost always the case with current treatment options).

Since multiple myeloma is a potentially fatal disease, it is useful to discuss the possibility of palliative care, which should involve not only doctors but also family members and friends of the patient. It is necessary to discuss issues such as the appointment of a guardian (who will also take orders of a medical nature), the use of a tube for artificial feeding, and pain relief.

In the treatment of multiple myeloma, the main goal set by specialists is to stop the progression of the disease, transfer it to a stable remission, prevent relapses and provide the patient with a good quality of life. This is achieved by destroying pathological cells, restoring hematopoietic processes, normalizing the qualitative composition of the blood, and relieving symptoms.

Our doctors are fluent in modern methods of treating oncohematological diseases and also use the latest generation of drugs. The appointment of treatment by a consultation of specialists makes it possible to take into account all the nuances of the disease and determine the most effective ways to influence pathological cells. Thus, even with a common disease, the patient gets the opportunity to improve well-being, restore the normal process of hematopoiesis and, accordingly, have a good quality of life.

Myeloma treatments that are used in LISOD:

1. Drug therapy:

Chemotherapy. Helps to stop the development of the disease, and destroys cancer cells. LISOD uses only high-quality drugs from official manufacturers.

Target therapy. The drugs that have made a breakthrough in cancer treatment have the ability to find abnormal plasma cells and block their further reproduction.

Immunotherapy. The drugs activate the patient's immune system, and “teach” it to find and destroy atypical cells.

2. Radiation therapy. The Israel Oncology Hospital LISOD has installed linear accelerators from VARIAN, the world's leading manufacturer of such equipment. Careful calculation of the dose and targeted treatment allows you to act precisely on pathological foci, while healthy tissues experience minimal radiation exposure. Affected bone tissues and other organs to which malignant cells have spread are irradiated.

Based on the patient’s well-being and according to the results of ongoing examinations, accompanying therapy may be prescribed. The Hospital presents the most modern protocols for the treatment of pain; patients have the possibility of round-the-clock monitoring by highly qualified specialists in the intensive care unit; can receive modern drugs to strengthen bone tissue, both targeted and bisphosphonates). With the development of complications of the disease or therapy, each patient receives high-quality accompanying therapy.

Each patient is the center of attention of a team of experienced doctors. LISOD specialists do their best to ensure that each patient who applies has received effective treatment in accordance with international recommendations.

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