Case Report

Hematological malignancies presenting as spontaneous tumor lysis syndrome: A case series

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Abstract

Tumor lysis syndrome is an oncological emergency caused by massive tumor lysis resulting in a constellation of metabolic abnormalities. It is observed most frequently in patients with high-grade hematological malignancies undergoing treatment. Tumor lysis syndrome can occur spontaneously and it can present as the first symptom of an underlying malignancy. Diagnosis should be considered if specific metabolic abnormalities are present even in the absence of previously diagnosed malignancy. We report three unusual cases of hematological malignancies, rare in view of the primary disease as well as its presentation as spontaneous tumor lysis syndrome where a high index of suspicion led to the final diagnosis.

Keywords: Cairo-Bishop definition, hyperuricemia, renal failure, spontaneous tumor lysis, underlying malignancy

Introduction

Tumor lysis syndrome (TLS) is an oncological emergency with high mortality rate characterized by specific electrolytic abnormalities. It is mostly seen following initiation of chemotherapy for high-grade hematological malignancies, like Burkitt lymphoma and acute lymphoblastic leukemia (ALL), but it has also been largely reported in a variety of solid tumors. TLS can rarely occur spontaneously which can be the initial presentation of an underlying malignancy.

Case Reports

Case 1

A 9-year old with a history of abdominal pain and vomiting of 10 days duration was evaluated in a nearby hospital. He had elevated serum amylase and lipase and bulky pancreas on ultrasonography. Later, he developed oliguria and was referred to our center. He had pallor, facial puffiness, and epigastric tenderness. He also had abnormal renal function with metabolic acidosis and was admitted with diagnosis of acute pancreatitis with secondary renal failure, and symptomatic treatment was started. On further investigation, elevated lactate dehydrogenase (LDH), hyperuricemia, hyperphosphatemia, and hypocalcemia [Table 1] were detected.

He also had anemia (hemoglobin 9 g/dL), leucocytosis (11,400 cells/cmm), thrombocytopenia (91,000/cmm), and elevated erythrocyte sedimentation rate (ESR) (54 mm/h). His renal function worsened despite clinically improving pancreatitis suggesting an alternate reason for renal failure. Meanwhile, peripheral smear examination revealed 17% blasts. Thus, a diagnosis of spontaneous TLS was considered. Bone marrow aspirate and biopsy showed 85% blast, morphology suggestive of ALL [Figure 1]. And, a diagnosis of ALL with spontaneous TLS and secondary renal failure was made.

Case 2

A 15-year-old boy was referred to our center with a history of anorexia, abdominal distension, and breathing difficulty. On

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Table 1: Relevant biochemical values in 3 cases

	Case 1	Case 2	Case 3	Reference range
Uric acid	32 mg/dL	18.3 mg/dL	20.1 mg/dL	2.6-7.2 mg/dL
Phospherous	7.7 mg/dL	5.9 mg/dL	-	4.5-5.5 mg/dL
LDH	4163 U/L	3953 U/L	428 U/L	85-227 mg/dL
Calcium	8.1 mg/dL	8.7 mg/dL	-	8.5-10.1 mg/dL
Pottassium	4.7 mE/dL	5 mE/dL	4.4 mE/dL	3.5-5.1 mgE/dL
Creatinine	6.5 g/dL	2.9 g/dL	1.6 g/dL	0.6-1.3 g/dL
BUN	127 g/dL	95 g/dL	41 g/dL	15-40 g/dL
HCO_3	10 mEq/L	14 mEq/L	-	22-28 mE/L

LDH: Lactate dehydrogenase; BUN: Blood urea nitrogen

admission, he had significant ascites and initial investigation revealed altered renal function. Ascitic fluid showed high cell count (2 lakh cells/cmm) but cytology showed only degenerated cells. Computed tomography (CT) abdomen revealed omental, peritoneal, and diaphragmatic thickening with caking, and differential diagnoses of peritoneal tuberculosis, peritoneal carcinomatosis, and peritoneal lymphomatosis were considered.

Later, he was found to have hyperuricemia, hyperphosphatemia, and high LDH [Table 1] which were suggestive of TLS, and symptomatic treatment for the same was initiated. On diagnostic laparoscopy, multiple subdiaphragmatic, peritoneal, and omental nodules were found along with 1 × 1 cm sized nodule in liver. Multiple biopsies were taken and lesions showed morphology suggestive of non-Hodgkin lymphoma [Figure 2a]. We proceeded with immunohistochemistry (IHC) [Figure 2b-d], and a final diagnosis of Burkitt lymphoma with spontaneous TLS and secondary renal failure was made.

