



Clinical case

Acute Myeloid Leukemia in a Geriatric Patient with a History of Minimal Change Disease

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Abstract

Background: The increase in the incidence of malignancies globally, and the increase in the usage frequency and types of new anti-cancer drugs, have made onconephrology more important in our clinical practice. Paraneoplastic glomerulonephritis constitutes an important part of this approach as well.

Purpose: The association of AML-nephrotic syndrome is relatively less defined in the literature compared to other hematological malignancies.

Case presentation: In this article, we present a case of acute myelocytic leukemia in a patient who was diagnosed with minimal change disease many years ago.

Discussion and Conclusion: Hematological malignancies-MCD association, is one of the best described examples of paraneoplastic glomerulonephritis. We know that cancer can be clinically diagnosed years after the detection of renal disease in paraneoplastic glomerulonephritis. In this case; rationality of follow-up, not only during the diagnosis of glomerulonephritis but also periodically in the long term, especially in clinical situations such as MCD that occur in geriatric patients, should be discussed.

Keywords: Acute myelocytic leukemia; minimal change disease; geriatrics; paraneoplastic glomerulonephritis.

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Leucemia mieloide aguda en un paciente geriátrico con antecedentes de enfermedad de cambios mínimos

Resumen

Introducción: El aumento en la incidencia de neoplasias malignas a nivel mundial, y el aumento en la frecuencia de uso y tipos de nuevos medicamentos contra el cáncer, han hecho que la onconeurología sea más importante en nuestra práctica clínica. Asimismo, la glomerulonefritis paraneoplásica también constituye una parte importante de este enfoque.

Propósito: La asociación de LMA-síndrome nefrótico está relativamente menos definida en la literatura a comparación de otras neoplasias malignas hematológicas.

Presentación del caso: En este artículo presentamos un caso de leucemia mielocítica aguda en un paciente al que se le diagnosticó enfermedad de cambios mínimos hace años.

Discusión y Conclusión: La asociación de neoplasias hematológicas malignas-MCD, es uno de los ejemplos mejor descritos de glomerulonefritis paraneoplásica. Sabemos que el cáncer puede diagnosticarse clínicamente años después de la detección de la enfermedad renal en la glomerulonefritis paraneoplásica. En este caso, debe discutirse la racionalidad del seguimiento, no solo durante el diagnóstico de glomerulonefritis, sino también periódicamente a largo plazo especialmente en situaciones clínicas como la ECM que se presenta en pacientes geriátricos.

Palabras clave: Leucemia mielocítica aguda; enfermedad de cambios mínimos; geriatría; glomerulonefritis paraneoplásica.

Case history

A 79-year-old male patient was admitted to the nephrology outpatient clinic with complaints of weakness, dizziness and bruising on the body for the last month. In his medical history, it was learned that he had a renal biopsy nine years ago (in 2011) due to nephrotic syndrome. In the renal biopsy; there were no findings other than mild congestion in 11 glomeruli, in immunofluorescence examination IgG-IgA-IgM-C1q-C3-C4 was negative, fibrinogen was fine, granular positive in the glomeruli, and, a diagnosis of MCD was made excluding secondary causes (Figure 1, 2). The patient responded to oral steroid treatment and was accepted in remission. In addition, there was a history of type 2 diabetes mellitus, coronary bypass surgery and benign prostatic hyperplasia. He did not describe any familial renal disease. In the physical examination; he was conscious and he was pale, his arterial blood pressure was 130/80 mmHg, heart rate 98/min and respiratory sounds were normal. The heart was tachycardic and there was a 2/6 systolic murmur in all foci. Several ecchymoses were seen on the patient's lower extremities and back, there was no organomegaly, palpable lymphadenopathy, and peripheral edema. The drugs he had been using were tamsulosin hydrochloride, isosorbide

mononitrate, metoprolol, acetylsalicylic acid, metformin, olmesartan medoxomil, furosemide and escitalopram. Laboratory values on admission are shown in the table (Table 1). Ultrasonography revealed cholelithiasis, a 17 mm diameter stone and caliectatic changes in the left kidney, and simple cortical cysts in the bilateral kidneys. The size and parenchymal thickness of the kidney were reported as normal. The patient, who came for a control 7 months ago and whose hemogram values were completely normal, was consulted with hematology because of bicytopenia. Blastic cells were detected in the peripheral smear. Upon bone marrow biopsy; cellularity was 50 %, increased interstitial blastic cells among marrow cells, and immunohistochemically, CD 34 (-), CD 117 (+), CD 33 (+), MPO (+), TdT (-) were detected in blastic cells (Figure 3, 4). In the genetic evaluation, monosomy 7, trisomy 8, 5q31 deletion, 7q31 deletion, 20q12 deletion and 20q13.2 deletion were not observed. With the present findings, the patient was diagnosed with acute myelocytic leukemia (M0). After the cardiological evaluation, subcutaneous azacitidine 75 mg/m² treatment was initiated. On the 5th day of the treatment, the patient died due to cardiovascular and septic reasons.

