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Assessment of tumor lysis syndrome cases

Tümör lizis sendromlu olguların değerlendirilmesi

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SUMMARY

Objective: Tumor lysis syndrome (TLS) is a clinical picture that occurs with the rapid destruction of tumor cells and with life-threatening metabolic disorders. The aim of our study is to evaluate the etiologic causes, diagnosis and treatment of TLS cases.

Method: The study was conducted between January 2015 and December 2017 in Kahramanmaras Necip Fazıl city Hospital. A total of 32 patients diagnosed with TLS were included in the study. Laboratory values of patients were scanned (blood urea nitrogen, creatinine, potassium, phosphorus, calcium, serum uric acid, lactate dehydrogenase) and diagnoses, chemotherapy and treatments were noted.

Results: Of the 32 patients who were included in the study, 17 were male and 15 were female. The average age of the patients was found as 62,06 ± 12,10 (35-86) years. Hematologic malignancy was detected in the etiology of 11 of the TLS cases and solid tumor was detected in 21 of the TLS cases. A total of 12 (37.5%) patients had spontaneous TLS (5 in haematological malignancy and 7 in solid tumor). Hyperpotassaemia 50%, hypocalcaemia 46.9%, hyperphosphatemia, hyperuricemia and acute kidney damage was present in all patients. Mortality rate was found as 40.6%.

Conclusions: In our study, spontaneous TLS was detected at a high rate. In addition, the mortality rate was also high. Early diagnosis and urgent treatment should be planned to avoid mortalities.

Keywords: Tumor lysis syndrome, malignancy, hyperuricemia, acute renal damage

ÖZET

Amaç: Tümör lizis sendromu (TLS), tümör hücrelerinin hızlı bir şekilde yıkılmasıyla ortaya çıkan ve yaşamı tehdit edebilen metabolik bozukluklarla seyreden klinik bir tablodur. Çalışmamızdaki amaç TLS olguların etyolojik nedenleri, tanı ve tedavilerini değerlendirmektir.

Yöntem: Çalışma Ocak 2015 ile Aralık 2017 tarihleri arasında Kahramanmaras Necip Fazıl Şehir hastanesinde yapıldı. Çalışmaya, TLS tanısı konan toplam 32 hasta alındı. Hastaların dosyaları taranarak laboratuvar değerleri (kan üre azotu, kreatinin, potasyum, fosfor, kalsiyum, serum ürik asit, laktat dehidrogenaz), tanıları, aldıkları kemoterapi ve tedavileri not edildi.

Bulgular: Çalışmaya alınan toplam 32 hastanın 17'si erkek, 15'i bayandı. Hastaların ortalama yaşları 62,06±12,10 (35-86) olarak saptandı. TLS olgularının 11'nin etiyolojisinde hematolojik malignensi, 21'inde ise solid tümör saptandı. Toplam 12 (37,5%) hastada spontan TLS (5'i hematolojik malignensi ve 7'si solid tümör) tespit edildi. Hiperpotasemi 50% oranında, hipokalsemi 46,9% oranında, hiperfosfatemi, hiperürisemi ve akut böbrek hasarı ise hastaların tümünde mevcuttu. Mortalite oranı 40,6% olarak saptandı.

Sonuç: Çalışmamızda spontan TLS yüksek oranda saptandı. Ayrıca mortalite oranıda yüksekti. Mortaliteden kaçınmak için erken tanı ve acil tedavi planlanmalıdır.

Anahtar sözcükler: Tümör lizis sendromu, malignensi, hiperürisemi, akut böbrek hasarı

INTRODUCTION

Tumor lysis syndrome (TLS) is a clinical picture that occurs with the rapid destruction of tumor cells and with life-threatening metabolic abnormalities. TLS spontaneous may develop after biopsy, after radiotherapy or chemotherapy. TLS is characterized by the presence of at least two of the laboratory findings, serum uric acid level ≥ 8 mg / dL or 25% increase in serum level, potassium level ≥6 mEq/L or 25% increase in potassium level, phosphate ≥ 4.5 mg/dL or 25% increase in phosphate level, calcium level ≤ 7 mg/dL or 25% decrease in calcium level together with the presence of at least one of the clinical manifestations of acute renal failure (AKI ()convulsions, arrhythmia / sudden death [1].

