

12. Bölüm

TÜMÖR LİZİS SENDROMU

Ahmet Bilgehan ŞAHİN¹

Giriş

Tümör lizis sendromu (TLS), tümör hücrelerinin parçalanması sonucu sistemik dolaşıma büyük miktarlarda potasyum, fosfat ve nükleik asit salımı ile karakterize onkolojik acil durumdur. Nükleik asitlerin ürik aside katabolizması hiperürisemiye yol açar. Ürik asit atılımındaki belirgin artış, renal tübüllerde ürik asidin çökmesine neden olur. Ayrıca renal vazokonstriksiyon, bozulmuş otheregölasyon ve inflamasyona bağı renal kan akışında azalma akut böbrek hasarıyla sonuçlanır. Böbrek tübüllerinde hiperfosfatemiye bağı kalsiyum fosfat birikimi de akut böbrek hasarına katkıda bulunur.

Tümör lizis sendromu en sık, Burkitt lenfoma gibi yüksek gradlı lenfomalı ve akut lenfoblastik lösemili hastalarda sitotoksik tedavinin başlamasından sonra ortaya çıkar. Bununla birlikte, TLS sitotoksik tedaviye duyarlılığı fazla olan diğere solid organ tümörlerinde görülebildiğı gibi yüksek proliferatif indekse ve ciddi tümör yüküne sahip tümörlerde tedavi almadan spontan olarak da görülebilir. TLS patogenezi, klinik bulguları, tanımı, etiyoloji ve risk faktörleri, risk sınıflaması, profilaksisi ve tedavisi aşağıda tartışılmıştır.

Patogenez

Yüksek proliferatif hız, fazla tümör yükü ve/veya tedaviye sensitif bir malignite durumunda, sitotoksik kemoterapinin başlatılması, sitolitik antikor tedavisi, radyasyon tedavisi veya bazen tek başına glukokortikoid tedavisi, tümör hücrelerinin hızlı lizisine neden olabilir. Yeni etkili ve hedeflenmiş antikanser

¹ Uzm. Dr., Bursa Uludağ Üniversitesi, Tıbbi Onkoloji Bilim Dalı, absahin@uludag.edu.tr

Sorular

1. **Kan ürik asit düzeyini en etkili düşüren hipoüremik ajan aşağıdakilerden hangisidir?**
 - A) Allopurinol
 - B) Febuksostat
 - C) Rasburikaz
 - D) Losartan
 - E) Furosemid
2. **Allopurinol kullanan hastalarda aşağıdaki ilaçların hangisinde oluşabilecek toksisiteyi engellemek için doz ayarı gerekir?**
 - A) Rasburikaz
 - B) Azatioprin
 - C) Azitromisin
 - D) Klaritromisin
 - E) Everolimus
3. **Aşağıdaki tedavi yaklaşımlarından hangisi tümör lizis sendromu profilaksisinde etkinliği kanıtlanmadığı için önerilmemektedir?**
 - A) Hidrasyon
 - B) İdrar alkalinizasyonu
 - C) Rasburikaz
 - D) Allopurinol
 - E) Fenobuksostat

Kaynaklar

1. Davidson MB, Thakkar S, Hix JK, et al. Pathophysiology, clinical consequences, and treatment of tumor lysis syndrome. *Am. J Med.* 2004;116:546–554.
2. van den Berg H, Reintsema AM. Renal tubular damage in rasburicase: risks of alkalinisation. *Ann Oncol* 2004;15:175–176.
3. Hande KR, Garraway GC. Acute tumor lysis syndrome in patients with high-grade non-Hodgkin's lymphoma. *Am J Med.* 1993;94:133–139.
4. Coiffier B, Mounier N, Bologna S, et al. Efficacy and safety of rasburicase (recombinant urate oxidase) for the prevention and treatment of hyperuricemia during induction chemotherapy of aggressive non-Hodgkin's lymphoma: Results of the GRAAL1 (Groupe d'Etude des Lymphomes de l'Adulte Trial on R. *J Clin Oncol.* 2003;21:4402–4406.

