CASE REPORT

Tumour lysis syndrome as a rare complication of chemotherapy in paediatric Wilms' Tumour: a case report

Sobia Qamar,[1] Irfana Ishaq Sindhu,[2] Najma Shaheen[3]

Abstract

Wilms tumour is the most common renal malignancy in children, with two-thirds of cases diagnosed before five years and 95 percent before 10 years of age. Over the last decade, the five-year survival rate has improved dramatically and now approaches 90 %. Tumour lysis syndrome, commonly seen in association with haematological malignancies, is rarely seen in Wilms tumour. We present two cases of Wilms tumour developing tumour lysis syndrome in the first week of initiation of chemotherapy. Both patients presented with huge abdominal masses causing mass effect on surrounding structures. Chemotherapy was administered as per International Society of Pediatric Oncology guidelines (SIOP). Both patients developed laboratory and clinical tumour lysis syndrome (TLS) after the first cycle of chemotherapy requiring continuous renal replacement therapy (CRRT). However, both died because of multiorgan failure.

Keywords: tumour lysis syndrome, Wilms tumour, chemotherapy, continuous renal replacement therapy, case report.

DOI: 10.47391/JPMA.6470

Submission completion date: 07-04-2022
Acceptance date: 04-08-2022

Introduction

Tumour lysis syndrome (TLS) is an oncologic emergency resulting from lysis of rapidly proliferating tumour cells, and is seen most often in patients with aggressive haematological malignancies.[1] It is rarely seen in tumours with a high proliferative rate, large tumour burden, or high sensitivity to cytotoxic therapy. But it remains unwanted in solid tumours like Wilms' tumour, and has rarely been reported.

In this article, we describe two patients with Wilms tumour who developed tumour lysis syndrome upon treatment initiation. Both patients presented with abdominal distention due to the presence of a tumour mass. Diagnosis was confirmed by tru-cut biopsy and preoperative chemotherapy was given in accordance to SIOP 2016 guidelines[2]. Both developed acute kidney injury (AKI), secondary to laboratory and clinical TLS, within 48 hours of starting chemotherapy. Their AKI was managed with hyperhydration and continuous renal replacement therapy (CRRT). Although TLS improved, both patients died due to multiorgan failure secondary to sepsis. The approval for publication of this case report was waived by the local Institutional Review Board (IRB# Ex-05-05-20-02).

The aim of this report is to make oncologists and paediatric intensivists aware of the possibility and occurrence of this exceptional complication in solid malignancies with large tumour size. Management of tumour lysis syndrome with continuous renal replacement therapy was a new modality for our 2 patients, as this facility is not commonly available in most tertiary centres of Pakistan. This case report was written after taking consent from both patients' parents. The consent was also documented in our patients' medical records. To the best of our knowledge, there is no local publication regarding tumour lysis syndrome in Wilms tumour.

Case 1

A two year old girl came to Sheikh Zayed Hospital, Rahim Yar Khan in September 2019 with progressive abdominal distention. There was no family history of malignancies. Previous medical and psychosocial history was unremarkable. An abdominal CT scan, done in the same hospital, showed a lesion in the upper pole of the right kidney, which was suggestive of Wilms tumour. On 24th September 2019, a repeat CT-scan of chest, abdomen and pelvis was done under sedation, to see interval progression of the disease and metastasis. Upon recovery from sedation, she was pale, well perfused and had developed tachycardia, tachypnoea, and intercostal retractions. She was admitted to the high dependency unit on the same day. Laboratory results from 24th September 2019 showed a low haemoglobin (Hb) level of 4.2 g/dL (11-14 g/dL), 16.1% haematocrit (Hct 34-40%), hypochromic, microcytic red blood cells, low serum iron

[1]Department of Pediatric Intensive Care, [2,3] Department of Pediatric Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan.

Correspondence: Irfana Ishaq Sindhu. Email: irfanaishaq@skm.org.pk
ORCID ID.