The incidence of TLS is highly variable and the frequency varies according to malignancy type. It is more common in haematological malignancies.

In the study of patients with acute leukaemia and non-Hodgkin's lymphoma (NHL) The frequency of TLS was found as 27.8% [2]. In another study (total 153 adult hematologic malignancies), laboratory TLS was found as 11.1% and TLS with clinically AKD was found as 19.6% [3]. In the study conducted in patients with acute myeloid leukaemia (AML) (772 adult patients), TLS was found as 17% (5% clinical and 12% laboratory TLS) [4]. It is rarely seen in solid tumors. The incidence of TLS in solid tumors is not known exactly. The incidence of TLS in solid tumors was found to be less than 0.3% [5]

MATERIAL AND METHODS

The study was conducted between January 2015 and December 2017 in Kahramanmaras Necip Fazıl city Hospital. A total of 32 patients diagnosed with TLS were included in the study. Patients' files were scanned (blood urea nitrogen, creatinine, potassium, phosphorus, calcium, serum uric acid, lactate dehydrogenase) and laboratory values, diagnoses, chemotherapy and treatments were noted. Patients' AKI staging was performed according to Kidney Disease Improve Global Outcomes (KDIGO). KDIGO stage 1 serum creatinine value is 1.5-1.9 times increase or ≥0,3mg/dl increase or urine flow for 6-12 hours <0.5 ml / kg / h, stage 2 serum creatinine increase is 2,0-2,9 times increase or <0.5 ml/kg/h for ≥12 hours of urine flow, during stage 3, ≥3 times increase compared to basic values or serum creatinine ≥ 4mg / dl or initiation of renal replacement therapy or under the age of 18, the glomerular filtration rate is <35ml / min or 12 hours anuria or for ≥ 24 h <0.3 ml / kg / h.

Statistical Analysis

For statistical analysis, Windows 20.0 (IBM SPSS Statistics for Windows, Armonk, NY, USA) Statistical Package for Social Sciences (SPSS) was used. Student t test (mean ± standard deviation) for analysis of normal distribution data, in non-normal distribution groups, Mann Whitney U test median and minimum-maximum and chi-square analysis for nominal data were planned to use. P<0,05 was considered statistically significant.

RESULTS

Of the 32 patients who were included in the study, 17 were male and 15 were female. The average age of the patients was found as 62,06 ± 12,10 (35-86) years. Hematologic malignancy was detected in the aetiology of 11 of the TLS cases and solid tumor was detected in 21 of the TLS cases. A total of 12 (37.5%) patients had spontaneous TLS (5 in hematological malignancy and 7 in solid tumor). Hyperpotassaemia 50%, hypocalcaemia 46.9%, hyperphosphatemia, hyperuricemia and acute kidney damage was present in all patients. Hypercalcemia was detected at 9.4%, two of the patients had multiple myeloma (MM) and one had prostate cancer. Metabolic acidosis was detected in 62.5% of patients. laboratory data of hematologic and solid tumors are given in Table 1. Fluid electrolyte regulation, allopurinol and hemodialysis were performed in the treatments. Of the total 10 cases treated with hemodialysis, one had end-stage renal failure, one had chronic kidney disease, and 3 patients had improvement. 5 patients died. A total of 13 patients (4 hematologic and 9 solid tumors) died. The overall mortality rate was 40.6% in malignancies with TLS. TLS mortality rate in hematological malignancies was found as 36.3% and mortality rate in solid tumors was found as 42.8%.

