Ukrainian Journal of Nephrology and Dialysis
Scientific and Practical, Medical Journal

Founders:

- State Institution «Institute of Nephrology NAMS of Ukraine»
- National Kidney Foundation of Ukraine

ISSN 2304-0238;
eISSN 2616-7352

Journal homepage: https://ukrjnd.com.ua

Clinical case reports

doi: 10.31450/ukrjnd.3(67).2020.05

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Tumor lysis syndrome associated with acute kidney injury as the first manifestation of essential thrombocytosis

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Citation:

Kemeç Z, Koçanoğlu A, Şıkgenç MM. Tumor lysis syndrome associated with acute kidney injury as the first manifestation of essential thrombocytosis. Ukr J Nephr Dial. 2020;3(67):28-32. doi: 10.31450/ukrjnd.3(63).2020.05

Article history:

Received March 26, 2020
Received in revised form May 04, 2020
Accepted May 24, 2020

Abstract. *In the present case, a 52-year-old female patient has no disease in her medical history. She was brought into the emergency department with muscle pain, nausea-vomiting, acute kidney injury (AKI), tumor lysis syndrome (TLS). Intensive hydration was performed. On the fourth day, venous blood gas, serum kidney function testing and electrolyte levels improved. Thrombocytosis was detected. Our patient with TLS-associated AKI was diagnosed with essential thrombocytosis. We have not previously observed such a case sample in the English literature in the extensive examination.*

Keywords: *acute kidney injury, tumor lysis syndrome, essential thrombocytosis.*

Conflict of interest statement. The authors declare no competing interest.

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УДК 616.61–008.6–036.11:616.155.2:

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Синдром лізису пухлин, асоційований з гострим пошкодженням нирок як перший прояв есенціального тромбоцитозу

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Резюме. *У представленому клінічному випадку, аналогів якому ми не знайшли в опублікованій науковій літературі, 52-річна пацієнтка не мала жодного захворювання в анамнезі. Її доставили у відділення невідкладної допомоги з болем у м'язах, нудотою, блювотою, клінічними проявами гострого пошкодження нирок (ГПН) та синдромом лізису пухлини (СЛП). На четвертий день інтенсивної гідратації у хворої покращився кислотно-лужний стан, функція нирок та рівень електролітів. Після стабілізації стану її перевели до відділення гематології у зв язку з вперше виявленим есенціальним тромбоцитозом.*

Ключові слова: *гостре пошкодження нирок, синдром лізису пухлини, есенціальний тромбоцитоз.*

Introduction. Essential thrombocytosis (primary thrombocythemia) is an asymptomatic, chronic myeloproliferative disease revealing itself with continuous megakaryocyte proliferation that causes to increase in a multitude of circulating platelets. Essential thrombocytosis is portrayed by a constantly increased number of platelets more than 450,000/μL, megakaryocytic hyperplasia, splenomegaly, a clinical trend involved with thrombotic or hemorrhagic chapters or both [1].

Tumor lysis syndrome (TLS) is a syndrome having the potential of leading to death, a medical condition observed in the initial stages of diagnosis and treatment of rapidly increasing fatal neoplasms. TLS is defined by quick start of hyperuricemia, hyperkalemia, hypocalcemia, hyperphosphatemia, and failure of a kidney after the release of intracytoplasmic ingredients in the course of cellular lysis. This has a firm relationship with hematological malignancies, especially with acute leukemias and non-Hodgkin lymphomas [2].

There are various mechanisms in terms of acute kidney injury (AKI) in cases diagnosed with TLS. The consumption of intravascular capacity may result in an inducing element for the reabsorption of uric acid and following net storage in distal tubules. The existence of low urinary pH encourages the precipitation of uric acid in the collection system of the kidney and distal tubules, resulting in uric acid nephropathy and oliguric AKI [3, 4].

Our patient with TLS-associated AKI was diagnosed with ET. As a result, we have not previously observed such a case sample in the English literature in the extensive examination. We present it as the first case.

Case report. A 52-years-old female patient has signed the informed consent. She was admitted to our emergency department with symptoms of muscle pain, nausea, vomiting, loss of appetite, a headache, weakness, which started a week ago. There was no fever, palpitations, cough, diarrhea, abdominal pain, difficulty urinating and change in urine color. Some diseases such as kidney disease, rheumatologic disease, iron deficiency anemia, uncontrolled blood sugar, hypertension, infection, smoking, alcohol, drugs (such as herbal medicine) and toxin use were excluded from our patient's past medical history.