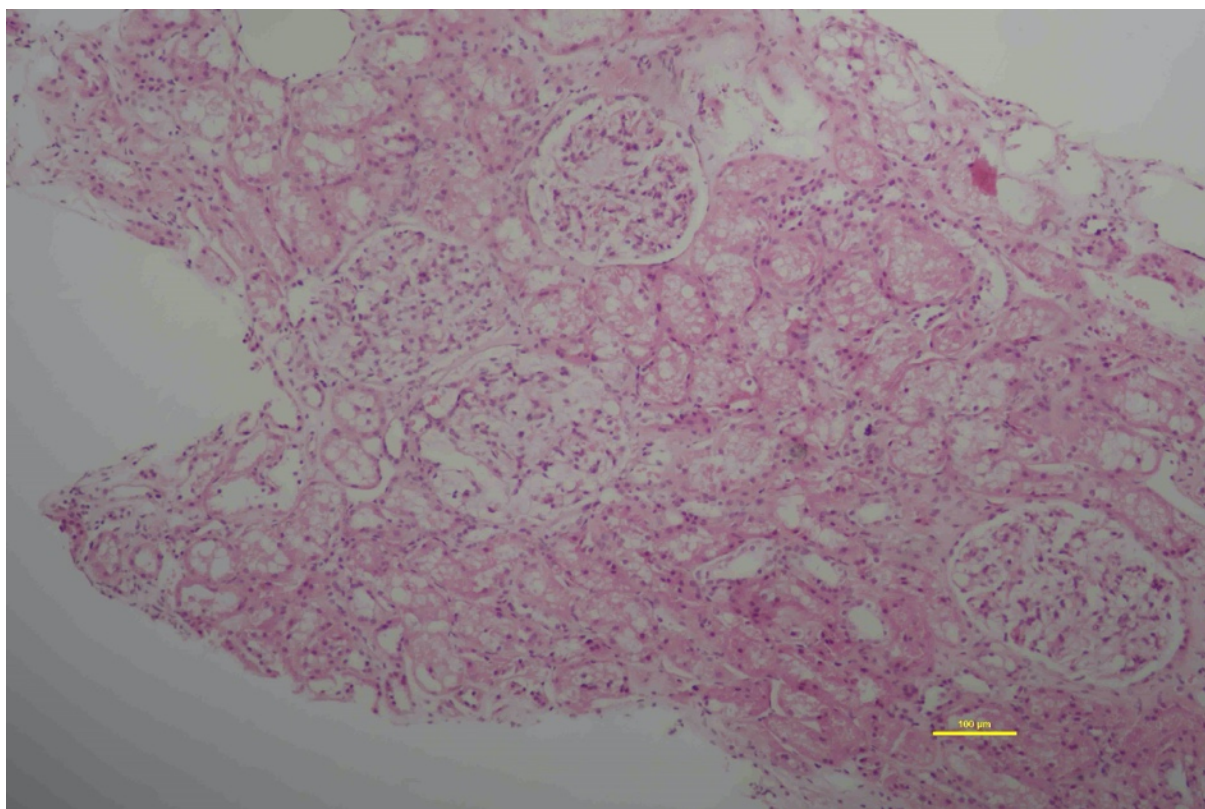


Figure 1. Renal biopsy specimen X100, Normal glomeruli and interstitial area

Source: The authors.