Case 3

A 28-year-old gentleman was on treatment for high-grade fever, rigor and chills, and cough for 4 months. CT thorax showed large pleural effusion. He was suspected to have tuberculosis and treatment was initiated. As he did not find any relief, he was referred to our center. On admission, he had altered renal function, anemia (Hb 4.2 g/dL), leucocytosis (TC − 111,000 cells/cmm), and thrombocytopenia (1 lakh/cmm). Further investigations showed elevated total protein (12 g/dL), globulin (9.7 g/dL), immunoglobulin G (7580 mg/dL), and ESR (140 mm/h). Serum electrophoresis showed monoclonal gammopathy with M band. He also developed hyperuricemia and high LDH giving rise to suspicion of TLS [Table 1].

The pleural fluid aspirate showed 1200 cells/cmm, predominantly plasma cells. Peripheral smear showed 14% plasmacytoid cells. Bone marrow showed 15% plasma cells, and following IHC, a diagnosis of plasma cell leukemia was made [Figure 3]. This case had not met the diagnostic criteria for plasma cell leukemia (≥20% plasma cells in peripheral smear) and we believed it was possibly due to tumor lysis.

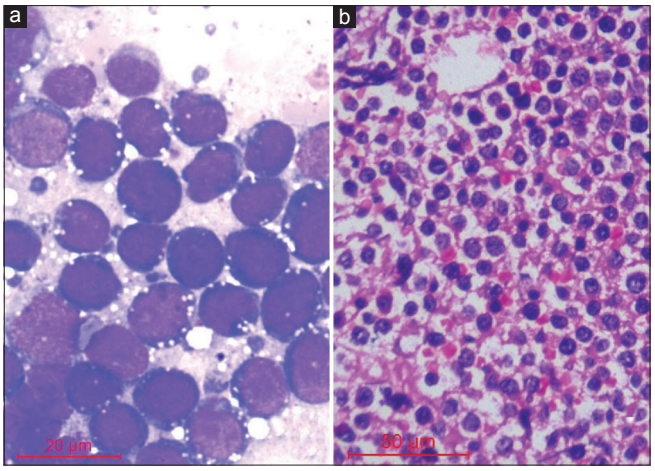

Figure 1: Bone marrow morphology: (a) bone marrow aspirate showing lymphoblast with vacuolated cytoplasm (Leishman stain) and (b) bone marrow biopsy showing lymphoblast (H and E)

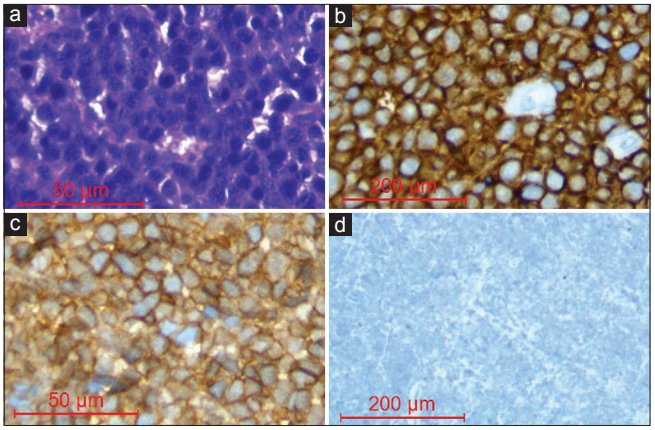

Figure 2: Peritoneal biopsy: (a) atypical lymphoid cells (H and E), (b) IHC – CD20 positive, (c) IHC – CD10 positive, and (d) IHC – CD5 negative

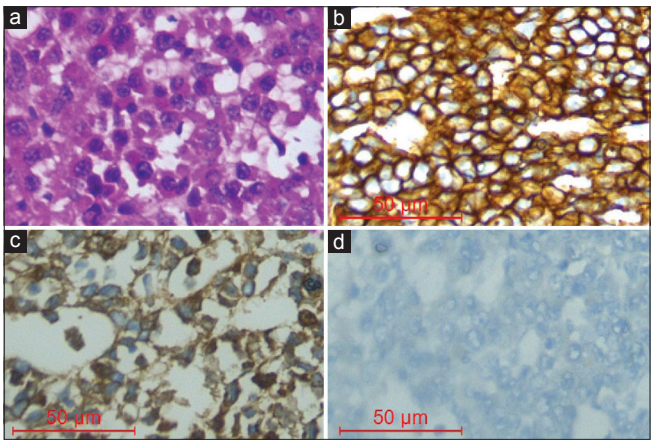

Figure 3: Bone marrow biopsy: (a) plasma cells (×40) (H and E), (b) IHC – CD138 positive, (c) IHC – kappa positive, and (d) IHC – CD5 negative

