Nephrotic syndrome as the first manifestation of Acute Myelogenous leukemia

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Abstract

The hematological malignancies associated with nephrotic syndrome are mainly hodgkin's and non-hodgkin's lymphomas and chronic lymphocytic leukemia. Acute myelogenous leukemia (AML) has rarely been described in associated with nephritic syndrome. We report a rare case of acute myelogenous leukemia who presented with nephrotic syndrome.

A previously healthy 62-year-old man was admitted in nephrology ward because of generalized developing pitting edema during last month. Simultaneously, he had generalized itching and urticaria, polyuria, polydypsia and low grade fever but had no history of weight loss, anorexia and sweating. In laboratory tests he had proteinuria above 3.5 gr/ day. Because of anemia, hematology consultation was done. In peripheral blood, there were myeloblast cells in the circulation at a ratio of 20%.

Bone marrow aspiration confirmed a diagnosis of AML M2, showing hypercellular bone marrow with 80-90% leukemic cells, increased M/E ratio, myeloblast (immature cell, fine chromatin, cytoplasmic granule) and these abnormal elements: myeloblast >50% and mature cell about 20%. Unfortunately, we hadn't renal biopsy as a consequent of patient illness and thrombocytopenia. He received induction chemotherapy, which led to a complete remission and decreasing urinary protein excretion during chemotherapy and no proteinurai at the end of it.

Now the patient has received second course of consolidation therapy and remained in complete remission, with no physical and laboratory evidence of proteinuria.

It can be concluded that nephrotic syndrome may be additionally associated with AML. In some cases, there is a direct causal effect of the leukemic process on renal function or even pathology, while in others it is exerted indirectly via other complications of the malignancy or the treatment.

Key words: AML, Nephrotic syndrome, Case report

Introduction:

Leukemia is a heterogeneous group of disorders characterized by malignant transformation of stem cells in the bone marrow.(1) Association of extra renal malignancies with nephrotic syndrome are well described and has been interesting subject of several reviews.(2- 4) The hematological malignancies associated with nephrotic syndrome are mainly Hodgkin's and non-Hodgkin's lymphomas and chronic lymphocytic leukemia.

In the leukemic patients with nephrotic syndrome, the association of chronic lymphocytic leukemia with membranoproliferative glomerulonephritis has been most frequently documented(6) and other types of glumerulopathy such as minimal change disease, membranous nephropathy, or focal glomerular sclerosis have also been described.(2,3) However, Acute Myelogenous Leukemia (AML) has rarely been described in association with the nephrotic syndrome.

We report here a rare case of Acute Myelogenous Leukemia (AML) who presented with nephrotic syndrome.

Case report

A 62-year-old man admitted in our hospital in nephrology ward for evaluation of edema. He had

no history of any underlying disease and was healthy until one month ago.

Legs pitting edema was the first symptom that begins from one month ago and gradually developed to other body areas and coincident symptoms were generalized itching and urticaria, polyuria, polydypsia, non exertional dyspnea, cough, muscle weakness and low grade fever. He had no history of weight loss, anorexia, sweating, drug consumption and any other problem.

In physical examination, he had pallor, normal thyroid size, left axillary lymphadenopathy (1.5×1.5 cm, immobile, non tender, firm), 5 cm subcostal enlargement of spleen, pitting edema in extremities and no hepatomegally and shifting dullness.

Laboratory studies at admission showed these data: leukocyte count, 15600/µL; hemoglobin, 8.7 gr/dL; platelet, 35000/µL; MCV, 62.3 fl; MCH, 19.1 pg; MCHC, 30.7 gr/dL; RDW, 14.4%; Albumin, 2 gr/L; BUN, 18 mg/dL; creatinine, 0.8 mg/dL; Serum iron, 50µg/dl; TIBC, 400µg/dl; CRP: ++; (Table- 1).

Table- 1. primary laboratory data of the patient on admission

Lab test	Result	Normal range (unit)
White Blood Cell (WBC)	15600 Immature cells (Myeloblast): 20%	4-10 (×1000/ml)
Red Blood Cell (RBC)	3.05	3.9- 5.8 (×10⁶/ml)
Hemoglobin	8.5	12-16 (g/dl)
Mean Corpuscular Volume	62.3	80-100 (fl)
Platelet	35,000	150-450 (/ml)
Erythrocyte Sedimentation Rate	60	<20 (/1st hour)
Blood Urea Nitrogen	18	8-20 (mg/dl)
Creatinin	0.8	0.6-1.3 (mg/dl)
Sodium	141	135-145 (meq/L)
Potassium	3.8	3.5-5.2 (meq/L)
Calcium	9	8.5-10.5 (mg/dl)
Phosphorus	4	2.5-5 (mg/dl)
Serum Albumin	2	3.5-5.3 (g/dl)
Prothrombin Time	13	11-13 (sec)
Partial Thromboplastin Time	33	30-45 (sec)
Aspartate-amino Transferase	16	0-41 (U/L)
Alanine-amino Transferase	12	0-37 (U/L)
Alkaline Phosphatase	183	64-306 (U/L)
Lactate Dehydrogenase (LDH)	750	225-500 (U/L)
Uric Acid	4.3	2.4 -7 (mg/dl)
Urinalysis	Protein 3+ Blood 3+ RBC: 16-18 WBC: 10-12 24h urine >3.5 gr proteinuria	