5. Boles J -M, Mialon P, Garre M, et al. Acute renal failure caused by extreme hyperphosphatemia after chemotherapy of an acute lymphoblastic leukemias. *Cancer*. 1984;53:2425–9.
6. Seegmiller JE. Xanthine stone formation. *Am J Med* 1968;45:780–783.
7. LaRosa C, McMullen L, Bakdash S, et al. Acute renal failure from xanthine nephropathy during management of acute leukemia. *Pediatr Nephrol* 2007;22:132–135.
8. Coiffier B, Altman A, Pui CH, Younes A, Cairo MS. Guidelines for the management of pediatric and adult tumor lysis syndrome: An evidence-based review. *J Clin Oncol*. 2008;26:2767–2778.
9. Montesinos P, Lorenzo I, Martín G, 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.
10. Cairo MS, Bishop M. Tumour lysis syndrome: New therapeutic strategies and classification. *Br. J. Haematol*. 2004;127:3–11.
11. National Cancer Institute (2017). *Common Terminology Criteria for Adverse Events (CTCAE).v.5.0*. (05/01/2021 tarihinde https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50 adresinde ulaşılmıştır).
12. Cairo MS, Coiffier B, Reiter A, et al. Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: An expert TLS panel consensus. *Br J Haematol* 2010;149:578–586.
13. Howard SC, Jones DP, Pui C-H. The Tumor Lysis Syndrome. *N Engl J Med* 2011;364:1844–1854.
14. Yang H, Rosove MH, Figlin RA. Tumor lysis syndrome occurring after the administration of rituximab in lymphoproliferative disorders: High-grade non-Hodgkin's lymphoma and chronic lymphocytic leukemia. *Am J Hematol* 1999;62:247–250.
15. Malik IA, Abubakar S, Alam F, et al. Dexamethasone-induced tumor lysis syndrome in high-grade non-Hodgkin's lymphoma. *South Med J* 1994;87:409–411.
16. Al-Kali A, Farooq S, Tfayli A. Tumor lysis syndrome after starting treatment with Gleevec in a patient with chronic myelogenous leukemia. *J Clin Pharm Ther* 2009;34:607–610.
17. Linck D, Basara N, Tran V, et al. Peracute onset of severe tumor lysis syndrome immediately after 4 Gy fractionated TBI as part of reduced intensity preparative regimen in a patient with T-ALL with high tumor burden. *Bone Marrow Transplant*. 2003;31:935–937.
18. Howard SC, Trifilio S, Gregory TK, et al. Tumor lysis syndrome in the era of novel and targeted agents in patients with hematologic malignancies: a systematic review. *Ann Hematol*. 2016;95:563–73.
19. Roeker LE, Fox CP, Eyre TA, et al. Tumor lysis, adverse events, and dose adjustments in 297 venetoclax-treated CLL patients in routine clinical practice. *Clin Cancer Res*. 2019;25:4264–4270.
20. UptoDate (2020). Tumor lysis syndrome: Definition, pathogenesis, clinical manifestations, etiology and risk factors. (05/01/2021 tarihinde <https://www.uptodate.com/contents/tumor-lysis-syndrome-definition-pathogenesis-clinical-manifestations-etiology-and-risk-factors> adresinden ulaşılmıştır).
21. Sklarin NT, Markham M. Spontaneous recurrent tumor lysis syndrome in breast cancer. *Am J Clin Oncol Cancer Clin Trials*. 1995;18:71–73.
22. Jasek AM, Day HJ. Acute spontaneous tumor lysis syndrome. *Am J Hematol*. 1994; 47:129–131.
23. Kjellstrand CM, Campbell DC, Von Hartitzsch B, et al. Hyperuricemic Acute Renal Failure. *Arch Intern Med*. 1974;133:349–359.
24. Coiffier B, Altman A, Pui CH, Younes A, et al. Guidelines for the management of pediatric and adult tumor lysis syndrome: An evidence-based review. *J Clin Oncol*. 2008;26:2767–2778.

