

CASE SERIES

PEDIATRIC INTENSIVE CARE

Spontaneous tumor lysis syndrome in pediatric patients: a case series

Muhammad Usman Ajmal¹, Rabia Saleem², Saad Ur Rehman³, Iqra Malik⁴, Muhammad Arslan⁵

Author affiliations:

1. Muhammad Usman Ajmal, Fellow Pediatric Critical Care, Shaukat Khanum Cancer Memorial Hospital & Research Center, Lahore, Pakistan; E-mail: usmanajmal230@gmail.com
2. Rabia Saleem, Senior Registrar, Punjab Institute of Neuro Sciences, Lahore, Pakistan; E-mail: rabiasaleem47@gmail.com
3. Saad Ur Rehman, Consultant Anesthesia and Critical Care, Shaukat Khanum Cancer Memorial Hospital & Research Center, Lahore, Pakistan; E-mail: saadurrehman@skm.org.pk
4. Iqra Malik, Medial Officer, Pediatric Oncology, Shaukat Khanum Cancer Memorial Hospital & Research Center, Lahore, Pakistan; E-mail: iqramalik@skm.org.pk
5. Muhammad Arslan, Fellow Infectious Diseases, Shaukat Khanum Cancer Memorial Hospital & Research Center, Lahore, Pakistan; E-mail: muhammadarslan@skm.org.pk

Correspondence: Muhammad Usman Ajmal; **E-mail:** usmanajmal230@gmail.com; **Phone:** 03336348281

ABSTRACT

Spontaneous occurrence of Tumor Lysis Syndrome (TLS) is very rare. Only 3 pediatric case reports were reported in literature. All 3 patients presented with therapy-sensitive disease. Unfortunately, only one patient survived. It is preventable in 100% of patients, but TLS is a hard nut to crack. We present three distinct cases of spontaneous tumor lysis syndrome within the pediatric population, each associated with different types of tumors.

A 3-year-old boy with mediastinal germ cell tumor of stage III, had hyperuricemia and hyperphosphatemia on presentation, tumor lysis syndrome improved but later died with sepsis, another patient of 4-year-old girl with precursor B cell acute lymphoblastic lymphoma had hyperkalemia, hyperuricemia and hyperphosphatemia on presentation and third patient was 6-year-old boy with abdominal Burkitt lymphoma stage III presented with hyperkalemia, hyperuricemia, hyperphosphatemia and Acute Kidney Injury (AKI) before initiation of chemotherapy. Later both these patients improved and survived. Spontaneous tumor lysis syndrome has high mortality, so it is of utmost importance to diagnose it timely. Swift and effective responses to spontaneous TLS can significantly reduce the risk of mortality linked to this critical emergency condition.

Abbreviations: AKI - Acute Kidney Injury; ASDII - secundum atrial septal defect; TLS - Tumor Lysis Syndrome;

Keywords: Pediatric Oncology; Sepsis; Tumor Lysis Syndrome;

Citation: Ajmal MU, Saleem R, Saad Ur Rehman SU, Arslan M, Malik I. Spontaneous tumor lysis syndrome in pediatric patients: a case series. *Anaesth. pain intensive care* 2024;28(2):372–375; DOI: [10.35975/apic.v28i2.2409](https://doi.org/10.35975/apic.v28i2.2409)

Received: January 18, 2024; **Revised:** February 10, 2024; **Accepted:** February 15, 2024

1. INTRODUCTION

Tumor Lysis Syndrome (TLS) is an oncologic emergency that is defined as an electrolyte instability due to rapid and extensive breakdown of cancer cells in blood stream as increased levels of uric acid, phosphate, potassium and hypocalcemia.¹ TLS typically manifests following the commencement of cytotoxic therapy in individuals diagnosed with acute lymphoblastic

lymphomas and high-grade lymphomas. TLS may manifest spontaneously and with other tumor types that are characterized by high proliferative rate and substantial tumor burden or high sensitivity to cytotoxic therapy. Spontaneous TLS can occur prior to the initiation of any cancer treatment, but it is a rare occurrence.²

Cairo-Bishop devised specific laboratory criteria for the diagnosis of TLS both at presentation and within seven days of treatment.³ Laboratory TLS was defined as any two or more serum values either above the upper limit of normal or 25 percent increase over baseline presented within 3 days before or seven days after instituting chemotherapy. Clinical TLS defined as Laboratory TLS plus one or more including increased serum creatinine, cardiac arrhythmia or sudden death or a seizure.

