CASE REPORTS

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Myeloma multiplex with pulmonary dissemination

Multipli mijelom sa pulmonalnom diseminacijom

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Abstract

Introduction. Multiple myeloma is a hemathological malignancy characterized by the clonal proliferation of plasma cells in the bone the marrow. Extramedullary dissemination of multiple myeloma is uncommon. In several cases only, the multiple myeloma malignant plasma cells had disseminated to the lung parenchyma. **Case report.** We presented a case of multiple myeloma with lung plasmacytoma, in a 79-year-old patient, hospitalized for febrility and infiltrative mass in the right lung. Two months before the patient was admitted, because of developing terminal renal failure, hemodialysis treatment had started three times a week. Since then, the patient was oliguric, but because of febrility and hemoptysis that appeared, at first he was treated with dual antibiotic therapy which resulted in temporary improvement of his general condition, but pleural effusion remained. After thoracocentesis, followed by myelogram, the multiple myeloma diagnosis was established. **Conclusion.** In patients of middle and older age, with general weakness, exhaustion, loss of weight, renal failure which progresses to the end stage rapidly, if symptoms of respiratory tract occur, consider this uncommon disease – extramedullary dissemination of multiple myeloma.

Key words:
multiple myeloma; neoplasm metastasis; lung; plasma cells.

Apstrakt

Uvod. Multipli mijelom je hematološko maligno oboljenje koje se odlikuje klonalnom proliferacijom plazma ćelija u koštanu srž. Ekstramedularna diseminacija multiplog mijeloma izuzetno je retka. U samo nekoliko slučajeva opisana je diseminacija multiplog mijeloma u pluća. **Prikaz bolesnika.** Prikazali smo bolesnika sa multiplim mijelomom plućne lokalizacije, starog 79 godina, koji je hospitalizovan zbog febrilnosti i infiltrativne promene u desnom pluću. Dva meseca pre prijema, zbog razvoja terminalne bubrežne slabosti, započeto je lečenje hemodijalizom, tri puta nedeljno. Od tog perioda bolesnik je bio oliguričan, a zbog pojave febrilnosti i hemoptizija lečen je najpre dvojnom antibiotskom terapijom, na čiju primenu je došlo do prolaznog poboljšanja opšteg stanja, ali bez povlačenja pleuranog izliva. Nakon učinjene torakocenteze, a potom i mijelograma, postavljena je dijagnoza multiplog mijeloma. **Zaključak.** Kod bolesnika srednjeg i starijeg životnog doba uz opštu slabost, malaksalost, gubitak telesne mase, bubrežnu insuficijenciju koja brzo progredira do terminalne, ukoliko se pojave simptomi u respiratornom traktu, diferencijalno dijagnostički treba razmišljati i o ekstramedularnoj, plućnoj diseminaciji multiplog mijeloma.

Ključne reči:
multipli mijelom; neoplazme, diseminacija; pluća; plazma ćelije.

Introduction

Multiple myeloma (MM) is a plasmaproliferative disease that is most often characterized with uncontrolled monoclonal proliferation of plasma cells in the bone marrow. As a consequence of tumor activity and its products, there are osteolytic lesions, osteopenia with pathologic fractures, followed with hypercalcemia, renal failure and hyperviscous syndrome [1, 2]. It appears in adults, more often male, the average age around 65 years and constitutes approximately 1% of all malignant diseases and slightly more than 10% of all hematologic malignancies [3–5]. The annual incidence in America is approximately 4−5 in 100,000 people and the similar trend is recorded in Europe, too [5–7].

Extramedullary plasmacytoma (EMP) represents approximately 3% of plasma cell neoplasms. EMP are uncommon and typically manifested like solitary plasmocytoma, and about 80% is in the upper respiratory tract, and less than

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5% of all extramedullary plasmocitomas is localized intrapulmonary [8]. Having in mind rates of occurrences of the abovesaid diseases, MM with pulmonary localization is considered as very uncommon.

Renal failure appears in this disease in approximately 50% of patients and is manifested as chronic, but rarely as acute renal failure. Whereas, it is a well-known fact that myeloma spreading to kidneys is an adverse prognostic sign [9, 10].

Chejfec et al. [11] defined even in 1983 the term "myeloma lung" with diffuse infiltrative plasma cells in pleural punctate or tissue samples obtained with needle biopsy and in rarely described cases, with MM spreading to lungs. The diagnosis is often established with biopsy, intraoperatively or by autopsy [11, 12].