Table- 2. laboratory data of the patient on 1 month after induction therapy

Lab test	Result	Normal range (unit)
Hemoglobin **WBC**	7.8 2000	12-16 (g/dl) Normal diff
Platelet	182,000	150-450 (/ml)
Blood Urea Nitrogen	18	8-20 (mg/dl)
Creatinin	0.8	0.6-1.3 (mg/dl)
Serum Albumin	3	3.5-5.3 (g/dl)
Lactate Dehydrogenase (LDH)	400	225-500 (U/L)
Urinalysis	Protein: -ve Blood: -ve RBC: 1-2 WBC: 2-3 24h urine= Negative for proteinuria	

WBC: White blood cell, diff.: Differential, -ve: Negative

Thyroid function tests: T3 RIA: 59 Ratio; TSH:4.3 µIU/ml and in ELISA:6.7; and AM Cortisol:24.3 µg/dl (Table- 1).

Hepatic function tests and serology: HBS Ag: (-); HBc Ab(Ig M): (-); HCV Ab: (-); SGOT: 16 u/l; SGPT: 12 u/l; Bilirubin total: 0.3mg/dl; Direct: 0.1 mg/dl; TG: 74 mg/dl; Chol: 213 mg/dl; LDH: 159 U/L; Anti-DNA: 4.2 ng/dl; C3: 160 ng/dl; CH50: 94 ng/dl; ANA: (-); (Table- 1).

First Urinalysis: 15- 16 Red Blood Cells, 6 to 7 white blood cells, blood (+), protein (+3) and more than 3.5 gr/day in a 24/h urine sample. Thus, he was diagnosed as developing nephrotic syndrome. (Table- 1).

In hematology consultation, blasts were seen in the circulation at a ratio of 20%. The diagnosis of Acute Myeloblastic Leukemia (M2) confirmed in bone marrow aspiration , that showing hypercellular bone marrow with 80-90% cellularity, increased M/E ratio, myeloblast (immature cell, fine chromatin, cytoplasmic granule) and these abnormal elements: myeloblast >50% and mature cell about 20%.

Because of patient illness and thrombocytopenia in serial CBCs, we couldn't take a renal biopsy and the patient received induction therapy as soon as possible which included: Daunorubicin 45 mg/square meter (for 3 days) and Cytarabine 100 mg/square meter (for 7 days).

In serial daily urinalysis, urinary protein excretion has a decreasing course and disappeared after the hematologic remission was achieved.

In abdominal ultrasound right and left kidney sizes were 116mm×46mm, 99mm×37mm, respectively. Increased parenchyma echo (grade II), normal pyelocaliciel system, mild hepatomegaly with

normal echo, splenomegaly (211mm.60mm) were seen. Portal vein, CBD, Splenic vein diameters were 13mm, 4mm and 10mm respectively.
After the end of chemotherapy, laboratory studies showed the following values:
leukocyte count, 2000/μL; hemoglobin, 7.8 gr/dL; platelet, 182000/μL; MCV, 77.8 fl; MCH, 21.3 pg; MCHC, 31.2 gr/dL; RDW, 20.3%; Blood Urea Nitrogen, 14 mg/dl; Creatinine, 0.8 mg/dl and normal serum electrolytes. (Table- 2)
Urinalysis showed 1 to 2 Red Blood Cells, 2 to 3 white blood cells and any evidence of proteinuria. (Table- 2)
Now the patient has received second course of consolidation therapy. In physical exam, he hasn't edema, and in laboratory exams he has no evidence of nephrotic syndrome or proteinuria. He remained in complete remission since the end of induction chemotherapy.

Discussion

The reported case shows a clinical picture characterized by nephrotic syndrome with severe proteinuria and anemia. There are many differential diagnosis for this condition. The clinical and laboratory data were inconclusive while a peripheral blood smear showed myeloblast cells in the circulation at ratio of 20% and bone marrow aspiration confirmed the diagnosis of AML M2 which presents with nephrotic syndrome.
Kidneys can be affected in a number of ways in this disease, including direct invasion, glomerulopathies, tubulointerstitial disease, fluid and electrolyte abnormalities, urinary tract obstruction (because of enlarged retroperitoneal lymph nodes), severe infection due to immunosuppression and as a complication of treatment.(7)
Renal enlargement in ultrasonography (37.5%), renal infiltration (47-61%), palpable kidneys (3-5%) and electrolyte imbalance has been seen in AML but nephrotic syndrome is very rare.(7)
In this case we didn't detect enlarged kidneys on USG, electrolyte imbalance and urinary tract obstruction.
It is likely that the patient had an underlying glomerular disease and we can not deny the possibility that several factors than immunologic reactions affect glomerular pathological changes. In a post mortem study, it was found that there is subclinical glomerular immune complex disease in patients with AML and demonstrated anantigen related to the interspecies antigen of mammalian oncornaviruses in the glomerular immune deposits.(6)
Therefore, the presence of massive immune deposits in the mesangium and the capillary walls in the biopsy specimen can suggest that the patient have underlying glomerular changes associated with leukemia based on the immunologic disorder.(6)
Negative urinary protein excretion at the end of induction chemotherapy means that there is a direct causal effect of the leukemic process on the renal function and even renal pathology in this case. While in other cases nephrotic syndrome can be an indirect association between leukemia and nephrotic syndrome.

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