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

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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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Introduction. Essential thrombocytosis (primary thrombocytethemia) 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 mEq/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).
### The laboratory values of the patient

| Parameter             | The first day | 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            |
| i.B (mg/dL)           | 0.45          | 0.32           | 0.46          | 0.37           | 0-0.7            |
| CK (U/L)              | 25            | 22             | 20            | 21             | 0 – 171          |
| Na (mEq/L)            | 132           | 130            | 137           | 146            | 136-146          |
| K (mEq/L)             | 5.8           | 4.5            | 3.9           | 3.9            | 3.5 – 5.1        |
| CL (mEq/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 (x10^9/L)         | 8.45          | 10             | 6.4           | 5.4            | 4.5-10.5         |
| RBC (x10^12/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 (x10^9/L)         | 1507          | 1204           | 765           | 799            | 130-400          |
| pH                    | 7.19          |                | 7.20          | 7.33           | 7.35 – 7.45      |
| PCO₂ (mmHg)           | 26.6          |                | 31.5          | 27.2           | 35-45            |
| HCO₃ (mmol/L)         | 12.1          |                | 13.1          | 19.2           | 22-30            |

*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.BIL: Direct bilirubin, I. BIL: 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, pCO₂: Carbon dioxide partial pressure, HCO₃: 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 is 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 in the kidney, arising from the release of adenosine into the bloodstream following lysis of tumor cells. 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.
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References:

1. Rumi E, Cazzola M. How I treat essential thrombocythemia. Blood. 2016;128(20):2403-2414. doi:10.1182/blood-2016-05-643346
2. Locatelli F, Rossi F. Incidence and pathogenesis of tumor lysis syndrome. Contrib Nephrol. 2005;147:61-68. doi:10.1159/000082543
3. Cancernetwork.com [homepage on the Internet]. We Treat Tumor Lysis Syndrome. Cancer Network; 2015. Available from: https://www.cancernetwork.com/view/how-we-treat-tumor-lysis-syndrome.
4. Schelling JR, Ghandour FZ, Strickland TJ, Sedor JR. Management of tumor lysis syndrome with standard continuous arteriovenous hemodialysis: case report and a review of the literature. Ren Fail. 1998;20(4):635-644. doi:10.3109/08860229809045157
5. Hoffman R. Hematology: Basic principles and practice. Essential thrombocythemia. Philadelphia, PA: Churchill Livingstone; 2012.
6. Fu R, Zhang L, Yang R. Paediatric essential thrombocythaemia: clinical and molecular features, diagnosis and treatment. Br J Haematol. 2013;163(3):295-302. doi:10.1111/bjh.12530
7. Soyer N, Haznedaroğlu İC, Cömert M, Çekdemir D, Yılmaz M, Ünal A, Çağlıyan G, Bilgir O, Ilhan O, Özdemirkiran F, Kaya E, Şahin F, Vural F, Saydam G. Multicenter Retrospective Analysis of Turkish Patients with Chronic Myeloproliferative Neoplasms. Turk J Haematol. 2017 Mar 1;34(1):27-33. doi: 10.4274/tjh.2016.0005.
8. Stapleton FB, Strother DR, Roy S 3rd, Wyatt RJ, McKay CP, Murphy SB. Acute renal failure at onset of therapy for advanced stage Burkitt lymphoma and B cell acute lymphoblastic lymphoma. Pediatrics. 1988;82(6):863-869.
9. Tosi P, Barosi G, Lazzaro C, Liso V, Marchetti M, Morra E, Pension A, Rosti G, Santoro A, Zinzani PL, Tura S. Consensus conference on the management of tumor lysis syndrome. Haematologica. 2008 Dec;93(12):1877-85. doi: 10.3324/haematol.13290.
10. McCurdy MT, Shanqholtz CB. Oncologic emergencies. Crit Care Med. 2012;40(7):2212-2222. doi:10.1097/CCM.0b013e31824e1865
11. Agha–Razii M, Amyot SL, Pichette V, Cardinal J, Ouiemt D, Leblanc M. Continuous veno-venous hemodialfiltration for the treatment of spontaneous tumor lysis syndrome complicated by acute renal failure and severe hyperuricemia. Clin Nephrol. 2000;54(1):59-63.
12. Sarno J. Prevention and management of tumor lysis syndrome in adults with malignancy. J Adv Pract Oncol. 2013;4(2):101-106.
13. Mika D, Ahmad S, Guruvayoorappan C. Tumour lysis syndrome: implications for cancer therapy. Asian Pacific J Cancer Prev. 2012;13(8): 3555–3560.
14. McBride A, Westervelt P. Recognizing and managing the expanded risk of tumor lysis syndrome in hematologic and solid malignancies. J Hematol Oncol. 2012;5:75. Published 2012 Dec 13. doi:10.1186/1756-8722-5-75
15. Mirrakhimov AE, Voore P, Khan M, Ali AM. Tumor lysis syndrome: A clinical review. World J Crit Care Med. 2015;4(2):130-138. Published 2015 May 4. doi:10.5492/wjccm.v4.i2.130
16. Rampello E, Fricia T, Malaguernera M. The management of tumor lysis syndrome. Nat Clin Pract Oncol. 2006;3(8):438-447. doi:10.1038/ncpnc0581
17. Darmon M, Guichard I, Vincent F. Rasburicase and tumor lysis syndrome: lower dosage, consideration of indications, and hyperhydration. J Clin Oncol. 2011;29(3):e67-e69. doi:10.1200/JCO.2010.32.6751
18. Johnson M, Gernsheimer T, Johansen K. Essential thrombocythemia: underemphasized cause of large vessel thrombosis. J Vasc Surg 1995;22(4):443-447. doi: 10.1016/S0741-5214(95)70013-7
19. Ganguli A, Chalokia RS, Kaur BJ. Obstructive Uropathy as an Initial Presentation of Primary Myelofibrosis: Case Report and Review of Literature. Indian J Hematol Blood Transfus. 2016;32(Suppl 1):117-120. doi:10.1007/s12288-016-0679-6

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