CASE REPORT


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# Acute kidney failure and extramedullary lung infiltration as the initial presentation of multiple myeloma: A case report

## Akutna bubrežna slabost i ekstramedularna infiltracija pluća kao inicijalne prezentacije multiplog mijeloma

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**Abstract**

**Introduction.** Kidney failure in multiple myeloma is sometimes initial symptomatology and a very serious complication with an unfavorable effect on the course and prognosis of the disease. Multiple myeloma is a disease characterized by the proliferation of plasmocytes in the bone marrow, and in rare cases, it can be extramedullary in various organs and systems. Pulmonary plasmacytoma localization is a rare extramedullary localization, especially when it represents one of the initial manifestations of multiple myeloma. **Case report.** We present a patient with progressive acute kidney failure who has started hemodialysis treatment. On chest radiography, a homogeneous shadow was observed along the left chest wall, and the multislice computed tomography (MSCT) pointed to the tumor formation in the pulmonary parenchyma in the projection of the left upper pulmonary lobe with signs of pleural infiltration, intercostal muscles, and V rib destruction. Laboratory examination indicated the presence of Bence-Jones proteinuria in the urine sample in addition to anemia syndrome and azotemia with hyperuricemia. After bronchoscopy and needle biopsy, diffuse infiltration of mature plasma cells was demonstrated in the cytological and histopathological findings of the lungs. The histopathological finding of bone marrow biopsy indicated multiple myeloma of Lambda type with infiltration of plasma cells – about 70%. The hematologist determined a diagnosis of multiple myeloma BJ lambda III BCS, with extramedullary lung infiltration and acute kidney failure. Further treatment was continued according to the hematological protocol while performing intermittent hemodialysis. **Conclusion.** Sometimes, extremely rarely, and in completely asymptomatic patients with massive pulmonary infiltration observed initially, the differential diagnosis may also represent an extramedullary presentation of multiple myeloma, which should be considered.

**Key words:**
**multiple myeloma; lung; acute kidney injury; diagnosis, differential.**

**Apstrakt**

**Uvod.** Bubrežna slabost u multiplom mijelomu ponekad predstavlja inicijalnu simptomatologiju i veoma ozbiljnu komplikaciju sa nepovoljnim uticajem na tok bolesti. Multipli mijelom je bolest koju karakteriše proliferacija plazmocita u koštanoj srži, a u retkim slučajevima mogu biti zastupljeni i ekstramedularno u različitim organima i sistemima. Plućna lokalizacija plazmocitoma je retka ekstramedularna lokalizacija, a pogotovo kada predstavlja i jednu od inicijalnih manifestacija multiplog mijeloma. **Prikaz bolesnika.** Prikazali smo bolesnika sa akutnom bubrežnom insuficijencijom, progresivnog toka, kod koga je započeto lečenje hemodijalizama. Na radiografiji grudnog koša zapažena je homogena senka uz levi lateralni zid grudnog koša, a multislajsna kompjuterizovana tomografija (MSKT) je ukazala na tumorsku formaciju u plućnom parenhimu u projekciji levog gornjeg plućnog režnja sa znacima infiltracije pleure, interkostalnih mišića i destrukcijom V rebra. Laboratorijskim ispitivanjem, osim

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anemijskog sindroma i azotemije sa hiperurikemijom, u urinu je dokazana Bence-Jones-ova proteinurija. Nakon bronhoskopije i iglene biopsije, u citološkom i patohistološkom nalazu pluća dokazana je difuzna infiltracija zrelih plazma ćelija. Patohistološki nalaz biopsije koštane srži ukazao je na multipli mijelom lambda tipa sa infiltracijom plazma ćelijama – oko 70%. Od strane hematologa postavljena je dijagnoza multiplog mijeloma BJ lambda III BCS, sa ekstramedularnim zahvatom pluća i akutnom bubrežnom insuficijencijom. Dalje lečenje nastavljeno je po hematološkom protokolu uz obavljanje intermitentnih hemodijaliza. **Zaključak.** Ponekad, izuzetno retko i kod potpuno asimptomatskih bolesnika, masivne plućne infiltracije, zapažene inicijalno, diferencijalno dijagnostički mogu predstavljati i ekstramedularnu prezentaciju multiplog mijeloma, o čemu treba razmišljati.