Spontaneous TLS is found to be linked with hyperuricemia without hyperphosphatemia. It has been proposed that rapidly growing cancers have high cell turnover rates and thus generating high serum uric acid levels through rapid nucleoprotein turnover. Interestingly, the tumor is able to reutilize released phosphorus for formation of new cancer cells.⁴ By contrast, TLS after chemotherapy is due to cell destruction without reuptake of phosphorus and thus hyperphosphatemia.

2. CASE SERIES

First Case

A 3-year-old boy presented in emergency with history of fever, cough and progressive shortness of breath for the last 3 weeks and significant past history of right sided orchiectomy due to enlarged right scrotal mass. On examination, this thin lean child was in obvious respiratory distress, with use of accessory muscles of respiration and he could not maintain oxygen saturation at room air. There was no air entry on his left side of chest. Baseline CT chest showed large anterior mediastinal mass extending to middle mediastinum measuring 17.4x12x9 cm, and causing mediastinal shift to right side. The mass encased left pulmonary artery and the arch of aorta and compressed superior vena cava. Right lower lobe was consolidated and the left lung had collapsed.

Patient was intubated due to respiratory failure and shifted to ICU on mechanical ventilation. Alpha feto protein 2699 IU/ml was administered. Biopsy of the mass showed germ cell tumor likely to be yolk sac tumor, labelled as stage II. Baseline white cell count was $22 \times 10^9/L$, Hb 8 g/dl and platelet count was $526 \times 10^9/L$. Sodium 140 mmol/L, potassium 6 mmol/L, Urea 40 mg/dl, creatinine 0.58 mg/dl, bicarbonate 15.5 mmol/L, phosphate 7.59 mg/dl and uric acid 11.62 mg/dL, which improved after a single dose of rasburicase. Tumor lysis profile improved within 3 days with sevelamer, alopurinol and hyperhydration.

On second day of ICU admission, JEB chemotherapy started, which is a chemotherapy combination used to treat childhood ovarian and testicular germ cell cancers

that have spread. It includes the drugs carboplatin (JM8), etoposide phosphate, and bleomycin sulfate. We replaced bleomycin with vincristine. Meanwhile, his tracheal aspirates yielded *Hemophilus influenza* and *Moraxella catarrhalis* growth. He developed post chemotherapy febrile neutropenia sepsis with multidrug resistant *Escherichia coli* bacteremia, which progressed to septic shock requiring inotropic support and ultimately leading to multi-organ failure. In spite of rigorous treatment, the patient did not survive and succumbed to death after 11 days of ICU stay.

Second Case

A 4-year-old girl presented with abdominal distension for 2 months and fever for one month, bleeding from nose for the last 2 weeks. Multiple transfusions of platelets and packed RBCs were given. History of secundum atrial septal defect (ASDII). On examination she was a severely malnourished girl having blood clots in nose, tachypneic with use of accessory muscles and not maintaining saturation even with hi-flow oxygen. Abdomen was distended with massive hepatosplenomegaly and multiple bruises over left thigh and palpable bilateral inguinal and axillary lymph nodes.

Her hematological investigations revealed Hb 4.9 g/dl, WBCs $8 \times 10^9/L$, platelets $5 \times 10^9/L$ and 21% blasts in peripheral smear. Uric acid was 12.38 mg/dl, which improved after rasburicase administration, potassium 6.39 mmol/L and phosphate 8.78 mg/dl, urea 0.21 mg/dl, creatinine 17 mg/dL, LDH 1409 U/L. She was diagnosed as pre B cell acute lymphoblastic lymphoma on bone marrow examination.