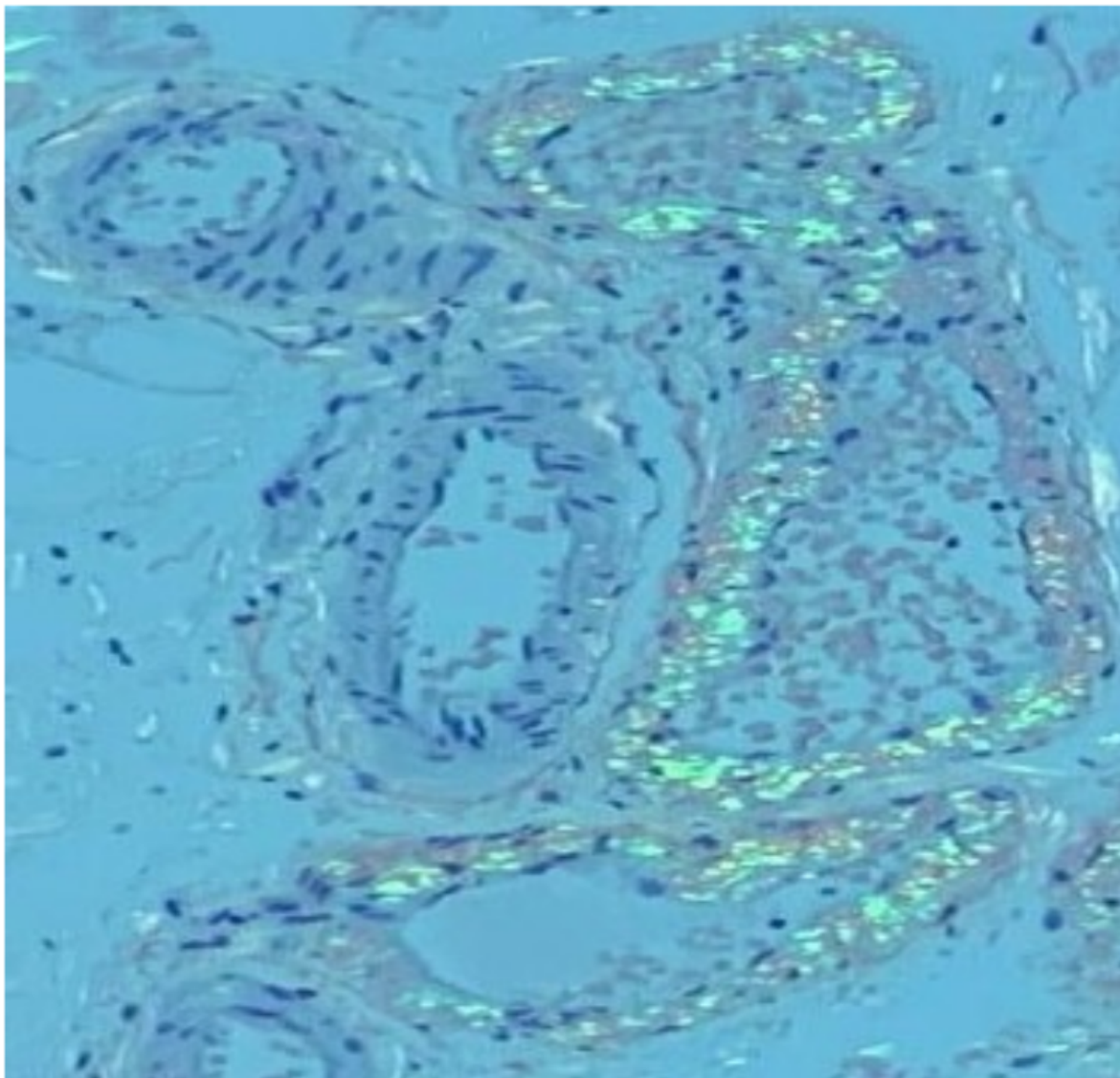


Figure 2. Renal biopsy specimen X200, Normal glomeruli and interstitial area

Source: The authors.

Discussion

MN is the most common paraneoplastic glomerulonephritis when all malignancies are evaluated and it seems to be often associated with solid tumors. When it comes to hematological malignancies (especially lymphomas), the incidence of MCD increases. In addition, MN, MPGN, FSGS and Ig A nephropathy may be associated with hematological malignancies.