**Ključne reči:**
**multipli mijelom; pluća; bubreg, akutna insuficijencija; dijagnoza, diferencijalna.**

## Introduction

Multiple myeloma (MM) is a plasma proliferative disease that is more common in the older population (above the age of 60), with an incidence of about 5 cases per 100,000 persons. It represents about 1% of all malignancies, while it is the second most common hematological disease (10% of cases) [1–5].

The occurrence of acute kidney failure in MM sometimes also represents the initial symptomatology of this disease and further complicates this quite serious disease. It is believed that, precisely because of this presentation, 50% of cases with MM are initially nephrology patients [6]. That is why many authors suggest mandatory MM-related evaluation in acute kidney failure patients [7–9].

The extramedullary (EM) plasmacytoma is malignant plasma cell proliferation, not localized in the bone marrow. It is described in 7–17% of patients at the moment of diagnosis of MM and in 6–20% of cases during the course of treatment of the disease. However, the data of recent studies state the occurrence in about 34% of cases where it represents a very poor prognostic parameter [10–15].

The most common EM localizations (about 85% of cases) are in soft tissues around the skeletal system, and the remaining cases (15%) of EM localization occur in lymph nodes, liver, kidney, respiratory tract, spleen, skin, CNS, and others [13, 14]. EM localization in the lungs is described in less than 5% of cases [16]. Very rarely, as in the case of our patient, simultaneous infiltration of the lungs and acute kidney failure is observed as the initial manifestation of MM.

## Case report

A 47-year-old male was admitted to the Clinic for Nephrology for acute kidney failure development, followed by arterial hypertension and anemic syndrome. The first complaints were reported one month before admission to the Clinic, in the form of fatigue, faster tiredness, and loss of appetite. At that time, elevated creatinine (683 µmol/L) and urine erythrocytes and proteinuria of 0.92 g/24 h were observed in laboratory analyses. The patient was sent to our institution for further assessment. At the time of admission, arterial hypertension (150/85 mmHg) was noted, along with paleness of skin and mucous membrane, while other results were within the normal range. The patient indicated that he was a long-term smoker who ceased smoking one month earlier. Laboratory analysis included the following: accelerated erythrocyte sedimentation rate (ESR 132 mm/h), anemia syndrome [hemoglobin (Hb) 97 g/L], azotemia (creatinine 876–1005 umol/L, urea 42,1 mmol/L), hyperuricemia (670 umol/L), total protein 72 g/L, albumin 50 g/L, and in the urine sample, hematuria with proteinuria of 0.656 g/24 h. Echotomographically, both kidneys were 12.8 cm in size with more echoing parenchyma and pronounced pyramids, and without hydronephrosis and calculus (Figure 1). Given the progressive course of kidney failure, a kidney biopsy was performed. In the meantime, oliguria with hypervolemia developed due to which a central venous catheter was placed in the right *vena jugularis*, and hemodialysis was started. Radiography of the chest revealed a homogeneous shadow of the polycyclic appearance on the