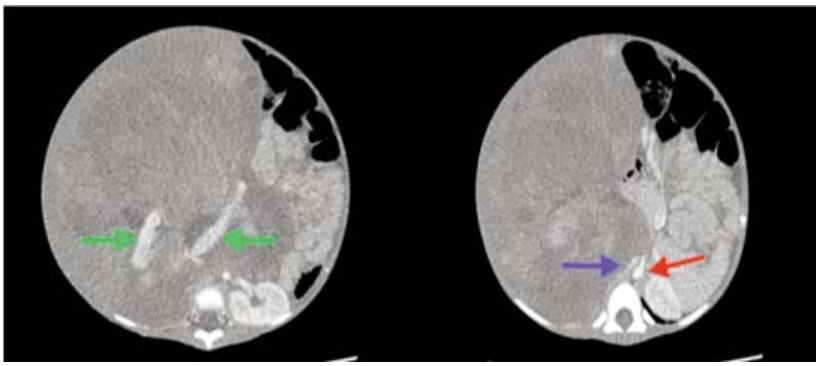

Figure-1: Left: Contrast enhanced CT showing a huge heterogeneously enhancing right hemi-abdominal mass extending across the midline with residual enhancing right renal parenchyma (arrows). It is encasing the left renal vessels at renal hilum. Right: IVC (red arrow) and aorta (green arrow) are compressed.

and normal ferritin. No metabolic or respiratory acidosis was found. Her condition improved with oxygen and red blood cell transfusion. Repeat Hb was 7.1 g/dL (11-14 g/dL) on 25th September 2019. Imaging revealed a 17x18 cm heterogeneously enhancing retroperitoneal mass originating from right kidney, encasing right renal vessels, and compressing the inferior vena cava (IVC) and abdominal aorta. The mass was extending across the midline into the pelvis and coming into contact with the under surface of the liver (figure 1). There were no osseous or lung metastasis. Ultrasound-guided deep trucut biopsy of the mass was done on 26th September 2019.

Chemotherapy was started on 30th September 2019, according to SIOP guidelines. Within 24 hours of receiving her first week of pre-operative vincristine and actinomycin chemotherapy, she developed oliguria, generalized body swelling and hyperuricaemia of 7.45 mg/dL (3.5-7mg/ dL). Veno-occlusive disease, as a differential diagnosis was ruled out as she had no tender hepatomegaly and serum bilirubin was 0.35mg/dl (1mg/dl). Allopurinol was started and patient was electively intubated for possible need of CRRT for TLS. Serial tumour lysis profile revealed uric acid 9.61 mg/dl (3.5-7mg/ dL), phosphorus 7.67 mg/dl (3.3 - 5.6 mg/dl), potassium 6.78 mmol/l (3.5 - 5.1 mmol/l), creatinine 0.44 mg/dl(0.31- 0.47 mg/dl), calcium 8.4 mg/dl(8.5 - 10.5mg/dl), serum bilirubin 0.3 mg/dl(1 mg/dl). Her urine output was 0.7ml/kg/hour (1-4ml/Kg/hour). After failure of medical potassium lowering measures, anuria, and resultant fluid overload (FO) continuous veno-venous haemodiafiltration (CVVHDF) was started on 31st December 2019. She remained on vasopressors during the therapy. Post chemotherapy drop in platelets and Hb was managed with transfusions. After 48 hours of continuous veno-venous haemodiafiltration (CVVHDF) therapy, TLS resolved, and anuria responded to intravenous frusemide with improvement in FO up to 14 %. She had poor lung compliance, with no triggering of ventilator and failed several trials of spontaneous breathing test. Histopathology report revealed biphasic nephroblastoma with rhabdoid differentiation. Continuing chemotherapy for 4 weeks followed by response assessment was planned, but second week of chemotherapy could not be given due to her critical condition. During her hospital stay, methicillin resistant Staphylococcus aureus, Burkholderia Cepacia and Pantoea growth was present in her tracheal aspirate, which were managed appropriately. Renal parameters and FO continued to worsen. On 8th January 2020, she had high serum bilirubin, intolerance to feeds, and neutropenia. After 48 hours, she had stage 3 AKI with increasing serum bilirubin level, bilious nasogastric tube aspirate with ileus, and was ventilator dependent. Due to her critical condition, multiorgan dysfunction and inability to give further chemotherapy, goals of care were revised after discussion with family. She ultimately died on11th January 2020.