Discussion

TLS is caused by massive tumor lysis resulting in a constellation of metabolic abnormalities. It is observed most frequently in patients undergoing treatment for high-grade hematological malignancies like Burkitt lymphoma and ALL. But it has also been largely reported in a variety of solid tumors. The intrinsic

risk factors for the development of TLS are high proliferation index and chemosensitivity of tumor, bulky disease, high LDH, pretreatment hyperuricemia, and renal failure.[1,2] The exact etiology of spontaneous TLS is unknown. Some suggest an intrinsic production of glucocorticoids or hyperthermia as a cause of tumor cell lysis.[3,4]

TLS is characterized by specific metabolic abnormalities such as hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. Elevated LDH is a typical finding in TLS. Pathogenesis of TLS is based on release of intracellular contents into the circulation following tumor cell lysis [Figure 4]. Spontaneous TLS may not show hyperphosphatemia as the released phosphorus may be reutilized for synthesis of new tumor cells.

The initial presentation may be vague with features like nausea, vomiting, fatigue, muscle cramps, etc., which could be encountered during routine practice. Laboratory TLS is diagnosed based on Cairo Bishop definition [Table 2].[5] Change in two or more should be present within 3 days before or 7 days after chemotherapy. Modification to this criteria was proposed in 2011.[6] When patients with laboratory TLS develop complications like seizure, renal failure, arrhythmia, or sudden death, it is called clinical TLS. However, these definitions are insufficient to accurately diagnose spontaneous TLS, which occurs independent of treatment. Management of established TLS includes adequate hydration, urate-lowering measures, management of hyperkalemia, and hemodialysis in refractory cases. Our patients were treated addressing hyperuricemia and other metabolic abnormalities, and after stabilization, they were transferred to oncology centers for definitive management.

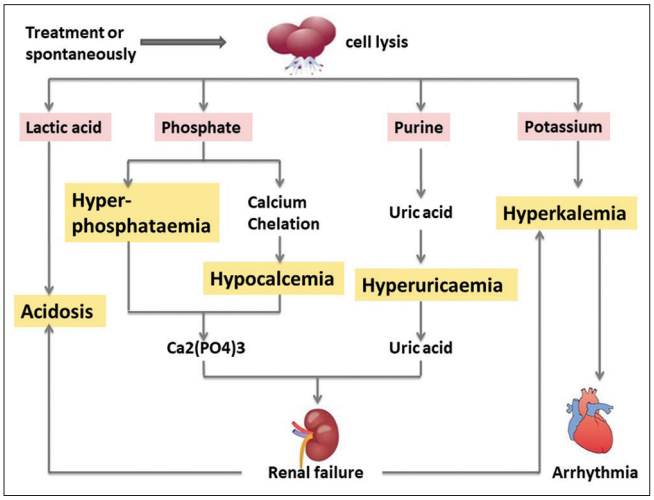

Figure 4: Pathogenesis of tumor lysis syndrome and its complications

Table 2: Cairo-Bishop definition of laboratory tumor lysis syndrome

Variable	Value	Change from baseline
Uric acid	≥8 mg/dL (476 mmol/L)	25% increase
Potassium	≥6 mEq/L (6 mmol/L)	25% increase
Phosphorus	≥4.5 mg/dL (1.45 mmol/L) for adults, ≥6.5 mg/dL (2.1 mmol/L) for children	25% increase
Calcium	≤7 mg/dL (1.75 mmol/L)	25% decrease

All the three cases we presented here were rare in view of the primary disease as well as its complication as spontaneous TLS. The first child had bulky pancreas. ALL infiltrating pancreas could be a possibility and a few similar cases have been reported.[7] Second case had lymphoma with extensive peritoneal and omental involvement which is considered to be unusual.[8] Plasma cell leukemia presenting at younger age group is extremely rare with a few reported cases in literature.[9]

Because of the unusual presentation, spontaneous TLS is often underdiagnosed. More dangerously, it may be the first symptom of underlying malignancy and diagnosis may be further delayed which gives an added risk to the patient. These cases highlight the fact that a high index of suspicion is needed even at primary care level, in diagnosis of spontaneous TLS, and diagnosis should be considered if specific metabolic abnormalities are present even in the absence of a previously diagnosed malignancy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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