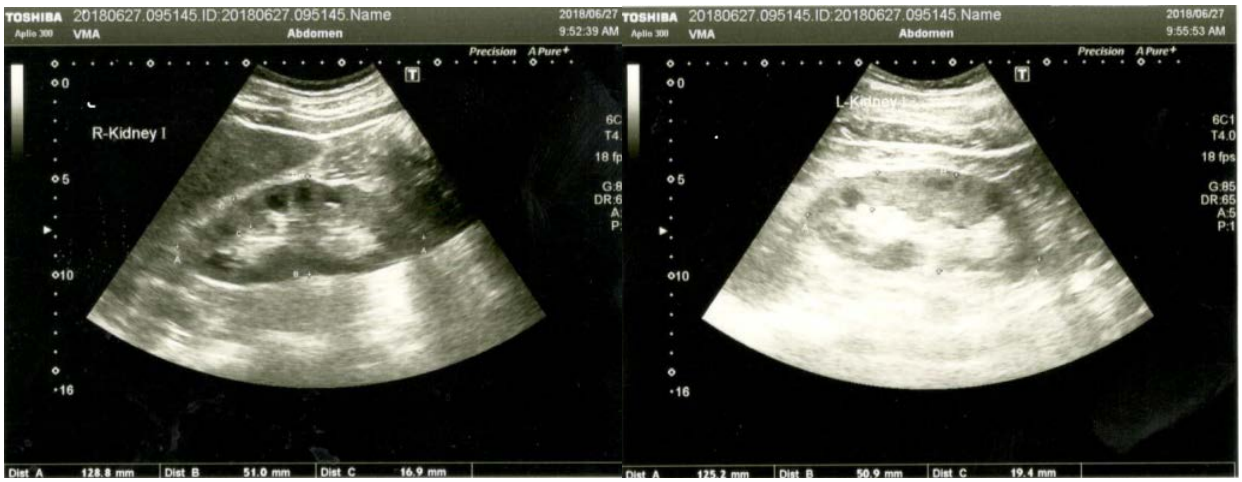


**Fig. 1 – Kidney ultrasound: points to enlarged kidneys, echogenic parenchyma, and pronounced pyramids.**

left side along the lateral wall of the thorax and multislice computed tomography (MSCT) was indicated (Figure 2). An infiltrative tumor formation was observed in the pulmonary parenchyma in the projection of the apical segment on the chest MSCT with dimensions 8 cm × 7 cm × 9 cm, with signs of pleural infiltration, intercostal muscles, and destruction of V rib (Figure 3).

Only then, did the patient recall that a year ago, he occasionally felt mild manifestations of unspecified disturbances on the left side of the chest, which he did not mention because he thought they were irrelevant. Discrete M-spike in the gamma fraction was found in the serum protein electrophoresis: 61.1% albumin, alpha-1 5.5%, alpha-2 13.6%, beta-1 5.3%, beta-2 4.8%, gamma 9.7%. The nephelometric finding indicated an extremely high concentration of Lambda F 5,820.0 mg/L (reference values 8.3–27.0 mg/L), which represents paraprotein seen as discrete M-spike in gamma region on serum electrophoresis. Levels of Kappa F 29.3 mg/L, IgL lambda light chain 1.62 g/L, and IgL kappa light chains 1.43 g/L, k/l ratio 0.88

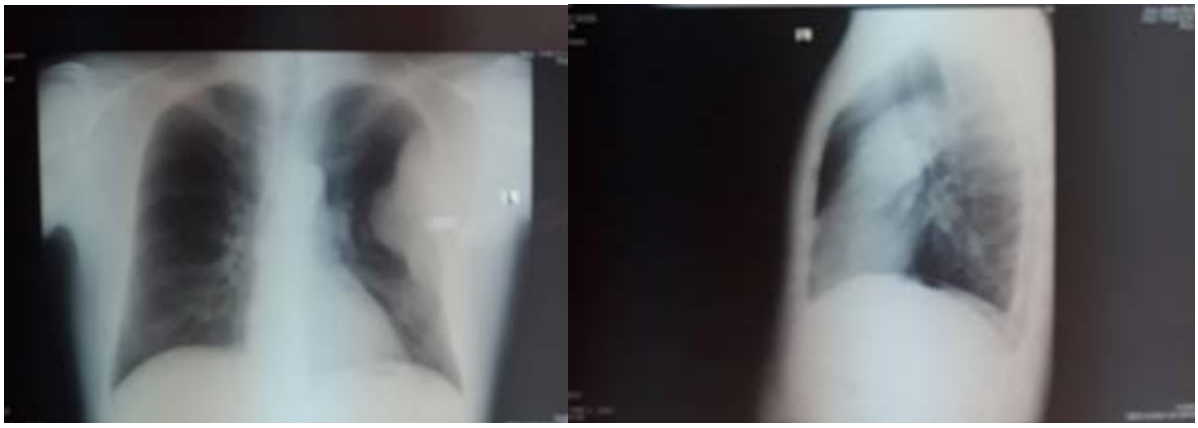

**Fig. 2 – A radiographic record of the thorax on which a homogeneous shadow along the chest wall is seen on the left side in the middle lung field.**