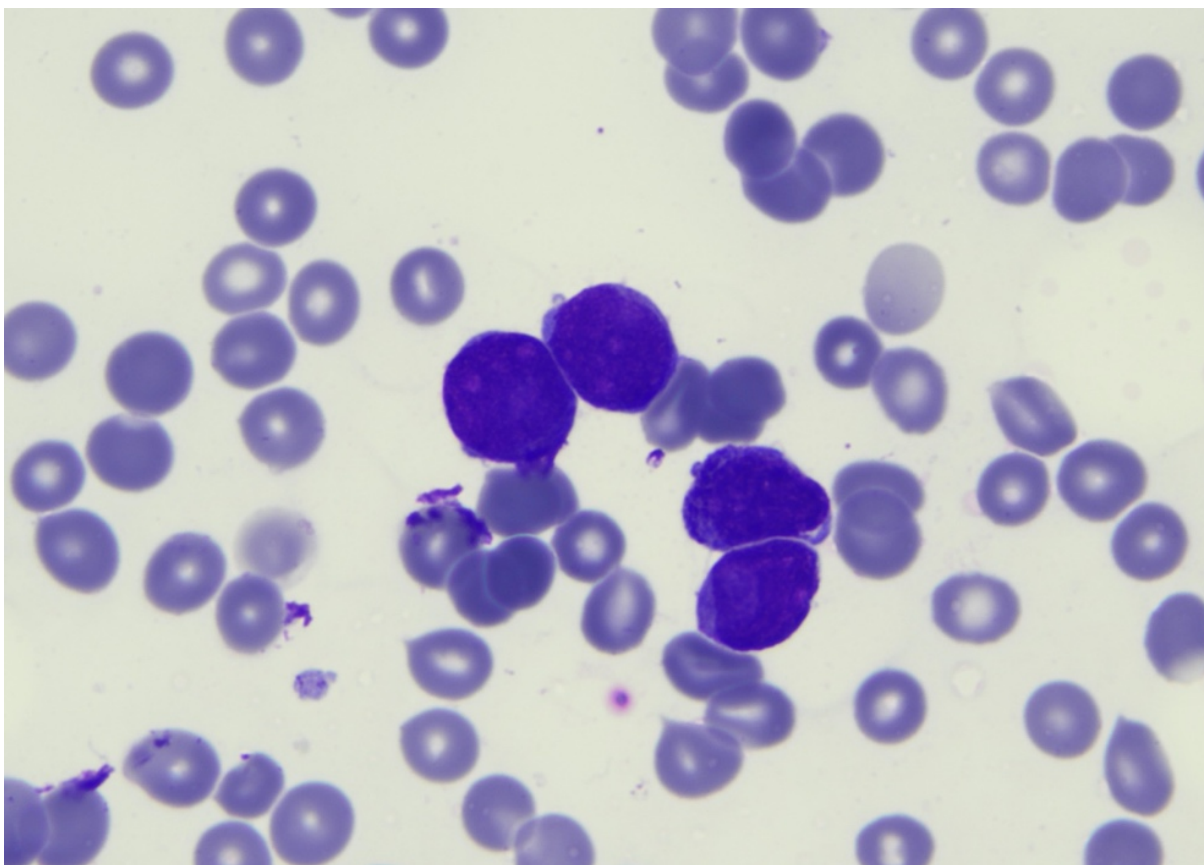


Figure 3. Interstitial blastic cells among marrow cells

Source: The authors.

Minimal change disease, is a type of glomerulonephritis that presents with nephrotic syndrome (proteinuria above 3.5 g/day, hyperlipidemia/lipiduria, hypoalbuminemia and edema) and is more common in the child/adolescent period compared to adulthood (90 % vs. 10 %). Glomerular immunoglobulin or complement accumulation is not observed and it is assumed that the main injury mechanism is podocytopathy. It is thought that the production of the glomerular permeability factor secondary to immune cellular dysfunction (especially immature and undifferentiated T cells (CD34 +)), and the effect of this factor on the glomerular capillaries, cause proteinuria and fusion in podocytes. There is strong evidence that this factor may be IL-13 [1]. MCD can be seen secondary to drugs (NSAI, antibiotics, lithium, etc.), infections, atopic/allergic conditions, and in the course of other glomerular diseases (IgA nephropathy, lupus nephritis). It can also be seen as paraneoplastic in the course of hematological malignancies (Hodgkin lymphoma, non-Hodgkin lymphoma, leukemias), and solid organ tumors (thymoma, renal cell carcinoma, mesothelioma), especially in middle and advanced ages. Hodgkin lymphoma-MCD association is one of the best described examples of paraneoplastic glomerulonephritis. In the most comprehensive study examining this association, 21 patients participated. In this multicenter study of French origin, MCD was detected

