

CASE REPORT
OPIS PRZYPADKU**MULTIPLE MYELOMA: CHALLENGES OF DIFFERENTIAL DIAGNOSIS (CLINICAL CASE)**

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The objective of our study was to interpret and discuss atypical multiple myeloma case. The article describes the case of clinical observation of a patient K, in which manifestations of chronic kidney disease and circulatory failure prevailed in clinical picture of the disease. The authors recommended an X-ray examination of skull and pelvic bones as a screening method suitable for elderly people with symptoms of chronic renal insufficiency and chronic bone and muscle pain resistant to treatment.

KEY WORDS: multiple myeloma, differential diagnostics, X-ray examination

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INTRODUCTION

Today we witness the stunning growth of incidence of tumor diseases, the mortality for which continues to concede only to cardiovascular diseases [3, 4, 5]. The complexity of diagnostics of the disease at initial stages is explained by a fuzzy and unspecific clinical picture, which requires careful differential-diagnostic search [6, 7, 8].

Multiple myeloma (MM) is considered a tumor disease with a low degree of malignancy, which morphological substrate is an uncontrolled synthesis of monoclonal protein, which leads to tumor-like transformations of individual precursor cells [8, 9].

MM is one of the infrequent pathologies, however, the disease is ranked second by prevalence after non-Hodgkin lymphoma (10%) among oncological blood nosologies. American oncologists are afraid that the number of newly diagnosed MM cases may bring the disease to five most common diseases of this profile in the United States. We assume this region of the world not endemic in terms of the oncological pathology, therefore, this trend may loom a global format [11, 12]. In recent years, the fact of underlying genetic anomalies that precondition development and progression of multiple myeloma has been proved, thus explaining family cases [13, 14, 15].

Compared to other oncological diseases, MM is characterized by slow progression, as twenty, and sometimes thirty years [16] may pass from primary tumor-like changes in precursor cells to the onset of clinical symptoms. However,

complications associated with acute infectious diseases and renal insufficiency can significantly reduce the life expectancy of patients [17]. The disease is characterized by positive response to treatment and high patient survival rate in the event of early diagnosis and timely treatment [18, 19]. Slow progression and long-lasting latent stage of the disease make the early MM diagnostics a tough case.

In 2014, members of IMWG (International Myeloma Working Group) reviewed and supplemented the diagnostic criteria. The presence of certain criteria undoubtedly confirms the MM diagnosis [1, 2].

MM is characterized by a variety of clinical manifestations. In most cases, the first symptom of multiple myeloma is a subacute continuous pain of migratory nature with a circadian rhythm [20, 21]. Over time, due to metabolic disturbances and formation of myelomic kidney, the patients present with edema syndrome and all other manifestations of chronic renal failure, which has an indolent course in almost 40% of cases [21, 22, 23]. Chronic kidney disease develops as a result of lesion of tubules due to deposition of light chains of immunoglobulins and leads to the development of renal failure. However, onset of the disease with symptoms of chronic kidney disease is quite uncommon [22].

Normochromic anemia develops as one of the hematological manifestations. Symptoms of intoxication [24, 25] come to the fore in the clinical picture of untreated MM cases or in the event of speedy progress of the disease.

Physical changes at the onset of the disease are minimal, with no characteristic features. In the osteolysis areas, bone palpation reveals uneven and painful surface. Hepatosplenomegaly with moderate enlargement of the liver is observed in approximately one third of the cases [26].

THE AIM

The clinical features of multiple myeloma options require a thorough differential diagnostics. The following case history is a vivid example that sustains the thesis. The clinical features of patient K. with MM are presented in this article.

CASE REPORT

Patient K., 58, a resident of the countryside of the Vinnytska region, was admitted to the General Medicine Department of the University Hospital of the Pyrohov Memorial National Medical University (Vinnytsya) on June 04, 2018 with complaints of expressed general weakness, rapid fatigability, shortness of breath and sensation of heaviness in the heart area under physical load, palpitation, edema of the legs, increased body temperature (up to 37.4°C), weight loss by 30 kg over two years, periodic pain in the right hypochondrium, the right hip and knee joints, space-occupying lesion in the left portion of the forehead (associated with a life trauma).