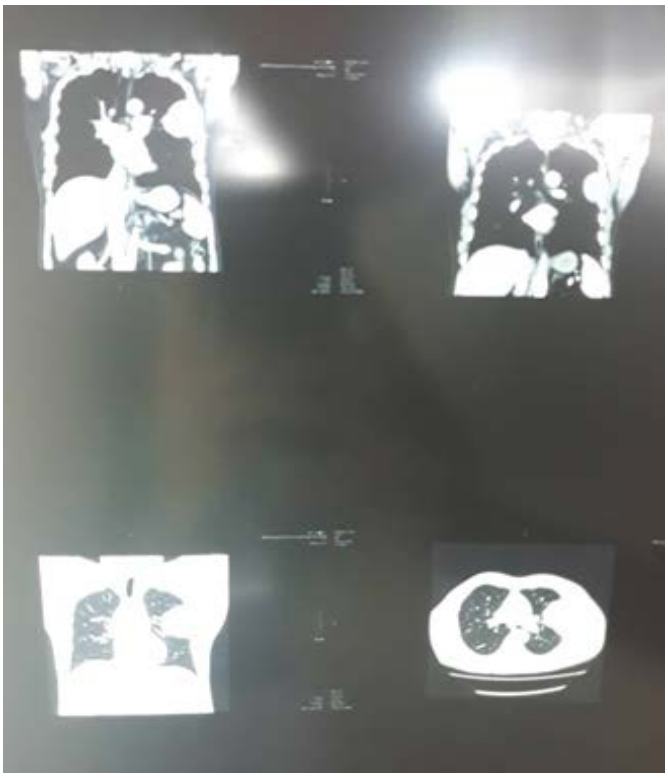

**Fig. 3 – Chest multislice computed tomography (MSCT) with infiltrative tumor formation in the pulmonary parenchyma in the projection of the apical segment of the upper lung lobes, dimensions 8 cm × 7 cm × 9 cm, with signs of the infiltration of pleura, intercostal muscles, and destruction of V rib on the left.**

(reference values 1.35–2.65 g/L), immunoglobulins IgG 7.2 g/L, IgA 0.68 g/l, IgM 0.18 g/L, and serum β2-microglobulin 29.7 mg/L (reference values 0.70–1.80 mg/L) were also determined.

With a diuresis of 700 mL and proteinuria of 0.656 g/24 h, protein electrophoresis in urine was performed: albumin 12.9%, alpha-1 5.9%, alpha-2 18.4%, beta 50.7%, gamma 12.1%, M-spike in the beta fraction. The nephelometric finding indicated: kappa F 29.3 mg/L, lambda F 5820.0 mg/L (reference values 8.3–27.0 mg/L), IgL lambda light chain 1.62 g/L, and IgL kappa light chains 1.43 g/L, k/l 0.88 (reference values 1.35–2.65), b2M 29.7 mg/L (reference values 0.70–1.80 mg/L). The presence of monoclonal light chain Lambda type (bound and free) and monoclonal free light chain lambda type was identified by immunofixation. The finding pointed to Bence-Jones proteinuria (Figure 4).

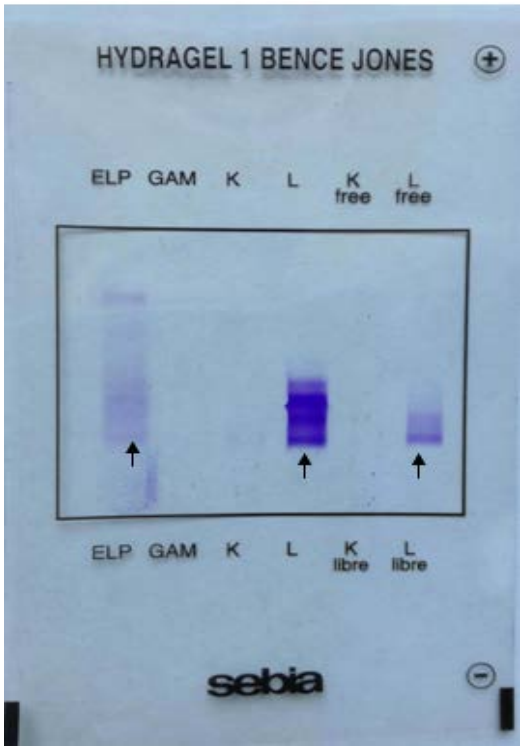


**Fig. 4 – Bence-Jones immunofixation of the patient's urine: the presence of a monoclonal tape derived from the monoclonal free light chain λ type is observed in regions of ELP urine, L-lambda (free and bonded light chains), and L free (free light chains).**