In the physical examination; pulse was 110/min (in sinus rhythm), blood pressure was 140/90 mmHg and body temperature was 37.5°. She didn't have a convulsion. The thyroid examination was natural. The spleen was handled under the rib. There was no pretibial edema in both legs. Her peripheral pulse was plump. The cardiac function was normal in echocardiography. Her electrocardiography was in sinus rhythm. In laboratory assessment; the following results were detected; calcium (Ca): 8.2 mg/dL, creatinine (Cr): 2.04 mg/dL, potassium (K): 5.8 mEql/L, uric acid: 8.96 mg/dL, alanine aminotransferase (ALT): 90 U/L, aspartate aminotransferase (AST): 52 U/L, lactate dehydrogenase (LDH): 480 U/L, gamma-glutamyl transferase (GGT): 215 U/L, alkaline phosphatase (ALP): 232 U/L, phosphor (P): 10.6 mg/dL, C-reactive protein (CRP): 6.8 mg/L, white blood cell (WBC): 8.45×109/L, platelet (PLT): 1507×109/L, pH: 7.19, HCO3: 12.1 mmol/L (Table 1).

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Table 1

The laboratory values of the patient

Parameter	The first dayX	The second day	The third day	The fourth day	Reference Values
Glucose (mg/dL)	122	125	125	100	70 – 110
Urea (mg/dL)	87	92	78	37	17 – 43
Cre (mg/dL)	2.09	2.4	1.44	0.64	0.7 – 1.3
Uric acid (mg/dL)	8.96	8.94	9.1	7.2	3.5 – 7.2
Alb (g/L)	51.1	45.8	33.7	32.5	35-52
ALT (U/L)	90	73	33	12	0 – 50
AST (U/L)	52	34	20.9	22	0 – 50
LDH (U/L)	480	423		248	0 – 248
GGT (U/L)	215	174	95	40	0-38
ALP (U/L)	232	197	133	113	30-120
T.B (mg/dL)	0.64	0.49	0.57	0.52	0.3-1.2
D.B (mg/dL)	0.19	0.17	0.11	0.15	0-0.2
İ.B (mg/dL)	0.45	0.32	0.46	0.37	0-0.7
CK (U/L)	25	22	20	21	0 – 171
Na (mEql/L)	132	130	137	146	136-146
K (mEql/L)	5.8	4.5	3.9	3.9	3.5 – 5.1
CL (mEql/L)	104	103	114	110	101-109
Ca (mg/dL)	8.2	8.2	8.8	9	8.8 – 10.6
P (mg/dL)	10.6	10.4	6	3.2	2.5 – 4.5
CRP (mg/L)	6.8	6.1	4.1	3.6	0- 5
WBC ($\times 10^9$/L)	8.45	10	6.4	5.4	4.5-10.5
RBC ($\times 10^{12}$/L)	5,78	5,36	4,23	4,01	4,2-6,1
HGB (g/dL)	16,7	15,8	12,3	12	12 -18
PLT ($\times 10^9$/L)	1507	1204	765	799	130-400
pH	7,19		7,20	7,33	7,35 – 7,45
PCO_2 (mmHg)	26,6		31,5	27,2	35-45
HCO_3 (mmol/L)	12,1		13,1	19,2	22-30

[x] the day of the patient's hospitalization.

Note: Since some of the data were not analyzed on certain days, related cells of the table were left blank"

Abbreviations. Cre: Creatinine, Alb: Albumin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase, GGT: Gamma-glutamyl transferase, ALP: Alkaline phosphatase, T.BIL: Total bilirubin, D.BİL: Direct bilirubin, İ. BİL: Indirect bilirubin, CK: Creatine phosphokinase, Na: Sodium, K: Potassium, CL: Chloride, Ca: Calcium, P: Phosphorus, CRP: C-reactive protein, WBC: White blood cell, RBC: Red blood cell, HGB : Hemoglobin, PLT: Platelet, pCO_2: Carbon dioxide partial pressure, HCO_3: Bicarbonate.

Plasma parathyroid hormone was found normal. Serum vitamin D3 levels were normal (1,25-OH: 37.6 ng/mL, 25-OH: 9.9 ng/ mL). Parathyroid hormone-related protein (PTHrP) could not be detected because it could not be measured in our hospital. Serum protein electrophoresis, thyroid hormones were in

the normal range. Vitamin B12, folate, ferritin levels were in the reference range. The urine test was normal. In Doppler ultrasound of the abdomen, the size and channels of the kidney are normal, renal artery and vein lumen are normal and spleen size found borderline. There was no feature on the chest X-ray. In peripheral smear; red blood cells normochromic normocytic, partly myelocyte-metamyelocyte, thrombocytosis, megakaryocytes, poikilocytosis and anisocytosis findings in platelets were detected.

She was diagnosed with acute kidney injury (AKI). There were no triggering factors except TLS. We assumed ET could have caused this. Bicarbonate hydration was performed. There was no problem with her urine output. Her dyspeptic complaints soon receded. Oral intake was provided. On 4th day, liver and kidney function tests, electrolytes improved. Metabolic acidosis responded to hydration. She did not need for rasburicase and hemodialysis. She was discharged after 1 week when she was stabilized. Since our medical center does not have a hematology unit, she was transferred to a university hospital. We have been in touch with the hematology unit. We have learned that she was diagnosed with ET with bone-marrow findings. The diagnosis we assumed has been confirmed.