ANAMNESIS MORBI

The patient has noted gradual, unprovoked deterioration of the health status during the last 3-4 months when the above-described complaints emerged. The patient complains of a week-long increased body temperature. According to the patient, she followed the diet and medicine treatment recommended by a traumatologist: the injectable (24 injections) and oral course of a chondroprotectors. She has been continuously taking acetylsalicylic acid (75 mg) and enalapril maleate (10 mg/day) for the last 6 months. From May 05, 2018 until June 01, 2018, she was admitted to the local district hospital with a diagnosis: IHD; atherosclerotic cardiosclerosis; aortosclerosis; hypertension Grade II; left ventricular hypertrophy; high risk of vascular complications; CF stage IIa, functional capacity II (NYHA); severe anemia of uncertain genesis. The prescribed therapy (torasemid, spironolactone, Corvitin, enalapril maleate, acetylsalicylic acid, bisoprolol fumarate, and meloxicam) was not sufficiently effective, and the patient K. was discharged home with a slight improvement.

THE MEDICAL HISTORY (ANAMNESIS VITAE)

For a long time, the patient has suffered from chronic cholecystitis. The osteochondrosis of the lumbosacral region of the spine, deforming osteoarthritis of the right hip and both knee joints have been troubling for 5-6 years. She has got a surgery for uterine fibroids (18 years ago) and fracture of the ribs (life trauma 5-6 years ago). For 20 years, she has

suffered from chronic kidney disease – pyelonephritis (last exacerbation 2 years ago). The patient denies the presence of viral hepatitis, tuberculosis, HIV, venereal diseases in the medical history; allergic history is not burdened.

OBJECTIVES DATAS

At examination, the state of the patient was of a moderate severity, stable; the patient was conscious, oriented, took active position in the bed. The skin was clean, pale, with a yellowish tinge, warm to the touch, of normal elasticity. Subcutaneous fat was well developed (BMI = 27.2), peripheral lymphatic nodes were not enlarged. Painless tumor-like mass (2 x 3 cm) of tight-elastic consistency was palpable the forehead area. Body T – 36.7°C, RF-20 per minute, BP-150/90 mm Hg, HR-76 bpm.

Nasal breathing was free; clear lung sounds over the lungs against percussion; vesicular breathing without deviation from norm at auscultation. The left cardiac border was shifted 1.5 cm to the left from the middle-clavicular line; the other cardiac borders were not changed; diffuse cardiac impulse. The first cardiac tone at the top was weakened; an accent of the second tone above the aorta was heard. The abdomen of the usual form; superficial and deep palpation was painless. The lower edge of the liver coincided with the edge of the rib arch, rounded, tightly elastic, painless with palpation. The spleen was not palpable. Gall bladder symptoms and peritoneal irritation symptoms were negative. Defecation was normal; the consistency of feces was normal. The Pasternatsky symptom was negative on both sides. Urination – 4-5 times a day, painless. Swelling of the legs of a tightly elastic consistency; no abnormality of color and integrity of the skin of lower extremities was found. The knee joints were slightly deformed. Palpation of the periarticular regions of the right hip and knee joints was moderately painful; the load symptoms were positive; the volume of passive and active movements was somewhat limited; the patient felt a “crunch” when moving.

Given the subjective and objective data, a preliminary diagnosis was established: Severe anemia of unspecified genesis (CKD? Multiple myeloma? Neoplastic process?); CKD Grade 0; chronic pyelonephritis in the remission stage; CKD Grade I; symptomatic arterial hypertension Grade II; hypertrophy of the left ventricle; IHD: diffuse cardiosclerosis, aortosclerosis; CF IIa, II (NYHA); sinus tachycardia; chronic cholecystitis in remission; osteoarthritis; Grade II-III deforming osteoarthritis with a predominant lesion of right hip and knee joints in the stage of unstable remission; Grade 2 arthrosis of metatarsophalangeal articulations (according to the results of the traumatologist's consultation).

Patient K. was examined in accordance with the National Clinical Recommendations for Diagnosis and Treatment of Multiple Myeloma [2, 6]. The examination report was approved by the Local Ethics Committee in accordance with the Declaration of Helsinki (2013).

The patient was assigned additional laboratory and instrumental examinations, the results of which are listed

