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CLINICAL CASE OF A FEMALE PATIENT WITH MULTIPLE MYELOMA

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ABSTRACT — The article presents a clinical case of a female patient with multiple myeloma. This bone malignancy occurring with increasing frequency in older adults is common in hematological practice, late diagnosed and poorly managed, with a high level of mortality.

KEYWORDS — multiple myeloma, plasma cell myeloma, incidence, chemotherapy, bortezomib.

Multiple myeloma (MM) is β-cell malignant tumor whose morphological substrate is plasma cells producing monoclonal immunoglobulin. According to the latest WHO classification, in 2017 the term *multiple myeloma* was replaced with *plasma cell myeloma*, a disease characterized by multifocal proliferation of neoplastic plasma cells associated with monoclonal immunoglobulin secretion [1].

MM represents approximately 1% of all malignant tumors, and accounts for 13% of all hematopoietic neoplasms. MM occurs with increasing frequency in older people, the median age at diagnosis being 63.7 years [2]. The prevalence of the disease among the population younger than 40 years does not exceed 2%. In Russia in 2017, the incidence of MM was 2.78 per 100,000 persons, with 4,075 new cases diagnosed. 2,587 patients died [3].

The duration of the disease before the onset of the first clinical symptoms can range from several months to 2–3 years [1]. The MM clinical manifestations are extremely diverse, but they are largely determined by infiltration of the bone marrow by the plasma cells (PCs) and organ damage. MM often presents with bone injuries, hypercalcemia, renal failure, amyloidosis, infiltration of the bone marrow by the myeloma cells, a decreased level of normal immunoglobulins, cryoglobulinemia, and hyperviscosity syndrome [4].

The purpose of our study was to present a clinical case of a patient with MM since it accounts for 60% mortality rate in Russia due to its multiple clinical manifestations and the diagnostic complexity.

Case description

A 69-year-old female patient M. who lives in the Tver Region presented to the Hematology Department of Tver Regional Clinical Hospital on January 2nd, 2019, with complaints of moderate general weakness, moderate pain in the lower extremities, ribs, left clavicle increasing with movement and palpation, a cranial bone growth.

According to the patient's history, for several years the woman had had minor bone pain for which she was not examined. In January 2018, she consulted her district physician about the painless growth in the left frontal area, increased bone pain, and general weakness. The initial examination and lab tests revealed mild anemia (Hg —102 g/l), accelerated ESR (108 mm/h), and moderate proteinuria (2.15 g/l). The patient was referred to a series of X-ray bone tissue examinations. The 2-projection skull radiographs (July 16th, 2018) showed multiple foci of bone destruction; the shoulder radiographs revealed multiple foci of bone destruction of both clavicles, shoulder blades, and visible parts of the ribs. There was a deformity of the 6th right rib and swelling of the acromial end of the left clavicle. The radiographs of the thoracic and lumbar spine and pelvis showed multiple foci of bone destruction, signs of bilateral peritrochanteritis, and pathological Th 5 and Th12 fractures. Given the total pronounced changes in the bone structures of flat bones associated with an evident pain syndrome, the district physician suspected MM, and the patient was referred to a hematologist.

During the examination, the immunochemical assay (ICA) was performed, as well as radiography of the upper extremities. The findings of the ICA (September 18th, 2018) revealed paraprotein represented by M-gradient, 20.5 g/l, Bence-Jones protein secretion. The urine M-gradient was 0.91 g/day. The X-ray of the upper extremities and clavicles (October 2nd, 2018) showed a fused fracture of the acromial end of the clavicle with a massive bone callus on the right, as well as multiple foci of destruction in the examined areas.

In order to clarify the diagnosis and start proper therapy, on October 10th, 2018, the patient was referred to the Hematology Department of the Tver Regional Clinical Hospital, where MM was diagnosed and the 1st bortezomib-based VCD chemotherapy cycle was started on October 11th, 2018. The patient responded to the therapy well and was discharged in

satisfactory condition. The next hospitalization was from December 10th to December 22nd,2018, during which the 2nd bortezomib-based chemotherapy cycle was performed. The patient's response to the regimen was positive, she showed some improvement, the bone pain decreased, the patient became more active, and became independent with her ADLs.

The next hospitalization for the 3rd chemotherapy cycle was from January 2nd to January 14th, 2019.