The pathohistological finding of the kidney biopsy indicated obstructive tubulopathy (in the lumen of the tubule crystalloid contents with the surrounding inflammatory reaction), and the characteristics of the "myeloma kidney" were present (Figure 5). In order to clarify the etiology of pulmonary changes, a video bronchoscopy with a needle biopsy of changes in the lungs was performed. The cytological smear of the needle biopsy already pointed to monomorphic cell populations, eccentrically arranged sails in the medium abundant, and basophilic cytoplasm suggesting an extramedullary plasmacytoma (Figure 6).

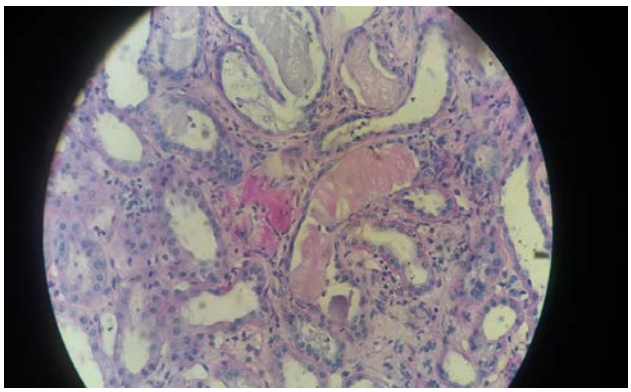

**Fig. 5 – Histopathological findings of the kidney biopsy: obstructive tubulopathy – in the lumen of the tubule, crystalloid content with the surrounding inflammatory reaction, characteristic of the "myeloma" kidney is present [hematoxylin-eosin (HE) staining, ×40].**

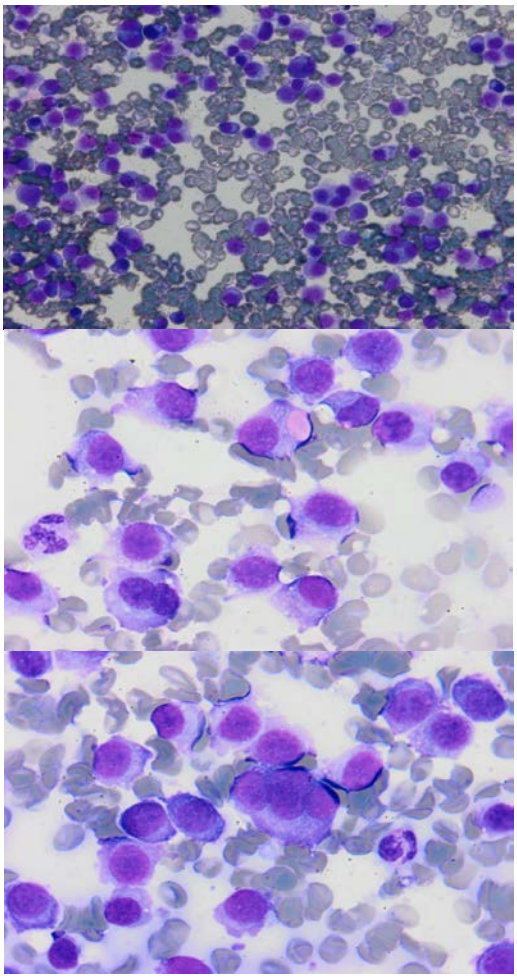

**Fig. 6 – Cytological smears of needle lung biopsies: monomorphic population of cells, eccentrically arranged nuclei in medium abundant, basophilic cytoplasm. In the cytoplasm of certain cells, the focus of the eosinophilic substance corresponding to the deposited immunoglobulins is observed. Multinuclear forms are also present [May Grunwald-Geimsa (MGG) staining, × 200, × 1000, × 100].**