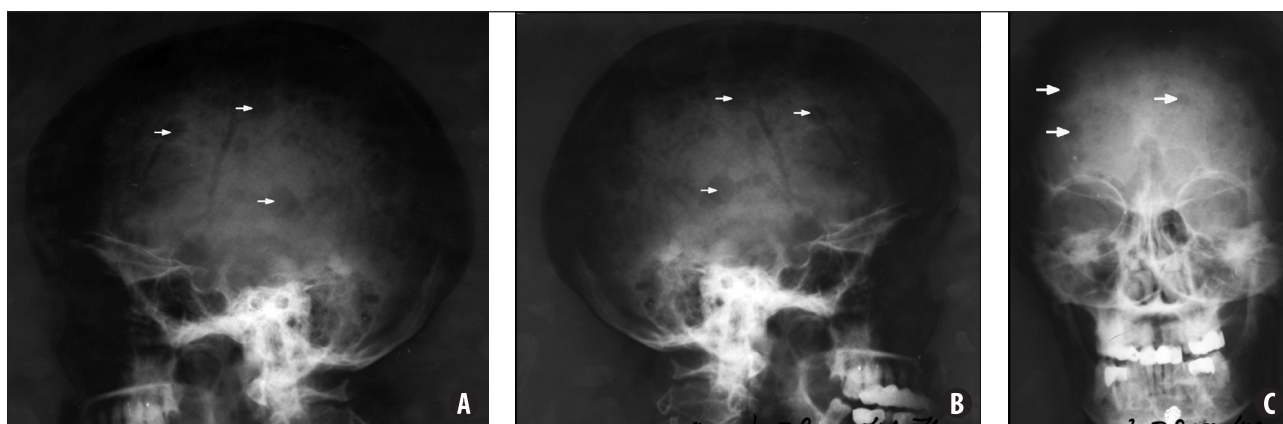


Figure 1. X-ray photos of skull in sagittal left (A), right (B) and front (C) views.

Notes: arrows show multiple focuses of destruction.

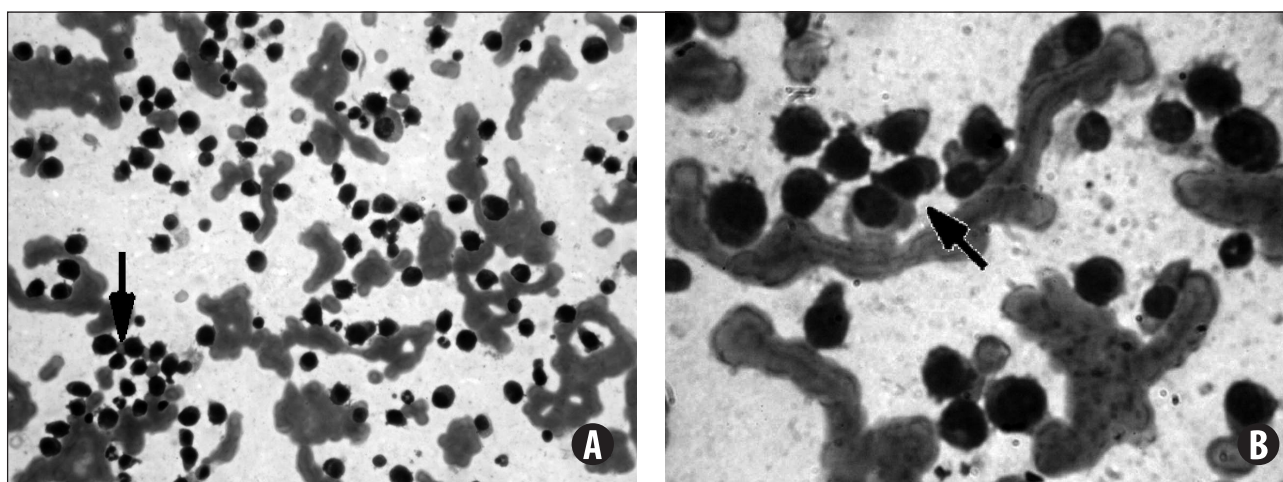


Figure 2. Blood smears photos (A, B).

Notes: arrows show clusters of plasmatic cells.

below. The results of the general blood count suggested the presence of severe hypochromic anemia (Hb – 63 g/l), decreased erythrocyte count ($2.0 \cdot 10^{12}/l$), pronounced anisocytosis, significant ESR growth (82 mm/hour); the leukocyte formula showed a left-handed shift of the formula (plasmatic cells – 2%, young granulocytes – 3%, stab neutrophils – 15%, segmental neutrophils – 55%, lymphocytes – 22%, monocytes – 3%); a slightly decreased platelet count ($140 \times 10^9/l$). The urinalysis revealed proteinuria (1.32%). The biochemical blood parameters, namely the level of bilirubin and its fractions, the intracellular hepatocytic enzymes, the level of total protein, indicators of the functional state of the excretory system and coagulogram were within the norm. The result of Wassermann reaction, viral hepatitis and HIV serological markers were negative. Deviations from the norm were observed as hypercholesterolemia and dyslipoproteinemia (cholesterol – 8.1 mmol/l, B-lipoproteins – 76 IU, triglycerides – 2.0 mmol/l), in the renal excretory function (urea – 10.2 mmol/l, creatinine – 120 $\mu\text{mol/l}$, GFR clearance – 35 ml/min), and indicators of acute phase inflammation (fibrinogen A – 7.6 g/l; fibrinogen B 3+; ethanol test 2+). Significant increase