25. Cairo MS, Coiffier B, Reiter A, et al. Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: An expert TLS panel consensus. *Br J Haematol.* 2010;149:578–586.
26. Mato AR, Riccio BE, Qin L, et al. A predictive model for the detection of tumor lysis syndrome during AML induction therapy. *Leuk Lymphoma* 2006;47:877–883.
27. Conger JD, Falk SA. Intrarenal dynamics in the pathogenesis and prevention of acute urate nephropathy. *J Clin Invest.* 1977;59:786–793.
28. UpToDate (2020). *Tumor lysis syndrome: Prevention and treatment.* 2020. *Tumor lysis syndrome_ Prevention and treatment – UpToDate.* (06/01/2021 tarihinde <https://www.uptodate.com/contents/tumor-lysis-syndrome-prevention-and-treatment> adresinden ulaşılmıştır).
29. Goldman SC, Holcenberg JS, Finklestein JZ, et al. A randomized comparison between rasburicase and allopurinol in children with lymphoma or leukemia at high risk for tumor lysis. *Blood.* 2001;97:2998–3003.
30. McLeod HL. Clinically relevant drug-drug interactions in oncology. *Br J Clin Pharmacol.* 1998;45:539–544.
31. Feusner J. Role of intravenous allopurinol in the management of acute tumor lysis syndrome. *Semin Oncol* 2001;28:13–18.
32. Jeha S, Kantarjian H, Irwin D, et al. Efficacy and safety of rasburicase, a recombinant urate oxidase (Elitek™), in the management of malignancy-associated hyperuricemia in pediatric and adult patients: Final results of a multicenter compassionate use trial. *Leukemia.* 2005;19: 34–38.
33. Cheuk DKL, Chiang AKS, Chan GCF, et al. Urate oxidase for the prevention and treatment of tumour lysis syndrome in children with cancer. *Cochrane Database Syst Rev* 2017;3:CD006945.
34. Cortes J, Moore JO, Maziarz RT, et al. Control of plasma uric acid in adults at risk for tumor lysis syndrome: Efficacy and safety of rasburicase alone and rasburicase followed by allopurinol compared with allopurinol alone - Results of a multicenter phase III study. *J Clin Oncol.* 2010;28:4207–4213.
35. Lopez-Olivo MA, Pratt G, Palla SL, et al. Rasburicase in tumor lysis syndrome of the adult: A systematic review and meta-analysis. *Am J Kidney Dis.* 2013;62:481–492.
36. Sonbol MB, Yadav H, Vaidya R, et al. Methemoglobinemia and hemolysis in a patient with G6PD deficiency treated with rasburicase. *Am J Hematol.* 2013;88:152–154.
37. Yamamoto T, Moriwaki Y, Fujimura Y, et al. Effect of TEI-6720, a xanthine oxidase inhibitor, on the nucleoside transport in the lung cancer cell line A549. *Pharmacology.* 2000;60:34–40.
38. Stamp LK. Safety profile of anti-gout agents: An update. *Curr Opin Rheumatol.* 2014;26:162–168.
39. Bellos I, Kontzoglou K, Psyrri A, et al. Febuxostat administration for the prevention of tumour lysis syndrome: A meta-analysis. *J Clin Pharm Ther.* 2019;44:525–533.
40. Howard SC, Jones DP, Pui C-H. The Tumor Lysis Syndrome. *N Engl J Med.* 2011;364:1844–1854.
41. Tonelli M, Pannu N, Manns B. Oral Phosphate Binders in Patients with Kidney Failure. *N Engl J Med.* 2010;362:1312–1324.
42. Jones GL, Will A, Jackson GH, et al. Guidelines for the management of tumour lysis syndrome in adults and children with haematological malignancies on behalf of the British Committee for Standards in Haematology. *Br J Haematol* 2015;169:661–671.