Rare presentation of renal failure related to tumor lysis syndrome

[DOR: 20.1001.1.24234729.2018.4.2.2.8]

[DOI: 10.22088/CJP.BUMS.4.2.313]

Case Report

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Received: 25 June 2018
Revised: 28 July 2018
Accepted: 25 Aug 2018

Abstract

Background: Tumor lysis syndrome (TLS) which mostly occurs in lymphoproliferative malignancies after the start of chemotherapy is an oncologic emergency. Manifestations of metabolic imbalance including increasing hyperkalemia, hyperphosphatemia, hyperuricemia and hypocalcemia are common presentation of TLS.

Case report: We present two cases of spontaneous TLS; a rare presentation of TLS before cytotoxic chemotherapy. These cases were admitted with presentation of TLS without any history of chemotherapy with mediastinal mass in chest X-ray (CXR) and subsequent diagnosis of lymphoblastic lymphoma and T-cell acute lymphocytic leukemia (ALL). After several hemodialysis sessions, their conditions were improved and they underwent chemotherapy.

Conclusions: It was found that the presentation of mediastinal mass in cases of lymphoma and acute leukemia might be associated with TLS before chemotherapy. In addition, it is important to pay attention to CXR, when we face to a patient with acute renal failure related to TLS.

Key Words: Childhood Neoplasms, Leukemia, Lymphoma, Tumor Lysis Syndrome

Citation:
Tamaddoni A, Sadr Moharerpour S, Asefi S, Tamaddoni B. Rare presentation of renal failure related to tumor lysis syndrome. Caspian J Pediatr Sep 2018; 4(2): 313-6.

Introduction

Tumor lysis syndrome (TLS) as a metabolic disorder includes oliguric renal failure (ORF), hyperuricemia, hyperphosphatemia and hyperkalemia and commonly occurs after the malignant cells are rapidly destructed, [1] leading to the release of uric acid, potassium, proteins, phosphate and other purine metabolites into the systemic circulation. The mentioned factors make excessive demands on the body's homeostatic mechanisms and overcome the capacity of the renal system to excrete normally these materials. As the renal clearance of these chemical substances is overcome, the secondary hypocalcemia, hyperkalemia, hyperphosphatemia and hyperuricemia will occur and at the same time, the serum lactate dehydrogenase (LDH) level is often enhanced, too [2]. Uncontrolled TLS results in acute renal failure (ARF) and lactic acidosis, clinically, leading to multi-organ defects including cardiac arrhythmias, acute kidney injury (AKI) as well as seizures or sudden death which needs intensive care. TLS is the most common oncologic emergency, and the mortality and morbidity increase without early diagnosis and prompt therapeutic intervention [3]. TLS is less common in solid tumors and more common in high-grade leukemia and lymphoma with high white blood counts. During taking chemotherapy and cytotoxic drugs, often, this syndrome is iatrogenic [1]. Few but remarkable case reports suggest that the TLS can happen in alternative conditions including the use of comparatively weak tumoricidal agents like glucocorticoids, treatment with radiation and administration of monoclonal therapy in addition to

traditional cytotoxic agents [4-6]. Spontaneous TLS which is much less common often occurs before cytotoxic therapy [7]. In recent decades, the incidence of TLS has declined due to the physicians' attention and knowledge of the existence of this syndrome using appropriate prophylaxis before the start of chemotherapy.

In the current study, we report two cases of renal failure related to TLS before diagnosis of malignancies, referred to hematology ward in Amirkola Children Hospital of Babol University of Medical Science.

Case Presentations

Case 1:

A 12-year-old boy with lethargy, diarrhea and vomiting from previous day was referred to Amirkola Children's Hospital. He had normal growth and development and no history of hospitalization. He was ill, pale and dehydrated on examination. Abdominal exam was normal and without organomegaly. Petechiae, ecchymosis and purpura were observed on his both legs.

Vital sign (VS): Blood Pressure (BP): 100/60 mm-Hg, Pulse Rate (PR): 110/min, Respiratory Rate (RR): 19/min and Body Temperature: 38.5˚ C.

There was nothing abnormal on auscultation of the heart and lung sounds as well as the patient was nonoliguric.

Laboratory data:

White Blood Cell (WBC): 7500/dL), Hemoglobin (Hb): 7.7 (g/dL), Platelet (plt): 12000/dL).

Venous Blood gases (VBG) PH: 7.11, PCO2: 31.5, HCO3: 10.2

BUN: 135 (mg/dL), Creatinine (Cr): 3.2 (mg/dL), Sodium (Na): 130 (mg/dL), Potassium (K): 4.6 (mg/dL), Calcium (Ca): 4.5 (mg/dL), Phosphorus (P): 13.1 (mg/dL), Uric acid: 30 (mg/dL), LDH: 4095 (U/L)

Coagulation and liver function tests and urine analysis (U/A) were in normal range.

Patient with primary diagnosis of ARF as a result of HUS underwent on the basis of data laboratory 4 times hemodialysis and after that, his renal function was improved and creatinine level decreased from 3.2 mg/d) to 0.9 mg/dL over 10 days. There was no finding in abdominal sonography except mild hydronephrosis in both kidneys. CXR indicated a 3-4 centimetere diameter mass in right hilar and paracardiac regions. The CT scan revealed 28-38-mm diameter mass with a clear border at the anterolateral of *superior vena cava* (SVC)-right atrium, which could be invasive thymoma or mediastinal mass. Finally, during the core needle biopsy of mediastinal mass with the guide of ultrasound sonography, the lymphoma was diagnosed and immune histochemistry staining reported lymphoblastic lymphoma. Then, after hydration, the serum alkalization and oral administration of allopurinol chemotherapy started following the initial hemodialysis sessions. The patient's condition was improved and no major complications were reported, thereafter.