The pathological findings of lung biopsy revealed diffuse infiltration of mature plasma cells. Immunohistochemical analysis in proliferating cells produced a diffuse membrane reaction for CD 138 and a focal membrane reaction for CD 56, while the cytoplasmic reaction for lambda light chains was apparent in a number of cells from the cytoplasmic reaction to kappa light chains (Figure 7). After consultation with a hematologist, a myelogram was performed, and infiltration of the plasma cells (25%) was observed in the cytological smear of the bone marrow aspiration (Figure 8). After that, a bone marrow biopsy was performed, which pointed to multiple myeloma–Lambda type (high infiltration of about 70%). Plasma cell immunophenotyped CD 138+/MUM-1+/Lambd +/Kapa+/CD20- (Figure 9). Flat bone radiography showed: on the bones of the skull, axial skeleton, and pelvis, no signs typical of the multiple myeloma were noticed. The diagnosis of multiple myeloma BJ lambda III BCS, with extramedullary lung infiltrations and acute kidney failure, was determined. Further treatment was continued according to the protocol by a hematologist while performing intermittent hemodialysis.

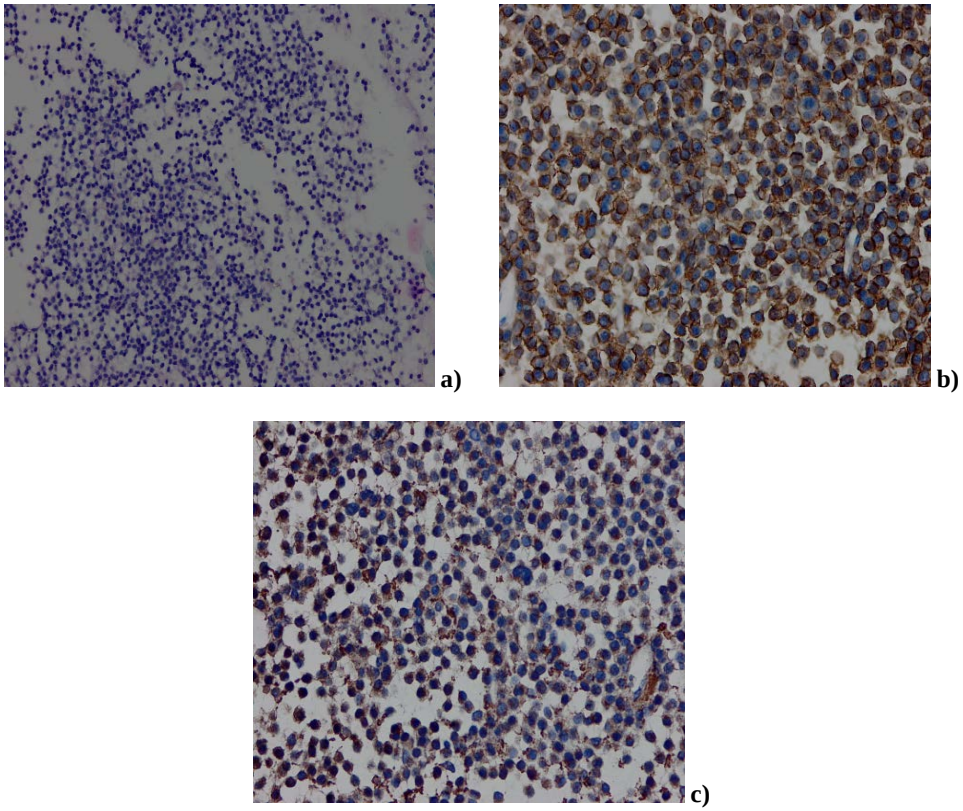


**Fig. 7 – Histoathological findings of pulmonary biopsy: a) proliferation of monomorphic plasmacytoid cells [hematoxylin-eosin (HE) staining, × 200]; b), c) immunohistochemical analysis in proliferating cells resulted in a diffuse membrane reaction CD 138 and cytoplasmic reaction for lambda-light chains (CD 138, lambda, × 400).**