Table 1: Laboratory data of the patients

	Total	**Hematologic**	**Solid tumour**
	32	11 (34,3%)	21 (65,6%)
Blood urea nitrogen	96,6±67,8 (27-283)	95,0±47,10	97,4±76,4
creatinine	3,95±3,06(1,6-22)	4,1±2,1	3,8±4,1
Potassium	5,93±1,8(3,2-11)	5,4±1,8	6,1±1,9
Uric acid	13,06±4,7(8,1-32)	15,7±6,6	11,8±3,1
Phosphorus	7,72±4,8(4,7-32)	10,0±7,8	6,6±2,0
Calcium	8,32±2,0(5,1-16)	8,8±2,9	8,0±1,3
LDH	1278,4±1317(193-4998)	871,0±767,6	1463,6±1481,3

	Diagnosis	**% (number)**	**Triggering factors**
Hematologic	Chronic lymphocytic leukaemia	%3,1 (1)	Rituximab
	Multiple myeloma	%15,6 (5)	Spontaneous (2)
			Lenalidomide(2)
			dexamethasone +Bortezomib (1)
	Non-Hodgkin lymphoma	%9,4 (3)	Spontaneous (1)
			R-CHOP (2)
	Myelodysplastic syndrome	%3,1 (1)	Spontaneous
	Chronic myeloid leukaemia	%3,1 (1)	Spontaneous
Solid tumor	Colon cancer	%9,4 (3)	Spontaneous (2)
			oxaliplatin, 5-fluorouracil (1)
	Lung cancer	%9,4 (3)	Spontaneous (1)
			After biopsy (1)
			Cisplatin, gemcitabine
	stomach cancer	%25 (8)	Spontaneous(3)
			Docetaxel, 5-fluorouracil (1)
			Gemcitabine,bevacizumab (1)
			After biopsy (2)
			capecitabine(1)
	Prostate cancer	%6,3 (2)	Spontaneous
			Leuprolide acetate +enzalutamide
	Oesophageal cancer	%3,1 (1)	Docetaxel, cisplatin, 5-fluorouracil
	Liver cancer	%3,1 (1)	Spontaneous
	Peritoneal carcinomatosis	%3,1 (1)	Glucocorticoids
	Endometrium cancer	%3,1 (1)	ifosfamide, Adriamycin
	Breast cancer	%3,1 (1)	Adriamycin, siklofosfamide Docetaxel

Table 2: Diagnosis and triggering factors of tumour lysis patients

Two patients with MM applied with TLS. Both patients applied to the clinic for the thoracic vertebra compression fracture. After the examinations performed, the patient diagnosed with TLS was diagnosed with MM. Patient admitted to general surgery clinic with NHL case with spontaneous TLS and pre-diagnosis of acute appendicitis also had TLS. The patient underwent colonoscopy and biopsied NHL was diagnosed. The patient underwent colonoscopy and was diagnosed with NHL at the end of the biopsy. Spontaneous TLS was detected after biopsy in two patients with gastric tumor. The malignant types of the patients and triggering factors are given in table 2. All solid tumors had extensive metastasis.

AKD was detected in all of the patients. According to KDIGO, AKD stage I was 12.5%, stage II was 25% and stage III was 62.5%.

DISCUSSION

TLS in malignant patients is one of the most important oncologic illnesses. Risk factors for TLS are tumor-related (large tumor burden, 10 cm large tumor, diffuse metastasis, extrinsic compression of the genitourinary tract by the tumor, high proliferation rate, high sensitivity to anticancer therapy, using combined chemotherapy, pre-treatment laboratory values (high LDH, serum creatinine, serum uric acid level, phosphorus level) and patient-related (low urine flow, dehydration or inadequate hydration, pre-nephropathy, exposure to nephrotoxic agents, hypotension and obstructive uropathy) [6]. In our study, common solid metastases are present in all solid tumors. In a case of hematologic malignancy, chronic kidney disease was previously present.

Spontaneous TLS is a rarely seen oncological emergency. Spontaneous TLS occurs in the absence of chemotherapy. Although spontaneous TLS is more common in hematological malignancies, it rarely develops in solid tumors. Small cell lung cancer, advance gastric cancer, endometrium cancer, hepatocellular carcinoma, colon carcinoma and over cancer from spontaneously TLS solid tumors have been described [7-10].

In our study, spontaneous TLS was detected in MM, Non-Hodgkin's lymphoma (NHL), myelodysplastic syndrome, chronic myeloid syndrome, colon cancer, lung cancer, stomach cancer, prostate cancer and liver cancer.