Case report

A 79-year old male patient was admitted to our department as a dialysis patient with temporary vascular access (CVC-right jugular vein), pronounced anemic syndrome, febrility and infiltrative mass in the right lung. Regular hemodialysis, three times a week lasting 4 hours, had started 2 months before he was hospitalized in our hospital, but additional difficulties had occurred 4 weeks before he was admitted with body temperature of up to 40°C. He was hospitalized in a regional hospital on suspicion of pleuropneumonia, and dual antibiotic therapy was introduced. This therapy led to lowering body temperature, but the increased levels of acute infection phase reactants remained with sedimentation rate 84 mm/h and C-reactive protein 103 mg/L. According to objective findings, the patient was markedly pale, with visible mucosa and with weakened respiratory murmur in the right lung, with a mass of inspirium crackles and inaudible breathing on the basis, left lung. The radiography of the lungs showed the infiltrative mass in the right lung with the presence of pleural effusion in both, more in the left (Figure 1), while the bronchoscopic findings were normal. The ultrasound of abdomen was almost normal, except the left kidney which was with a larger number of cysts, and the largest one was around 45 mm.

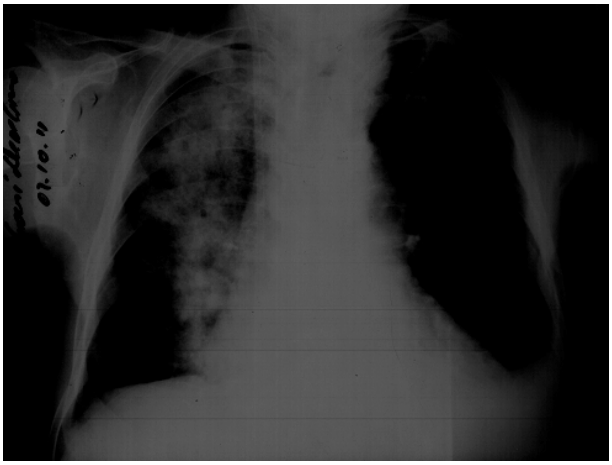

Fig. 1 − Infiltrative mass in the right lung, and the presence of pleural effusion in the left one.

Computed tomography (CT) of the chest confirmed the existing pleural effusion in both lungs and in the right, the zones that would most likely correspond to pneumonitis. Additionally, at the level of the thoracic vertebral body Th9-Th10, there was a hyperdense, solid mass with the diameter of 32 × 19.5 mm, while the other was with the diameter of up to 18 mm at the level of transversal L4 (Figure 2). Osteolytic changes were not observed.

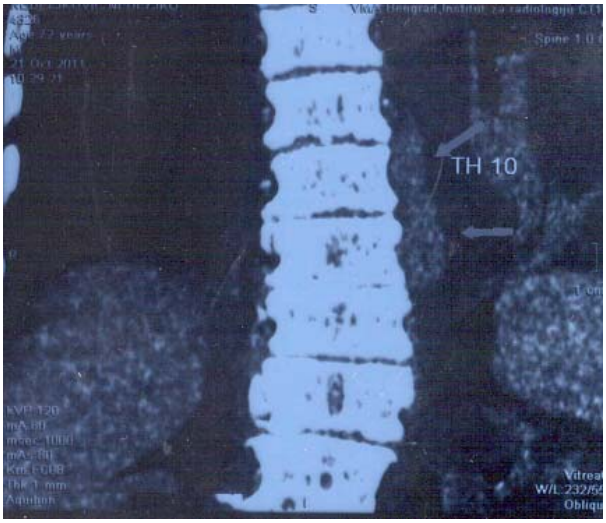

Fig. 2 − Magnetic resonance imaging – a paravertebral tumor mass.

Magnetic resonance imaging (MRI) of the thoracic and lumbar spine confirmed the existence of paravertebral tumor mass on both sides, without any sign of bone destruction.