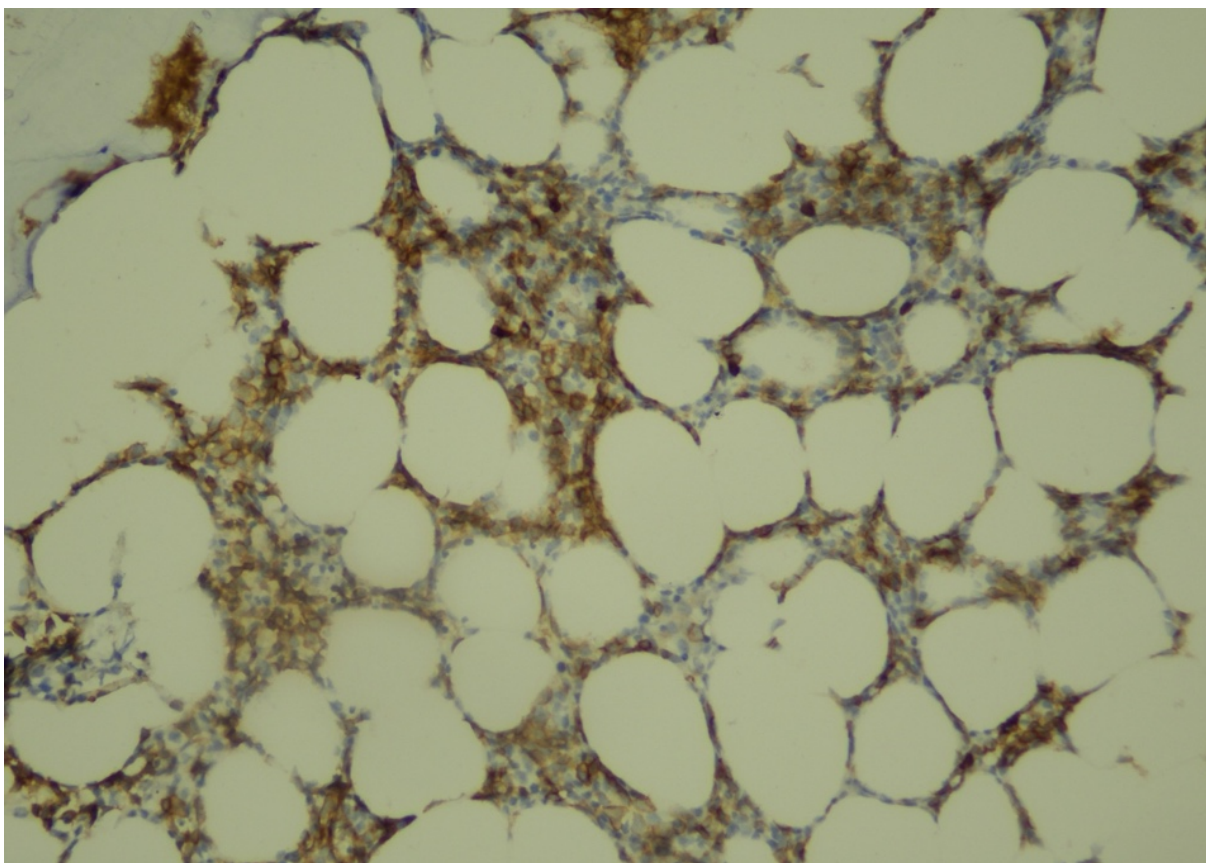


Figure 4. CD 117 positivity, blastic cells

Source: The authors.

in 8 of 21 patients before the diagnosis of lymphoma, additionally the mean time between MCD-Hodgkin lymphoma in these patients was 28.8 months, and the longest was 10 years [2].

Acute myeloid leukemia is a clinical condition that occurs as a result of clonal proliferation of myeloid precursor cells. It may be presented with varying degrees of cytopenia's, due to leukemic blast deposits in peripheral blood, bone marrow and other organs. Furthermore, it constitutes 80 % of acute leukemias in adults, and the average age at diagnosis is approximately 65. Renal involvement in the course of AML usually includes tumor lysis syndrome or acute kidney injury (prerenal injury, drug/antibiotic associated renal damage). As in other hematological and solid organ tumors, paraneoplastic glomerulonephritis can be seen simultaneously before or after AML diagnosis. Cancer can be clinically diagnosed years after the detection of renal disease in paraneoplastic glomerulonephritis. Therefore, some authors recommend routine, periodic screening (every 5 years under 50 to 60 years of age, and every 3 years if older) in late-onset types of glomerulonephritis, due to the lack of clear guidelines on this subject [3].