TLS is very rare in MM. Singh et al. found that spontaneous TLS developed in 3 cases of 7 multiple myeloma patients detected in TLS. In this study, hyperuricemia and renal dysfunction were found in all patients, hyperkalaemia in 4 patients, hyperphosphatemia in 6 patients, hypercalcemia in 2 patients and increase LDH in 6 patients [11]. Sezer et al. have published TLS that induces bortezomib in 7 patients with MM. Supportive treatment in their treatment and 2 patients underwent hemodialysis. One of the patients died (12).

In a study by Firwana et al. 105 patients with TLS were examined, 62% of which were hematologic malignancies and 38% were solid tumors. Besides The most common haematological malignancies ALL, and KLL, AML, KML, Hodgkin's lymphoma, NHL, MM were also detected. It is the most common gastrointestinal cancer (hepatocellular carcinoma, colorectal cancer, stomach neuroendocrine tumor, gastrointestinal stromal tumor), lung cancer, castleman disease, melanoma, over cancer, neuroblastoma, prostate cancer, renal cancer, breast cancer, testicular cancer, thymoma, uterus and pelvic cancer in solid tumors. Among the factors that trigger TLS in this study were 57.1% after chemotherapy, 25.7% spontaneously, 6.7% glucocorticoid, 2.9% radiotherapy, 6.7% others. Renal replacement therapy was required in 40% of patients [13]. In the study by Vodopivec et al. 58% chemotherapy, 14% spontaneously, 5% hormonotherapy, 6% immunotherapy, 7% radiotherapy, 3% transarterial catheter embolization, 7% others (such as surgery, bisphosphonate, radiofrequency) are in TLS etiology [6]. In the study conducted by Caravaca-Fontán et al., spontaneous TLS was detected in 47% of the patients. Spontaneous TLS in three of 8 patients with lung cancer, spontaneous TLS in one of two patients with oesophageal cancer, spontaneous TLS in a patient with colon cancer, spontaneous TLS in a patient with stomach cancer, spontaneous TLS in one of two patients with endometrium cancer, , spontaneous TLS in a patient with breast cancer, spontaneous TLS in a patient with prostate cancer, spontaneous TLS in a patient with germinal tumor, spontaneous TLS in a patient with germinal tumor, spontaneous TLS in a patient with liposarcoma and spontaneous TLS in a tumor of unknown origin were found [14]. In our study, TLS was detected after 46.8% 'indole chemotherapy, 37.5%' spontaneously, 9.3% after biopsy.

In a study of 63 TLS patients with hematologic malignancies, the 6-month mortality rate was found as 46% in total, %66 in patients and 21% in non-patients. The mortality rate in hospitalized patients was 32% in total, 51% in patients with, and 7% in non- patients. In this study, renal replacement therapy was required for 76% of patients. There were no AKI in 17 patients who underwent renal replacement therapy and the mortality rate was 6%, the mortality rate was found to be 55% in 31 patients with [15]. In hematological malignancies in intensive care unit, the TLS frequency is 9.3%. The mortality rate was 44.3% in patients with AKD and 25.4% in those with no development [16]. In the study, it was emphasized that the mortality rate in solid tumors was 35% and higher than [hematological mignans 17]. In our study, the mortality rate was higher in solid tumors than in haematological malignancies.

Acute renal failure is often oliguric and can lead to volume increase, pulmonary oedema, and hypertension. TLS treatment requires the administration of medicines as well as supportive

treatments such as hydration and alkalinisation. The duration and intensity of treatment should be adjusted according to the patient. Allopurinol is a xanthine oxidase inhibitor and inhibits the development of urate nephropathy and subsequent oliguric renal perfusion. Rasburicase should be considered as an alternative effective but expensive product in severe TLS cases where allopurinol is not used or ineffective [18].

As a result, spontaneous TLS is not uncommon in malignancies. While MM is the most common in TLS hematological malignancies, stomach cancer is most commonly found in solid tumors. The mortality rate was high in our study. Risk factors for TLS should be identified and closely monitored in malignancy patients to reduce the mortality rate. Perhaps this rate can be lowered by giving TLS diagnosis early and giving emergency treatment.

REFERENCES

1. Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol 2004; 127: 3-11.

2. Annemans L, Moeremans K, Lamotte M, Garcia Conde J, van den Berg H, Myint H, et al. Incidence, medical resource utilisation and costs of hyperuricemia and tumour lysis syndrome in patients with acute leukaemia and non-Hodgkin's lymphoma in four European countries. Leukemia& lymphoma 2003;44:77-83.