On admission, the patient's condition was estimated as satisfactory without any signs of mental confusion. The body temperature was 36.6 C. The patient walked using a walker, and was active in bed. There were multiple dense growths on the skull, the skin over them was not changed, painless on palpation, the maximum size in the frontal left area was up to 6×3 cm. On palpation, the left clavicle, sternum, and ribs on the anterior surface were moderately painful. The patient had normal constitution, height — 160 cm, weight — 70 kg. The body mass index was 27.34 kg/m^2 corresponding to being overweight. The skin was pale pink, of normal moisture, no swelling. The shape of the chest was correct, normosthenic, the respiratory rate was 16/min. The BP was 120/70 mm Hg, the heart rate was 76 BPM, the borders of the heart were expanded to the left by 1.5 cm, the heart tones were rhythmic, muted. No abnormalities were detected in the other organs and organ systems.

The examination showed mild anemia (RBCs — 3,2 · 10^{12}/L, Hg — 103 g/l). Blood biochemistry revealed no deviations from normal parameters. Urinary Protein Excretion Estimation was negative. An ECG was also performed, which showed signs of incomplete left bundle branch block.

Clinical diagnosis

C90. 0 Multiple myeloma, M-gradient in blood serum, with Bens-Jones proteinuria, osteodestructive process, anemia, soft tissue growths in the skull, stage IIA, ISS stage III. Condition after 3 VCD cycles.

Associated complications

Severe osteoporosis. Thinning of the cortical layer of the humerus. The acromial end of the clavicle is swollen.

The 3rd bortezomib-based chemotherapy cycle was performed: days 1, 4, 8, 11 — 1.3 mg/m^2 — 0.9 ml sub-Q. The treatment regimen included: dexamethasone 40 mg IV drip per 200 ml of normal saline on the days of bortezomib administration, Endoxan 400 mg IV drip per 200 ml of normal saline on days 1 and 8. In order to exclude the development of gastropathy, the therapy was supplemented with omeprazole 20 mg 2 times daily 30 minutes before meals on the days of dexamethasone administration. For pain, Ketorol 3% solution was administered — 2.0 ml IV given over a constant infusion rate. On January 13th, 2019, for the purpose of osteoclast hyperactivation zoledronic acid was administered IV drip as a single 4 mg dose in 200.0 ml of normal saline. The patient responded to the therapy well, without complications, with improvement. Upon discharge, the patient's Hb was 111 g/l, RBCs — 3.7 · 10^{12}/l, WBCs — 9.60·10^9/l, PTLs — 172 · 10^9/l. The patient was discharged with recommended follow-up by the district physician and hematologist. The next hospitalization was due in 3 weeks for the 4th cycle of bortezomib-based chemotherapy.

Maintenance therapy of bortezomib-based increases the rate of complete remission, progression-free survival, and survival to progression. Since there is no conclusive evidence of an increase in overall survival, according to ESMO recommendations, maintenance therapy in elderly patients is not recommended [5].

DISCUSSION

The main negative prognostic factors for MM include high levels of β2-microglobulin, decreased serum albumin, elevated LDH, cytogenetic abnormalities: t (4; 14), t(14;16), del17p13, del13q, 1q amplification, 13q deletion. Initial prognostic signs allow predicting the life expectancy of patients and their response to therapy, but they do not determine the choice of adequate treatment tactics for MM patients [2]. In our clinical case, there were no such factors. The timely MM therapy using the VCD regimen, as well as the absence of complications, made it possible to improve the patient's condition after the 3rd cycle (the bone pain reduced, the patient became more active) and slow down the disease progression. It is undoubtedly necessary to continue the therapy until complete remission has been achieved. The positive effect of the therapy has led to an increase in the patient's quality of life and, it can be assumed, the complete remission, when achieved, will increase its duration.

Thus, medical awareness of more frequent and characteristic clinical and laboratory manifestations of MM will allow detecting this disease at an early stage and timely start polychemotherapy thereby reducing the MM-related mortality rate.

Contributors

Elmira Aliyeva and Angela Asedova — literature review, clinical case description, submission for publication. Olga Poselyugina — clinical case selection, patient supervision, provision of data for the article. All the authors took equal part in writing the article. All the authors made an equal contribution to the

conception, design, and interpretation of the reported study. All the authors have equal rights.

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