Patient was shifted to ICU after intubation because of respiratory failure and mechanical ventilation started. Shock required inotropes, multiple blood product transfusions, and hyper-hydration. Alopurinol and sevelamer were given. TLS improved within 4 days. Chemotherapy UK regimen A with 3 drug induction (intrathecal methotrexate, IV vincristine and intramuscular pegaspargase) was started on second day of ICU admission. She remained intubated for 10 days, after which her condition improved, was extubated and sent to floor, after 13 days of ICU stay. Currently she is on maintenance chemotherapy.

Third Case

A 6-year-old boy presented in Emergency Room (ER) with low grade fever, weight loss and cough for 2 months, and progressive abdominal distension with pain for one month. He had shortness of breath and generalized body swellings for one week. Laparotomy was done and a biopsy before admission favored abdominal Burkitt lymphoma and stage III as per staging scan. On examination he was a thin lean child with

obvious respiratory distress, using accessory muscles. On auscultation there was decreased air entry on both sides of chest, and he did not maintain oxygen saturation at room air. His abdomen was distended with slit like umbilicus and fluid thrill present. He was immediately shifted to ICU and intubated as blood gas analysis indicated respiratory failure type II. There was moderate to large bilateral pleural effusion on chest X-ray.

Hematological investigation showed white cells 16,000, Hb 13g/dl, platelets 407,000, uric acid 19 mg/dl, for which rasburicase was injected and he improved. Calcium was 8.34 mg/dl, potassium 6 mmol/L, phosphate 8.9 mg/dl, urea 31 mg/dL, creatinine 0.89 mg/dL and bicarbonate 15 mmol/L. LDH 5948 units/L.

COP protocol (cyclophosphamide, vincristine and intrathecal methotrexate) 2 cycles were given during ICU stay. The tumor lysis initially worsened after initiation of the chemotherapy, but improved over 5 days. Bilateral chest tube was inserted and peritoneocentesis was done as well. He remained on mechanical ventilation for 7 days; however, his ICU stay was complicated with covid pneumonia, candidemia, and multi drug resistant *Klebsiella pneumoniae pneumonia*. All of these conditions were managed appropriately. He was successfully discharged to ward after 29 days of ICU stay and is currently on maintenance chemotherapy.

3. DISCUSSION

Spontaneous tumor lysis syndrome is an emergency in cancer patients which results in electrolyte disturbances due to the rapid destruction of cancer cells causing spill-over of intracellular contents into the blood. This condition is frequently associated with malignant tumors with rapidly growing cells.⁴ Three cases occurring at the ages of 13 years, 6 and 10 months were published earlier. Our patients were 3, 4 and 6 years of age; 2 of them were male and one was female.

TLS is characteristically associated with undifferentiated, high-grade lymphomas and acute lymphoid leukemia (ALL), but rarely reported in acute myeloid leukemia (AML) and other blood cancers.⁵ Previously reported patients in literature were associated with pineal germinoma, AML and hepatoblastoma, but our patients were diagnosed as mediastinal yolk sac tumor, ALL and Burkitt lymphoma.

The clinical presentation of spontaneous TLS can vary, but it typically involves a combination of symptoms and laboratory abnormalities with different renal, cardiac, neurological and respiratory derangements. Its management involves prompt multidisciplinary approach and depends upon patient factors and severity of the clinical presentation including hydration, optimization of electrolytes, uric acid lowering drugs,

renal replacement therapy, treatment of underlying malignancy and supportive care in a critical care settings. Two of the patients reported earlier were treated with hydration, allopurinol and chemotherapy and the third one received rasburicase in addition to the usual treatment.^{5,6,7} While all three of our patients received rasburicase along with hydration and chemotherapy.