3. Darmon M, Vincent F, Camous L, Canet E, Bonmati C, Braun T, et al. Groupe de Rechercheen Réanimation Respiratoire et Onco-Hématologique (GRRR-OH). Tumour lysis syndrome and acute kidney injury in high-risk haematology patients in the rasburicase era. A prospective multicentre study from the Groupe de Rechercheen Réanimation Respiratoire et Onco-Hématologique. Br J Haematol. 2013;162:489-97.

4. Montesinos P, Lorenzo I, Martín G, Sanz J, Pérez-Sirvent ML, Martínez D, et al. Tumor lysis syndrome in patients with acute myeloid leukemia: identification of risk factors and development of a predictive model. Haematologica. 2008;93:67-74.

5. Mott FE, Esana A, Chakmakjian C, Herrington JD. Tumor lysis syndrome in solid tumors. Support Cancer Ther 2005;2:188–91.

6. Vodopivec DM, Rubio JE, Fornoni A, Lenz O. An unusual presentation of tumor lysis syndrome i patient with advanced gastricadenocarcinoma: cas e report and literature review.Case Rep Med 2012; 2012:468452.

7. Goyal H, Sawhney H, Bekara S, Singla U. Spontaneous acute tumour lysis syndrome in gastric adenocarcinoma: a case report and literature review.J Gastrointest Cancer 2014;45:208-11.

8. Weerasinghe C, Zaarour M, Arnaout S, Garcia G, Dhar M. Spontaneous Tumor Lysis Syndrome in Small-Cell Lung Cancer: A Rare Complication. World J Oncol 2015;6:464-71.

9. Sommerhalder D, Takalkar AM, Shackelford R, Peddi P. Spontaneous tumor lysis syndrome in colon cancer: a case report and literature review. Clin Case Rep 2017;5:2121-6.

10. Harada S, Nagaharu K, Baba Y, Murata T, Mizuno T, Kawakami K. Spontaneous Tumor Lysis Syndrome in a Patient with a Dedifferentiated Endometrial Adenocarcinoma. Case Rep Oncol Med 2017;2017:5103145.

11. Singh A, Gupta S, Yim B, Thekkekara R. Tumor Lysis Syndrome in Multiple Myeloma: An Increasingly Recognized Risk-A Report of Seven Cases. Indian J Hematol Blood Transfus 2017;33:41-4.

12. Sezer O, Vesole DH, Singhal S, Richardson P, Stadtmauer E, Jakob C, et al. Bortezomib-induced tumor lysis syndrome in multiple myeloma. Clin Lymphoma Myeloma 2006;7:233-5.

13. Firwana BM, Hasan R, Hasan N, Alahdab F, Alnahhas I, Hasan S, et al. Tumor lysis syndrome: a systematic review of case series and case reports.Postgrad. 2012 ;124:92-101.

14. Caravaca-Fontán F, Martínez-Sáez O, Pampa-Saico S, Olmedo ME, Gomis A, Garrido P. Tumor lysis syndrome in solid tumors: Clinical characteristics and prognosis. Med Clin (Barc) 2017;148:121-4.

15. Darmon M, Guichard I, Vincent F, Schlemmer B, Azoulay E. Prognostic significance of acute renal injury in acute tumor lysis syndrome. Leuk Lymphoma 2010;51: 221–7.

16. Darmon M, Vincent F, Canet E, Mokart D, Pène F, Kouatchet A, et al. Acute kidney injury in critically ill patients with haematological malignancies: results of a multicentre cohort study from the Groupe de Rechercheen Réanimation Respiratoireen Onco-Hématologie. Nephrol Dial Transplant. 2015;30:2006-13.

17. Tosi P, Barosi G, Lazzaro C, Liso V, Marchetti M, Morra E, et al. Consensus conference on the management of tumor lysis syndrome. Haematologica 2008;93:1877–85.

18. Goldman SC. Rasburicase: potential role in managing tumour lysis in patients with hematological malignancies. Expert Rev Anticancer Ther 2003;3:429-33.