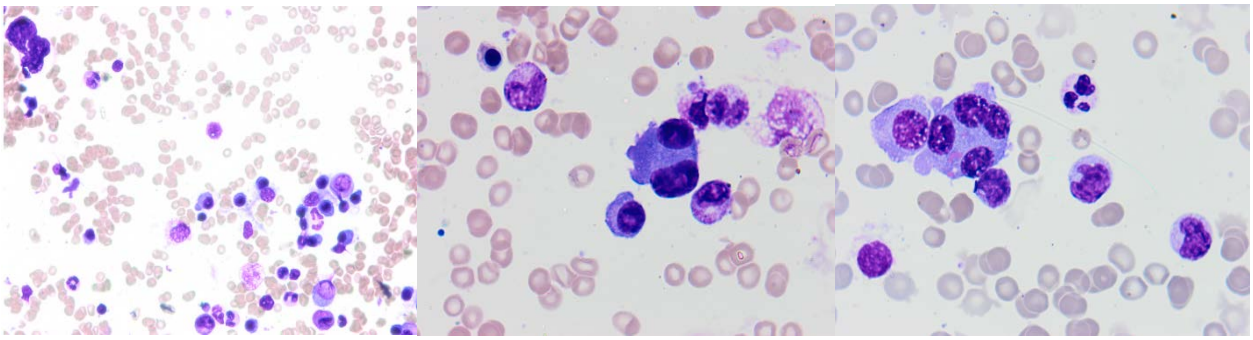

**Fig. 8 – Cytological smear of bone marrow aspiration (MGG, ×10, ×100, ×100). In the lightly hypocellular bone marrow, 25% of plasma cells were found, including binucleate and multinucleate forms present [May Grunwald-Geimsa (MGG) staining, × 100, × 1000, × 1000]).**

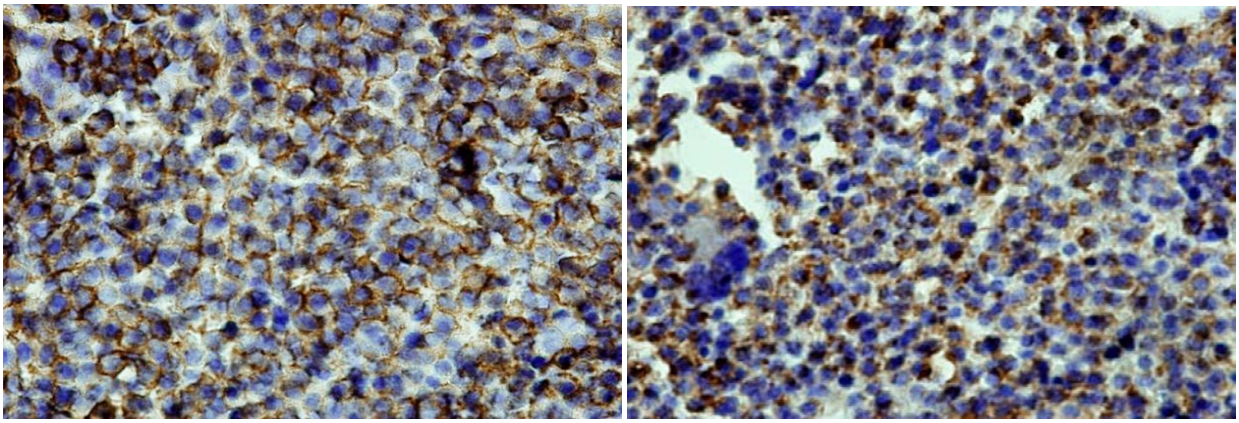

**Fig. 9 – Pathohistological findings of bone marrow biopsy. Immunohistochemical analysis in proliferating cells resulted in a diffuse membrane reaction CD138 and cytoplasmic reaction for lambda-light chains (CD138, lambda, × 400).**

## Discussion

Kidney lesion in MM is a very serious condition with a significant impact on the survival of patients. Sometimes the occurrence of acute kidney failure is the initial manifestation of multiple myeloma, with kidney damage most often being the consequence of the so-called cast nephropathy or "myeloma kidney", which represents tubular damage caused by precipitation of light chain immunoglobulins, followed by deposits of light chains, amyloidosis, hypercalcaemia, drugs, etc. [17, 18]. At the moment of diagnostic MM, the existence of acute kidney failure is described in 20–40% of cases, and in severe cases, it is accompanied by oliguria, thus dialysis is necessary, as was the case with our patient [19].

In patients with MM and kidney failure, Dimopoulos et al. [19] describe median survival of 29–32 months mainly due to the new therapeutic modalities.