Discussion. Clinical symptoms of ET could be defined mainly as neurological (e.g., headache, dizziness, and short-term ischemic attack), microcirculatory (e.g., acroparesthesia, odontalgia and defect of vision), gastrointestinal (e.g., nausea, vomiting) and hemorrhagic (e.g., nasal bleeding, ecchymosis, etc.). Thrombotic and hemorrhagic problems are the primary causes of death in adult cases diagnosed with ET [5-7].

TLS-associated hyperphosphatemia can give rise to AKI. Precipitation of calcium phosphate in the kidney tubule the main mechanism involved. Another possible mechanism that leads to AKI is vasoconstriction in the kidney, arising from the release of adenosine into the bloodstream following lysis of tumor cells [8]. TLS-related AKI has a multitude of results that may end up with speedy clinical breakdown of the patient. Oliguria can give rise to volume overcharge, secondary hypertension and pulmonic edema. Increased blood urea nitrogen may cause strong pericarditis and platelet disorder [9]. Anion gap metabolic acidosis is the principal irregularity based on acid, and it can exacerbate electrolyte disparities [3, 8, 10].

The prognosis of TLS associated AKI depends on the severity of TLS and electrolyte disparities. The gravest and often deadly shapes of TLS arise in patients with the impromptu form of the condition. AKI is related to high death rates [11].

In the management of obvious TLS, it must be focused on correcting the ordinary concentrations of extracellular solutes. On condition that complete loss of kidney function has not been reached, volume extension is beneficial to increase solute secretion of the kidney. Furthermore, escalating the secretion of K, P, and uric acid, retain sufficient urinary volumes and decrease precipitation of calcium phosphate crystals in tubules of the kidney [12-16].

Intravenous (IV) administration of fluids is recommended with 2–3 L/m^2/day to keep diuresis in the rate between 100–200 mL/h in adult cases without contraindication for volume expansion, as is the case in patients diagnosed with cardiac insufficiency. Ideally, IV hydration in high-risk patients should begin 24–48 hours before the start of cancer therapy and may be continued for 48–72 hours after the finalization of chemotherapy. Diuretics can be used to pursue proper urinary volumes only after the adjustment of hypovolemia [17].

In the laboratory of our case, hyperuricemia, hyperkalemia, the height of LDH, hyperphosphatemia, hypocalcemia supplied TLC criteria. Azotemia, metabolic acidosis was in favor of AKI. The peripheral smear and blood count made ET possible. A week after discharge, the diagnosis of ET was confirmed by a bone marrow analysis performed at a hematology clinic. There was no reason to make TLS-associated AKI except ET.

Our case is unique in some ways. Our case, which had no previous history of hematologic disease, was admitted with TLS-associated AKI. Quite simply, the patient got better quickly with fluid treatment. There was no need for hemodialysis, which required an interventional procedure. No expensive treatment was needed such as rasburicase. The patient was diagnosed ET with bone marrow finding at the hematology unit clinic. When English literature was examined inclusively, patients diagnosed with ET, AKI related to TLS was not detected.

There are AKI reports in the literature due to complications of ET-associated venous obstruction [18] and obstructive uropathy [19]. In the imaging tests of our case (e.g. ultrasonography), the large kidney vessels were open and no obstruction could block the flow of urine. Vasoconstriction, glomerular toxicity, and tubule obstruction may be present in vascular structures of the kidney due to electrolyte imbalance occurring in the TLS table [8]. In myeloproliferative disorders, platelet plug [18] may be present in the renal capillaries due to high turnovers. The lack of oral intake and fluid loss due to nausea and vomiting of our patient revealed a tendency for hypovolemia. In these ways, it is possible that acute tubular necrosis may occur in our case. Our patient's liver enzyme elevation may also be due to the platelet plug of the hepatocyte capillaries.

Conclusion. ET should not be forgotten in patients admitted with TLS-associated AKI clinic. TLS is a hematologic-oncologic emergency defined by the generation of hyperuricemia, AKI, and electrolyte imbalance that can be deadly. It is critical to identify patients who are at high risk for this syndrome for immediate detection of those patients diagnosed with TLS eligible to receive early treatment. ET management requires proper fluid resuscitation, use of hypouricemic agents, renovation of kidney replacement therapy, and rectification of electrolyte disparities.

Conflict of Interest Statement. There is no conflict of interest in this study.

Financial Disclosure. This study is not supported by any external funding.

Authors contribution. ZK, AK and MŞ contributed to the design and implementation of the research, to the analysis of the results and the writing of the manuscript.

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