Laboratory analyses showed anemic syndrome which required substitution (red blood cells 2.87 − 3.33 × 10^{12}, hemoglobin 83−101 g/L, hematocrit 0.26−0.29), while the differential blood test found monocytosis (16−17.3% Mo) with white blood cells 14.9−9.31 × 10^9. The values of urea and serum creatinine were such that the patient was on regular hemodialysis program three times a week (creatinine around 700 μmol/L and urea 20 mmol/L; creatinine clearance rate was of around 6 mL/min). The patient was anuric. The values of alkaline phosphatase ranged from 317−838−407 IU/L, lactate dehydrogenase 914−843 IU/L and once serum hypercalcemia was recorded to be up to 2.71 mg/dL, while the values of total proteins were from 75−87 g/L with normal and slightly lower albumins (35−31 g/L). The completed serum protein electrophoresis indicated M-peak in gamma globulins (36.2%), albumins 44.1%, α1 globulins 4.9%, α2 globulins 7.8%, β1 globulins 2.4%, β2 globulins 4.6%. Immunoglobulin (Ig) λ light chains were 11.8%, and κ light chains 2.49%. The ratio κ/λ was 0.21. Because of the aforementioned pleural effusion, thoracocentesis was done, but the cytological findings of pleural punctuate corroborated plasmacytic infiltration (Figure 3), while in myelogram done subsequently, all the 3 lineages of hematopoiesis were suppressed with 65% by plasma cell infiltration (Figure).

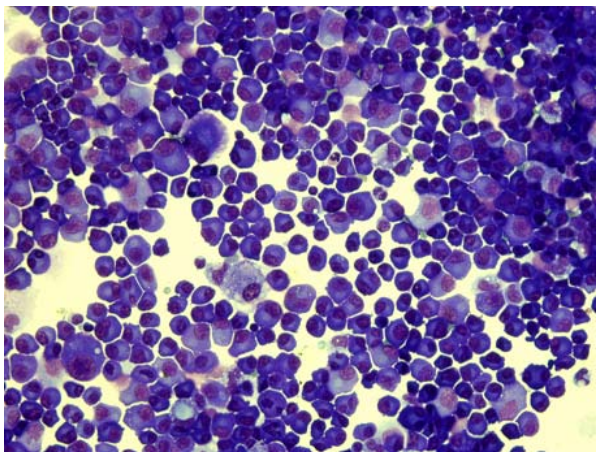

Fig. 3 − Centrifuged deposit of pleural fluid showed plenty of plasmacytoid cells, including binucleated and multinucleated ones admixed with a few reactive mesothelial cells and macrophages (MGG, ×200).

anemic syndrome, and if also spread to the respiratory system, there are symptoms in the upper part of the respiratory tract, too [1–9].

Myeloma cells found at extramedullary site may be because of EMP or due to extramedullar dissemination of multiple myeloma. EMP is an uncommon variant of MM, end it manifests as solitary plasmocytoma. Solitary plasmocytomas occur most commonly in the nasal cavities, paranasal sinuses, nasopharngs lymph nodes, lung, intestinal tract, without bonemarrow involvement. This tipe of plasmocytoma is responsive to local irradiation and has very good prognosis.

Intrapulmonary plasmocytoma is uncommon representing less than 5% of all EMP [8]. In the MM with pulmonary localization there is plasma cells infiltration of the bone marrow and myeloma plasma cells in the lung mass [9]. Several cases of extramedulary plasmocytoma with the involvement of lung parenchyma were only described.