Case 2

A four year old girl was evaluated for progressive abdominal distention since four weeks, in February 2020 in Pakistan Institute of Medical Sciences, Islamabad. There was no family history of malignancy. Previous medical and psychosocial history was normal. Her last ultrasound; done in January 2020; in Holy Family Hospital Rawalpindi, showed a large heterogenous mass replacing the right renal parenchyma, which was suggestive of neoplasm. She came to our hospital on 5th March 2020. A baseline CT scan from chest to pelvis done on 6th March 2020 revealed a 13x11 cm tumour of the right kidney with

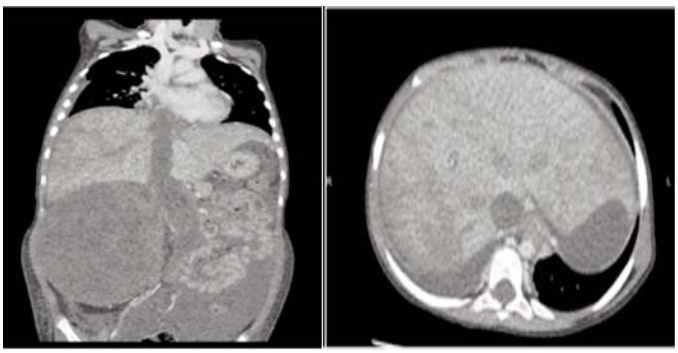

Figure-2: Contrast enhanced CT Chest, abdomen, and pelvis. Coronal and axial images showing large right hemi abdominal Wilms tumour with tumour thrombus involving IVC, extending superiorly to right atrium.

heterogenous enhancement abutting the under surface of the liver and extending across the midline. There was complete thrombosis of the IVC extending up to the right atrium (figure 2). Thrombosis also extended into intrahepatic veins with heterogenous attenuation of liver parenchyma. She also had right pleural effusion but no pulmonary nodularity or metastatic lesions in visualized skeleton.

On 11th March 2020, she presented with prolonged multifocal clonic convulsions, which were aborted with intravenous midazolam. Her arterial blood gas had mixed acidosis with lactate of 19.3 mg/dL (4.5 - 19.8 mg/dL). She was intubated on the same day for low GCS and type 2 respiratory failure and required high ventilator pressures; likely due to abdominal splinting. Notable laboratory abnormalities were Hb 8.9 g/dL(11-14 g/dL), Hct 27.8% (Hct 34-40%), with hypochromic microcytic red blood cells, leucocyte count 38.59x103/microliter (5 – 13) with 63% neutrophils, ALT 339 U/L (<34 U/L), AST 543 U/L(<33 U/L), albumin 2.64 gm/dL (3.5 - 5.2gm/dl), Prothrombin time 21.5 seconds (9.9 - 11.8 Seconds), INR 2.12(1.08), BUN 15(5 – 18 mg/dl) and serum creatinine 0.27(0.31- 0.47 mg/dl),. Treatment was initiated for suspected meningitis. CT scan of head was unremarkable. CSF analysis was done after 72 hours of management of fits; delayed due to persistent coagulopathy despite plasma transfusion. Persistent seizures was suggestive of partially treated meningitis with glucose 74 mg/dl (50-80mg/dl), lactate dehydrogenase (LDH) 206 U/L(40U/L), protein 157 mg/dl(15-45mg/dl), WBC 25/microliters(<5cells) with 88 % neutrophils. She required high oxygen and ventilator pressures. Ultrasound guided deep tissue tru-cut biopsy of renal mass was done on13th March 2020. A multidisciplinary team decided to start chemotherapy as per the SIOP 2015 guidelines; based on imaging consistent with the diagnosis of Wilms tumour. The first week of vincristine dose, modified for acute liver injury, was given on 16th March 2020. She was extubated to nasal CPAP via nasal pillow, but re-intubated in 10 hours due to persistent tachycardia, tachypnoea, and respiratory secretions on the same day.