Case 2:

The patient was an 11-year-old girl with severe respiratory distress from 2 days ago. She had the history of admission 2 months ago with renal failure post gastroenteritis with diagnosis of HUS and she underwent hemodialysis for five times and her creatinine level decreased from 5.7 mg/dL to 0.8 mg/dL during 12 days. Next, she was discharged with good general condition and normal kidney function test and normal kidneys by abdominal ultrasonography.

At the time of second admission, she was ill with intercostal and suprasternal retraction, wheezing on lung auscultation and jugular venous were prominent and her face seemed plethoric. CXR showed a large mass that occupied two-thirds of thoracic cage. Therefore, the SVC syndrome as an emergency case suggested the probability of lymphoma or leukemia.

When we assessed her last CXR in previous admission (2 months ago), she had small mediastinal mass at that time.

VS: BP: 105/60 mm-Hg, PR: 108/min, RR: 43/min and body Temperature: 37˚C

Laboratory data:

WBC: 9500/dL, Hb: 13.5 (g/dL), Plt: 372000/dL

VBG: PH: 7.27, PCO2: 38.9, HCO3: 17.6

BUN: 58 (mg/dL), Cr: 5.7 (mg/dL), Na: 129 (mEq/L), K: 4.9 (mEq/L), Ca: 7.2 (mg/dL)

P: 6.8 (mg/dL), Uric acide: 9.3 (mg/dL), LDH: 953 (U/L)

U/A: WBC: 2-4, RBC: many, SG: 1006

Coagulation and liver function tests were in normal range.

Bone marrow aspiration operation and immune phenotype by flow cytometry suggested the diagnosis of T-cell acute lymphocytic leukemia (ALL). The

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patient underwent on chemotherapy, per protocol, with no further TLS related complications. Over subsequent weeks, the tumor mass shrank dramatically and the patient had good general condition.

Discussion

Both patients in this study presented with hyperuricemia, hyperphosphatemia and renal failure before diagnosis and starting chemotherapy named spontaneous TLS. Unlike the normal feature of TLS and in disagreement with Enomoto et al.'s study [7], our patients were not oliguric or hyperkalemic.

Moreover, the hyperphosphatemia is less commonly observed with spontaneous TLS since the phosphate released in the spontaneous setting is deemed to be reapplied in the generation of new neoplastic cells which are less likely to assimilate with chemotherapy administration [8].

Our findings were based on Cairo and Bishop modified criteria of TLS, commonly used as classification system. This system is represented in table 1 [2, 9].

It is assumed that the metabolic derangement would less often take place with spontaneous TLS due to the hypocalcemia resulting from serum calcium binding to excess phosphate [10]. Unlike study of Kjellstrand CM.et al [8], our cases had hyperphosphatemia and hypercalcemia. Moreover, the presence of mediastinal mass is a considerable finding emphasizing that the chest X-ray (CXR) should be exactly seen in spontaneous TLS.

A natural product of purine catabolism is considered as uric acid. Massive TLS, either in the context of cytotoxic therapy or spontaneous, can lead to acute hyperuricemia, causing a risk for renal failure (RF) secondary to uric acid nephropathy in patients [11]. Both patients of the current study suffered from ARF. Today, it is believed that uric acid causes renal injury through inflammation and endothelial dysfunction though it is traditionally defined as an obstructive nephropathy because of intrarenal uric acid crystal deposition [11].

Through initial diagnosis of RF, two patients of the present study were firstly undergone hemodialysis, an important way to treat RF. However, hemodialysis in children involves some risks and even leads to death due to their inappropriate arteries and presence of abdominal tumors or severe thrombocytopenia. Thus, the best way to deal with this problem is prevention including four main matters. The first one is proper hydration to increase urine volume. Secondly, the administration of sodium bicarbonate should be done to maintain urine PH>7 in order to enhance the solubility of uric acid [12]. Thirdly, to decrease the serum uric acid level, the agents like rasburicase and allopurinol must be used [13] and finally taking drugs that increase serum urate or acidify urine such as thiazides or salicylates should be avoided [14].

In conclusion, according to our cases, it is important to pay attention to mediastinal mass in CXR when we face to a patient with ARF related to tumor lysis syndrome.

Table 1. Cario-Bishop definition of laboratory tumor lysis syndrome and clinical tumor lysis syndrome

Laboratory Tumor lysis syndrome	
Metabolite or electrolyte	**criterion for diagnosis**
Uric acid	≥8mg/dL or 25% increase from baseline
Potassium	≥6meq/L or 25% increase from baseline
Phosphorus	≥6.5 mg/dL (children) ,≥4.5 mg/dL (adult) or 25% increase from baseline
Calcium	≥25% increase from baseline

Clinical tumor lysis syndrome:

LTLS* and one or more of the following: 1) creatinine × ≥1.5 ULN* (age>12 years of age or age adjusted) 2) cardiac arrhythmia or sudden death 3) seizure

* LTLS: Laboratory tumor lysis syndrome, ULN: Upper limit of normal

Acknowledgment

The authors are grateful to the Clinical Research Development Committee of Amirkola Children's Hospital and Non-Communicable Pediatric Diseases Research Center of Babol University of Medical Sciences for their contribution to this study.

Funding: None.

Conflict of interest: There was no conflict of interest.

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