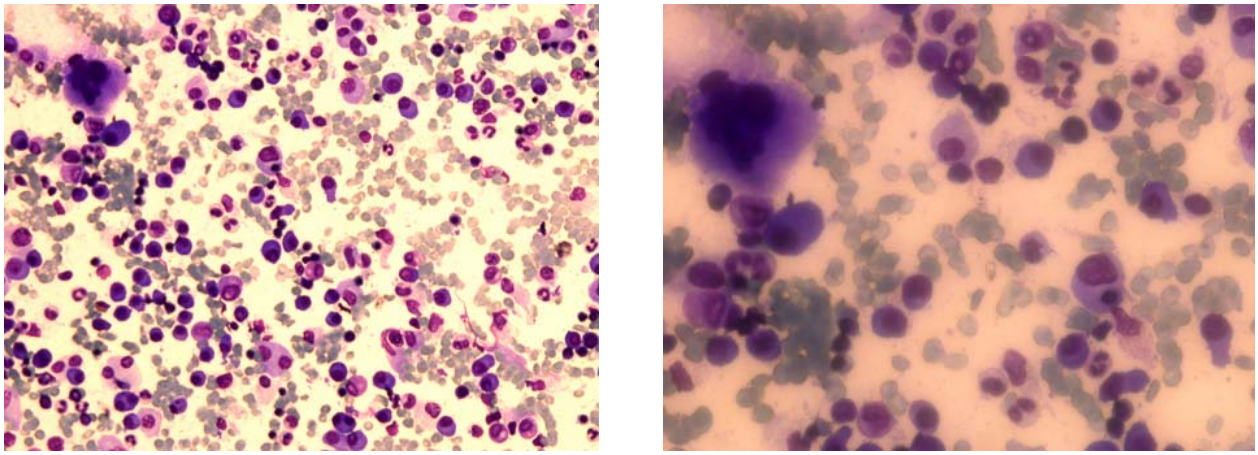

Fig. 4 – Bone marrow examination revealed hypercellular marrow with depression of erythropoiesis and leukopoiesis and adequate megakaryopoiesis, and a large number of plasma cells, above 65% of nucleated cell population, including binucleate and multinucleate forms (MGG: left × 200; right × 400).

Therefore the final diagnosis was multiple myeloma with myelomatous involvment of pleura.

Flat bones radiography, except degenerative changes to pelvis, found no other pathologic changes.

On the account of technical reasons, it was not possible to begin chemotherapy in accordance with the protocol for plasmaproliferative disease so the patient was referred to the competent regional hospital for further treatment. Three days after the patient was transferred, his general condition worsened in terms of his state of consciousness, which was up to the level of somnolence, so that the prescribed therapy was not administered. On the seventh day after his transfer, respiratory arrest appeared which resulted in lethal outcome.

Discussion

In multiple myeloma, the bone marrow is infiltrated with abnormal plasma cells leading to multifocal destructive bone lesions. Clinical presentation of MM is seen in the appearance of general weakness, exhaustion, loss of weight, pain in lumbar spine area, various degrees of renal failure,

In the presented patient, renal failure was the first manifestation of MM, and later pulmonary simptomatology occurred. Because of the infiltrative mass in the lung parenchyma, pulmonary examination was initiated. Computer tomography of the chest showed pleural effusion, but also the tumorous mass paravertebrally bilaterally, while the conducted MRI of the thoracolumbar spine showed no significant changes on bone structures [13–15]. In the course of further examination in order to do diagnostic puncture of pleural effusion, thoracocentesis was done, while cytological findings of pleural punctuate showed numerous plasma cells. Concurrently, laboratory analysis of serum protein electrophoresis showed M-peak in the gamma region [12, 14, 16]. The MM diagnosis was confirmed with biopsy of the bone marrow and the results of more than 65% of plasma cells in myelogram.

Renal failure developed at the very beginning of the disease, while the need for continuous hemodialysis procedures as a sign of irreversible renal failure also corroborated the gravity of the disease and shorter median survival of these patients (on the average 4 months from the first symptoms of the disease).

Dissemination of EMP in the lung is exceptionally rare, and shows up in about 3% of a total number of patients diagnosed with MM [11–13]. Malignant pleural effusion combined with pleural infiltration represents one of the late complications of the disease [17]. The appearance of pleural effusion is an adverse prognostic indicator as well as the resistance to the applied therapy, but also there are great chances for the relapse of the disease despite conducting the radio-and/or polychemotherapy. In some cases, regardless of the therapy, it is also necessary to perform pleurodesis so as to improve the general condition of the patient.

The literature lists the facts that very often, after the appearance of pleural effusion, even with the applied chemotherapy, there is a fatal outcome in the period of less than 4 months.

The presented patient had had the first symptoms of the respiratory tract 3 months before the diagnosis of MM with pulmonary localization was established. In that time, there was a sudden worsening of respiratory symptomatology and progression of pleural effusion so that chemotherapy could not be applied, but the condition resulted in lethal outcome.

Conclusion

Extramedullary dissemination of multiple myeloma in the lung is very uncommon and the prognosis of patients with it is very poor, oppositely to patients with primary pulmonary plasmocytoma to long survival rates. Multiple myeloma is a disease of aged population, with its severe clinical prognosis, heterogeneous symptoms, and the diagnosis is difficult.

Because of that, in patients of middle and older age, with general weakness, exhaustion, loss of weight, anemia, and renal failure, if symptoms of respiratory tract occur, consider this uncommon disease – multiple myeloma with lung involvement.

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