Extramedullary localization of MM is more common among males (about 3–4 times more frequent than in females), with only 1/3 of patients being younger than 50, as was the case with our patient [20–24].

In a study involving 1,027 patients with MM, Kyle et al. [21] described the extramedullary occurrence of MM before diagnosis in 4 patients (0.4%), and the median of the time interval was 18 months. According to anamnestic data, our patient experienced some unspecified difficulties on the left side of the chest a year earlier. Varettoni et al. [11] describe the occurrence of EM plasmacytomas in 13% of patients, with 7% having a pronounced EM plasmacytoma localization at the time of MM diagnosis, whereas in 6% of patients, there was a subsequent manifestation of EM plasmacytoma localization. Varga et al. [14] described that about 34% of patients treated for MM also express EM localization during treatment.

Data from other authors describe EM plasmacytoma in 20% of cases of plasma proliferative neoplasia, and the observation that the growth frequency is increasing is explained by the fact that the diagnostics are more sensitive, as well as the new treatment protocols that affect the survival of these patients [10–12, 23].

Five-year survival in patients with MM and EM plasmacytoma is described in 31% of cases, and in patients with MM but without EM plasmacytoma, in 59% of patients [24]. In MM light chains, the incidence of extramedullary localization is described initially in 2.1% of patients, and during the monitoring and treatment in 33.3% of cases, according to Zhang et al. [25]. EM plasmacytoma is sometimes described in patients who have previously been in remission, while in the course of the disease, relapse multiple organ involvement is observed – pancreas, kidney, adrenal glands, liver, lung skin, spleen, and lymph nodes [26]. The study of Oshima et al. [27] encompassed a period of twenty years and analyzed autopsy findings in 53 patients with multiple myeloma, and in 2/3 (63.5%), extraosseous localization was most represented in the spleen, kidney, and liver (about 30%), while pulmonary infiltration was observed in 15.4%.

Extramedullary localization in the respiratory tract is described in approximately 80% of patients, most often localized in the upper respiratory and nasopharyngeal tract (65–80%), while lung involvement is described less often, in 3–5% of cases [16, 20, 28, 29].

In a study published in 2004, in describing the cases of patients with pulmonary plasmacytoma (endobronchial localization), Edelstein et al. [30] state that only 22 proven cases of pulmonary infiltration have been described with immunohistochemical and other confirmatory assays. In a study published in 2011, in demonstrating a case of a patient with pulmonary plasmacytoma who had been experiencing difficulties in the form of shortness of breath, chest pain, cough, and loss of appetite, Prasad et al. [31]compare case studies of different authors with a review of pulmonary plasmacytoma, which is a rare occurrence (they describe 35 cases).

Extramedullary pulmonary plasmacytoma in our patient also represents the initial manifestation of multiple myeloma, which was clinically almost asymptomatic. The mild, nonspecific complaints of pain on the left side of the chest, which occasionally occurred, did not attract attention. At the moment of diagnosis, pulmonary changes were 9 cm in size, with pleural infiltration, intercostal muscles, and destruction

of the V rib. Only the occurrence of general signs of weakness and fatigue with laboratory confirmation of the patient's uremia brought the patient to a medical institution, where lung infiltration was observed during the examination of the etiology of kidney failure, and then multiple myeloma diagnosis was determined. EM pulmonary localization can clinically range from completely asymptomatic form to symptomatology in the form of cough, shortness of breath, and elevated temperature [32, 33].

Ravinet et al. [34] describe the case of a patient with a diagnosed MM who has experienced chronic respiratory insufficiency and emphysema, which had progressed to acute dyspnea and interstitial lung disease that was refractory to applied therapy. Postmortem autopsy analysis in the lungs verified nodal plasma cell infiltrates. Radiological investigations of pulmonary localization of plasmacytomas can present as infiltration in the form of a solitary mass of the nodular form, as in our patient, or as diffuse lung infiltration, which can sometimes occur on both sides [27, 35, 36].

## Conclusion

The case of our patient confirms the opinion that the diagnosis of acute kidney failure should always be completed with screening for multiple myeloma. Extraosseus localization with pulmonary infiltration represents a rather rare presentation of multiple myeloma, indicating the aggressive course of this disease especially given the association with renal impairment and consecutive treatment limitations.

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