of alkaline phosphatase levels (4882 nmol/l), GGT (2.7 $\mu\text{kat/l}$), uric acid (880 mmol/l), and hypercalcaemia (3.5 mmol/l) were also observed. The results of the instrumental research were characterized by vast deviations from the normative readings. For example, X-ray examination of the chest revealed signs of age-related changes in the pulmonary tissue, aortic sclerosis, left ventricular hypertrophy, and signs of multiple consolidated fracture of the ribs. The ultrasound examination revealed signs of diffuse changes in the parenchyma of both kidneys and pancreas, fatty involution of the mammary glands, and nodal goiter. An electrocardiographic study recorded left ventricular hypertrophy and sinus tachycardia.

The patient was examined by a surgeon and an ophthalmologist with following opinions presented: fibrolipoma of the frontalis, and retinal angiosclerosis of both eyes, respectively.

The X-ray examination of the skull bones presented isolated multiple destruction phenomena of the round form with a diameter of 2-3 cm with clear contours and signs of osteolysis. The conclusion: signs of multiple myeloma (Fig. 1).

The data obtained narrowed the diagnostic search and the patient was referred for consultation by a hematologist. The sternal puncture revealed 11% of plasmatic cells (Fig. 2).

The diagnosis of multiple myeloma in a patient was confirmed according to the criteria recommended by the International Myeloma Working Group (2017) [6]. The therapy was continued at the hematological department.

DISCUSSION

The classical debut of the multiple myeloma is considered a pain syndrome associated with osteolysis. In elderly patients, one third of all cases of the pathology could be manifested as signs of cardiac and chronic renal insufficiency [4, 21, 22]. However, clinical manifestations of joint pathology, as signs of the bone and muscular system pathology are observed in almost all patients after the age of 60 [27].

In the given clinical case, the complaints of the patient, the history of the disease and life, the results of physical examination and additional research methods, at first glance, corresponded to a picture of chronic cardiac or chronic renal pathologies, or a combination thereof. For example, subjective (weakness, shortness of breath, palpitations, etc.), objective data (displacement of the left cardiac border, the accent of the second tone above the aorta, edema of lower extremities), the results of ECG and X-ray examination of the chest, hypercholesterolemia, and dyslipidemia suggested a cardiovascular pathology. However, slowly progressing edema of the lower extremities, changes in laboratory parameters (severe anemia, high ESR, elevated enzyme count and indicators of acute phase of inflammation and chronic renal failure) were considered as signs of chronic kidney disease. It should be noted that unreasonable subfebrile condition, weight loss, a significant ESR increase, a leukocyte formula left-hand shift, hyperuricaemia and hypercalcaemia did not fit the cardiovascular and excretory system chronic pathology pattern and did not present any answers without additional research. The debut of the disease in the presented clinical case confirmed the data obtained by other researchers regarding MM variants with dominant signs of heart failure and chronic kidney disease [21, 22]. The presence of so-called “red flag” or “alarm” symptoms among the subjective and objective signs in the clinical picture of the patient’s K disease entertained the idea of a possible oncological pathology.

These same ambiguous clinical cases call for an expanded differential diagnostic search with the involvement of specific laboratory and instrumental tests recommended by the WHO clinical protocols.

Special attention of general practitioners regarding MM manifestations should be paid to a combination of the following symptoms and syndromes: moderate and severe anemia, a significant ESR growth, changes in laboratory parameters characteristic for osteolysis and chronic renal failure, even in the absence of characteristic pelvic pain. On the other hand, the resistance of pain syndrome to NSAID

therapy also requires a differential diagnostic search. A specific cytological pattern of bone marrow showed by a sternal puncture made it possible to finally confirm the diagnosis of multiple myeloma. The problem of untreated cases of the disease consists in the fact that, on the one hand, patients with unclear clinical picture, the symptoms of osteolysis and the absence of characteristic bone pain rarely agree to sternal puncture, on the other hand, joint pain, changes in laboratory parameters of elderly patients are considered by family doctors as age-related. Therefore, X-ray of flat bones of the skull and pelvis remains one of the simplest available screening diagnostic methods, which allows to detect the osteolysis foci.

CONCLUSIONS

1. Multiple myeloma, especially in recent years, has gained a worldwide trend of growing incidence.
2. Subacute onset, slow progression, various clinical options of the disease, and the presence of comorbid pathology cause difficulties in timely diagnosis of the disease in elderly people.
3. Radiography of flat bones of the skull and pelvis is one of the viable screening methods for detection of multiple myeloma in the primary medical care system.

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The Authors declare no conflict of interest

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