Table 1. Laboratory values on admission

Urea (mg/dl)	40	WBC	7050	Folate	5,03	C3 (g/L)	1,23
Creatinine (mg/dL)	0,8 3	Neutrophile	540	INR	1,28	C4 (g/L)	0,35
Na (mmol/L)	137	Lymphocyte	4090	Afp	1,1	Cea	3,21
K (mmol/L)	4,0	Monocyte	2410	Ca 19-9	9,08	Ca 125	11,5
Calcium (mg/dL)	8,6 5	Hemoglobin (gr/dL)	7,6	Ca15-3	22,6	Fecal occult blood test	Negative
Phosphorus (mg/dl)	4,5	Hematocrit (%)	22,8	HbsAg	Negative	AntiHbs	Negative
Uric acid (mg/dL)	6,7	MCV (fL)	98,3	Anti HCV	Negative	HIV	Negative
Albumin (gr/dL)	3,5 8	MCH (pg)	32,8	PTH (pg/ml)	39,9	24h proteinuria (mg/d)	256
Ferritin (ng/ml)	656	RDW (%)	15,9	24h albuminuria (mg/d)	35	Vit B12	2000<
ALT (U/L)	5	Platelet	8400 0	Ig G(g/L)	17,23	Ig M (g/L)	0,65
LDH (U/L)	148	Sedimentation (mm/ h)	140	Ig A(g/L)	5,62	Kappa Light chain (g/L)	4,808
LDL (mg/dl)	114	Triglyceride (mg/dl)	162	Lambda light chain (g/L)	3,212	TIT	Ery +, protein negative, dansity 1017, ph 5

Source: The authors.

In the study conducted by Bjørneklett *et al.*, it was shown that there could be patients who could be diagnosed with cancer up to 157 months after MN was detected. In this study, it was shown that the probability of renal biopsy-cancer detection increased statistically and significantly (standardized incidence ratio of 2.30) in the following 5 to 15 years period, as in the first 5 years after renal biopsy. It has been shown that the increased risk of cancer is not limited only to the short term immediately after the diagnosis of renal disease, but that this risk continues for many years after the renal disease diagnosis [4].

The pathophysiological relation between MCD and cancer is not as clear as the relation between MN and cancer. The most obvious mechanism to blame is VEGF-related. It is stated that the glomerular effect of anti-VEGF agents is TMA (with endothelial damage) or MCD/FSGS (with podocytopathic effect). These immunohistological effects are similar to HIV associated nephropathy (loss of certain podocytes differentiation markers and proliferation

of glomerular epithelial cells as indicated by KI-67 staining). In particular, it is emphasized that podocytopathy secondary to tyrosine kinase inhibitors occurs. In this study in which the renal effects of anti VEGF agents were monitored, it was observed that histochemically, Wnt-1 expression was decreased, c-mip accumulation, absence of synaptopodin in podocytes and KI-67 staining, were significantly higher in the group with MCN/cFSGS-like lesions. The reduced presence of VEGF in the glomeruli may have deleterious effects on kidney function since the glomerular filtration barrier may be particularly susceptible to toxicity from VEGF inhibitors [5]. Taniguchi *et al.* presented a case with coexistence of rectal adenocarcinoma and MCD. In this case, it was shown that the preoperative plasma VEGF level (1,880 pg/ml) significantly decreased (52.3 pg/ml) 3 months after the primary cancer was resected [6].

The association of AML-nephrotic syndrome is relatively less defined in the literature compared to other hematological malignancies (CLL, Hodgkin lymphoma, non-Hodgkin lymphoma). Chahal *et al.* reported graft versus host disease-associated MCD in a patient who had a stem cell transplant for AML at 18 months [7]. AML associated with membranous nephropathy was reported by Sahiner *et al.*, in this case, 3 months after the diagnosis of membranous nephropathy, the patient was clinically diagnosed with AML [8].

An interesting point in our case was the diagnosis of AML as long as 9 years after the diagnosis of MCD and when the renal disease was already in remission. This time-in terms of the coexistence of these two clinical conditions has been evaluated as the longest period that can be detected in literature. Was this just a coincidence? In our opinion, considering the association of hematological malignancies with nephrotic syndromes, it does not seem like a coincidence. It should be kept in mind that in geriatric patients with diagnoses such as MCD and MN, any cytopenia during follow-up should be considered, and it is thought that it may be an indicator of an underlying hematological malignancy. It seems rational to perform this follow-up not only during the diagnosis of glomerulonephritis but also periodically in the long term; especially in clinical situations such as MCD that occur in geriatric patients, this approach becomes even more important.

Conflict of interests

The authors have declared that no conflict of interest exists.

Ethical considerations

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent was obtained from all individual participants included in the study. Written informed consent was obtained from the patient for their anonymized information to be published in this article.

Authors' contribution

Conception and design: AA, GP. Drafting the manuscript: AA. Critical revision of the manuscript: MÇ.

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