On17th March 2020, she developed stage 2 acute kidney injury, haemodynamic instability, high lactate of 37.3 mg/dL (4.5-19.8 mg/dL)., thrombocytopenia of 49x103/microliter(150-450x103/microliter), leukocytosis and biochemical workup showed urea nitrogen 48.76 mg/dL(5 – 18 mg/dl), creatinine 1.1 mg/dL(0.31- 0.47 mg/dl), potassium 5.18(3.5 - 5.1 mmol/l), uric acid 10.54 mg/dL(3.5-7mg/ dL), phosphorus 6.38 mg/dL(3.3 - 5.6 mg/dl), corrected calcium 8.4 mg/dl(8.5 - 10.5mg/dl), LDH 2083 U/L (200-400U/L) with anuria over the preceding 6 hours. CVVHD was started on 17th March 2020 for TLS, AKI, and FO of 26 %. She also had worsening of liver function tests ALT 315 U/L(<34 U/L), AST 1466 U/L(<34 U/L), GGT 24 U/(8 – 61U/L), bilirubin 6.15 mg/dl (1mg/dl), albumin 2.67gm/dl (3.5-5.2mg/dl), INR 3.34(1.08), fibrinogen 47.4 mg/dL (200 to 400 mg/dL) and FDP <5 microgram/ml(<0.5 microgram/ml). Serum lactate and metabolic acidosis continued to worsen though biochemical markers of TLS improved. Fluid removal, under observation, was planned after 24 hours of CVVHD. Fluid removal target could not be achieved due to increasing need for noradrenaline, leading to worsening fluid overload. On 20th March 2020, she was critically sick with multiorgan dysfunction and was ventilator dependent. Surgery review ruled out the possibility of intervention due to current condition and inferior vena cava tumour thrombosis. Due to her critical condition, guarded prognosis and surgically non-salvageable tumour; further chemotherapy seemed unlikely. Goals of care were revised with a ceiling of care. Unfortunately, she died on 22nd March 2020.

Discussion

TLS is an oncological emergency mostly seen in association with malignancies with high proliferative rates such as acute lymphoblastic leukaemia, Burkitt leukaemia/lymphoma and diffuse large B-cell lymphoma. It may also be seen in tumours with high sensitivity to chemotherapy. But it has rarely been reported in solid tumours and is associated with high mortality.[3]

For Wilms tumour management, our institution follows SIOP guidelines. These guidelines recommend four weeks chemotherapy followed by surgical resection, staging and histological classification, further followed by postoperative chemotherapy. Based on typical clinical presentation, radiologic findings, and large tumour size with mass effect on surrounding structures, chemotherapy was given before histopathology results became available. Due to the patient's complicated clinical course, early surgical resection was considered but rendered surgically non-salvageable due to extensive local disease, encasement of renal vessels, proximity to aorta in first patient and extensive IVC and hepatic vein thrombosis in the second.

High tumour burden, elevated LDH and high chemosensitivity predisposes patients to high risk of TLS.[4,5] Patients with pre-existing renal insufficiency are also more likely to have TLS with chemotherapy. Both our patients had large tumours (case 1 17x18 cm and case 2 13x11 cm) at the time of diagnosis, with one having had high LDH with renal impairment, hence increasing the risk of TLS.

TLS following chemotherapy for Wilms tumour has rarely been described in literature, in which a patient developed TLS within a few days of vincristine, doxorubicin and actinomycin administration.[6,7] Our patients developed TLS following the first course of chemotherapy. The first patient received vincristine and actinomycin, while the second patient received vincristine only. TLS is categorized into laboratory (LTLS) and clinical (CTLS) varieties. LTLS is characterized by a set of biochemical abnormalities, including hyperuricaemia, hyperkalaemia, hyperphosphataemia with resultant hypocalcaemia- all present during the same 24-hour period and within three days before or up to 7 days after the initiation of chemotherapy. CTLS requires the presence of LTLS plus one of the consequential toxicities i.e., elevated creatinine, cardiac arrhythmias, or seizures. Both our patients had all the biochemical abnormalities of LTLS and elevated creatinine (CTLS), but did not have arrhythmias or seizures.

TLS is a potentially reversible condition. Management focuses on having a high index of suspicion, identifying those at higher risk and implementing prophylactic measures. Any child with a new malignancy should have a baseline measurement of serum uric acid, potassium, phosphorus, and calcium, along with renal functions. Those with an increased likelihood must be on prophylactic regimen of intravenous hydration without potassium and close monitoring for fluid overload. Loop diuretics may also be used to optimize urinary flow and avoid FO, as we used in one of our patients.