With advances in medical care and improved understanding of TLS, the prognosis has improved in many cases.⁸ One patient who received rasburicase survived in the previous three case reports, while among our three patients two survived. The one who died had developed septicemia which complicated the overall condition. The results are comparable to previous reported cases.

We observed that the mortality in patients with TLS in solid tumors is higher as compared to hematological cancers.⁹ Hydration and uric acid lowering drugs should be started at least 24 hours before the initiation of chemotherapy. Rasburicase is a urate oxidase, an enzyme that converts uric acid to allantoin, and is the most effective drug to reduce uric acid levels rapidly, but it is cost intensive.

4. CONCLUSION

Screening patients with a high burden of tumor cells before the commencement of chemotherapy is imperative. Timely diagnosis and effective management are critical not only for averting complications but also for ensuring the success of cancer treatment. This proactive approach also reduces the risk of mortality associated with potential complications.

5. Ethical issues

Institutional Ethical Committee approval was obtained to publish this case report.

6. Conflict of interest

The authors declare no conflict of interests. No external or industry funding was involved in the case management.

7. Authors' contribution

MU: Case report Writing

RS: Literature Review

SR: Concept

IM: Data Collection

MA: Analysis and Quality insurer

8. REFERENCES

1. D'Alessandro V, Greco A, Clemente C, Sperandeo M, De Cata A, Di Micco C, et al. Severe spontaneous acute tumor lysis syndrome and hypoglycemia in patient with germ cell tumor. *Tumori*. 2010; 96(6):1040–3 PMID: [21388073](#)

2. Cairo, M.S. and Bishop, M. (2004), Tumor lysis syndrome: new therapeutic strategies and classification. *Br J Haematol.* 2004 Oct;127(1):3-11. PMID: [15384972](#) DOI: [10.1111/j.1365-2141.2004.05094.x](#)
3. Kjellstrand CM, Cambell DC 2nd, von Hartitzsch B, Buselmeier TJ. Hyperuricemic acute renal failure. *Arch Intern Med.* 1974 Mar;133(3):349-59. PMID: [4283735](#)
4. Murray MJ, Metayer LE, Mallucci CL, Hale JP, Nicholson JC, Kirolos RW, Burke GA. Intra-abdominal metastasis of an intracranial germinoma via ventriculo-peritoneal shunt in a 13-year-old female. *Br J Neurosurg.* 2011 Dec;25(6):747-9. doi: [10.3109/02688697.2011.566383](#). Epub 2011 Apr 18. PMID: [21501064](#) DOI: [10.3109/02688697.2011.566383](#)
5. Shenoy MT, D'Souza B, Akshatha LN, D'Souza V, Rajan MG. Spontaneous Tumor Lysis Syndrome in an Infant: A Case Report. *Indian J Clin Biochem.* 2015 Jul;30(3):360-2. PMID: [26089626](#) PMCID: [PMC4469048](#) DOI: [10.1007/s12291-014-0472-y](#)
6. Vadlapudi et al, Spontaneous tumour lysis syndrome at presentation in an infant with hepatoblastoma: A rare occurrence, *Pediatric Hematology Oncology Journal* 2021;6(4):186-189, ISSN 2468-1245 DOI: [10.1016/j.phoj.2021.10.004](#)
7. Froila'n Torres C, Castro Carbajo P, Pajares Villarroya R, Plaza Santos R, Go'mez Senent S, Marti'n Arranz MD, et al. Acute spontaneous tumor lysis syndrome in a patient with Crohn's disease taking immunosuppressants. *Rev Esp Enferm Dig.* 2009;101(4):288–94.PMID: [19492906](#)
8. Riccio B, Mato A, Olson EM, Berns JS, Luger S. Spontaneous tumor lysis syndrome in acute myeloid leukemia: two cases and a review of the literature. *Cancer Biol Ther.* 2006;5(12):1614–7. PMID: [17204864](#) DOI: [10.4161/cbt.5.12.3610](#)