Patients with hyperkalaemia must be monitored for arrhythmias. Medical management includes prompt administration of calcium gluconate, insulin, beta adrenergic agonists and potassium binding resins such as sodium polystyrene sulfonate.[1] Serum potassium in our first patient could not be corrected with these measures. Allopurinol can be used in patients with normal or mildly elevated serum uric acid, as was used in one of our patients. Rasburicase must be given in those with uric acid levels higher than 8 mg/dL with a rapid rise (>25 % from baseline).[8] Allopurinol was given to our first patient who did not show adequate response. Both our patients had high serum uric acid level along with hyperphosphataemia, rising creatinine, oliguria and fluid overload necessitating renal replacement therapy. The prognosis for complete recovery of renal function is excellent if dialysis is initiated early. Oliguria also responds quickly as the serum uric acid concentration falls below 10 mg/dL. However, CRRT may be associated with electrolyte, mineral, and acid-base imbalances; hypotension; infection; bleeding; and hypothermia. Our patients had hypotension; which required vasopressors; and suffered from hypothermia- but no electrolyte or acid base balance.

Large tumour size not only predisposes patients to TLS but also leads to increased risk of organ dysfunction due to pressure effects.[9] Both our patients had reduced lung compliance due to abdominal splinting, high intra-abdominal pressure affecting gastric and renal function as part of abdominal compartment syndrome. Tumour thrombosis of IVC and hepatic vein led to acute liver failure in the second patient.

The strength of this study was the mention of a common paediatric oncologic emergency such as tumour lysis syndrome in Wilms tumour and its management with CRRT. The limitation of this study was that it mentioned tumour lysis syndrome in a small number of patients and more studies are required to note its incidence in solid tumours.

Conclusion

TLS, largely known to be associated with haematological malignancies, has rarely been reported with Wilms tumour. Our cases illustrate that large sized Wilms tumour can be associated with TLS. Hence routine assessment of renal function, uric acid, phosphorus, potassium and LDH should be advised in such patients. Also, TLS prophylaxis should be considered before initiation of chemotherapy.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Disclosure: None to declare.

References

1. Russell TB, Kram DE. Tumor Lysis Syndrome. Pediatr Rev. 2020; 41:20-6. doi: 10.1542/pir.2018-0243.
2. Van Den Heuvel-eibrink MM, Hol JA, Pritchard-Jones K, Van Tinteren H, Furtwängler R, Verschuur AC, et al. Position paper: Rationale for the treatment of Wilms tumour in the UMBRELLA SIOP–RTSG 2016 protocol. Nat Rev Urol. 2017; 14:743-52. doi: 10.1038/nrurol.2017.163.
3. Caravaca-Fontán F, Martínez-Sáez O, Pampa-Saico S, Olmedo ME, Gomis A, Garrido P. Tumour lysis syndrome in solid tumors: Clinical characteristics and prognosis. Med Clin. 2017; 148:121-4. doi: 10.1016/j.medcli.2016.10.040.
4. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome.N Engl J Med. 2011; 364:1844-54. doi: 10.1056/NEJMra0904569.
5. Cairo MS, Coiffier B, Reiter A, Younes A. 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; 149:578-86. doi: 10.1111/j.1365-2141.2010.08143.x.
6. Matsukura H, Ibuki K, Nomura K, Higashiyama H, Takasaki A, Miyawaki T, et al. Intracranial calcification in a uremic infant with Wilms' tumor in a solitary kidney. CEN Case Rep 2012; 1:86-9. doi: 10.1007/s13730-012-0019-0.

7. Carmichael SP, Pulliam JF, D'Orazio JA. Delayed tumor resection in a 5-year-old child with bilateral Wilms tumor. J Surg Case Rep. 2013; rjt012. doi: 10.1093/jscr/rjt012.
8. Galardy PJ, Hochberg J, Perkins SL, Harrison L, Goldman S, Cairo MS. Rasburicase in the prevention of laboratory/clinical tumour lysis syndrome in children with advanced mature B NHL: a Children's Oncology Group Report. Br J Haematol. 2013; 163:365-72. doi: 10.1111/bjh.12542.
9. Xiang ZL, Hao WY, Na L, Lin QR, Jia ZJ, Li JW, et al. Analysis of treatment of large abdominal malignancies in children complicated with abdominal compartment syndrome: Report of six cases. Medicine (Baltimore). 2017; 96: e6705. doi: 10.1097/MD.0000000000006705.