

## Hypercalcemia in Context of Tumor Lysis Syndrome in a Patient with Multiple Myeloma

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### ABSTRACT

**Purpose:** The purpose of this report is to increase awareness into various forms of tumor lysis syndrome (TLS) in patients with multiple myeloma, prompting recognition and management.

**Case Presentation:** We herein describe a patient with multiple myeloma who developed hypercalcemia in the setting of tumor lysis syndrome while receiving therapy. On the eighth day after treatment with Bortezomib and dexamethasone, our patient developed abdominal pain and obstipation. Examination revealed borderline vital signs along with signs of peritonitis. Biochemical profile revealed evidence of hypercalcemia in context of TLS and an acute kidney injury. Imaging showed signs of small bowel obstruction. The patient improved with aggressive hydration, anti-hyperkalemic measures, Rasburicase and Dexamethasone, after which she underwent urgent exploratory laparotomy with resection and anastomosis for impeding perforation. Although our patient had some reported risk factors for developing TLS, the case was atypical in terms of delayed presentation as well as an uncharacteristic presentation and biochemical findings in relation to TLS.

**Conclusion:** As TLS is a condition associated with high morbidity and mortality, the presence of hypercalcemia in context of an appropriate clinical setting should not delay or derail recognition and management of TLS.

### Keywords

Bortezomib, Hypercalcemia, Multiple myeloma, Tumor lysis syndrome (TLS).

### Introduction

Tumor lysis syndrome (TLS) is a combination of clinical and biochemical manifestations that include Hyperkalemia, hyperuricemia, hyperphosphatemia and hypocalcemia. It is known to occur most commonly in lymphoproliferative disorders, either spontaneously or in response to cytotoxic therapies. Multiple myeloma is a low proliferative tumor with rare incidence of tumor lysis in the pre-Bortezomib era. This report describes an uncommon presentation of hypercalcemia in the context of TLS in a patient with Multiple myeloma.

### Case Presentation

We report a case of a fifty eight year old woman who was

recently diagnosed with IgA Kappa restricted multiple myeloma based on serum protein electrophoresis M band, protein immune fixation revealing Kappa light chain and serum immunoglobulin IgA level of 18.7 gm/L, bone marrow aspiration smear showed abnormal plasma cells, bone marrow biopsy showed plasma cells accounting for 80%. Urine Bence Jones protein was positive.  $\beta_2$ -micro-globulin was 4.7 mg/L and serum lactate dehydrogenase (LDH) was 150 U/L (normal: 106-211 U/L). FISH probe was negative for common cytogenetic abnormalities including 13q deletion. The patient was diagnosed with Kappa light chain multiple myeloma, International Staging System (ISS) stage III.

The patient was started on VDR protocol that included Bortezomib, Lenalidomide, Dexamethasone and Zoledronic acid. On the eighth day of the first cycle of the protocol, she presented to the hospital with generalized abdominal pain for three days, associated with history of constipation and obstipation for five days, along with

reduced oral intake. Vital signs were documented as blood pressure of 105/74 mmHg, heart rate of 101 beats/min, and temperature of 36.6 degrees Celsius. Physical examination was remarkable only for a tender abdomen all over with generalized guarding. Biochemical profile of the patient was found to have a serum creatinine of 103mcmol/L, BUN 15.6 mmol/L, albumin 19.05 gm/L, calcium 2.49 mmol/L, corrected calcium 2.8 mmol/L, potassium 5 mmol/L, uric acid 504 mmol/L, white blood cell count of 3.1, hemoglobin 83.5 gm/L, platelets 55. A computerized tomography showed distal small bowel loop high grade obstruction with possibility of closed loop obstruction. So along with the obstruction, she was diagnosed with tumor lysis syndrome with hypercalcemia. Treatment was initiated with aggressive hydration, Rasburicase and Dexamethasone. After which all of her biochemical profile normalized, including the acute kidney injury and electrolytes. She has also underwent exploratory laparotomy with findings of non-viable impending perforation of a small segment of small bowel, mandating resection and anastomosis.

## Discussion

Tumor lysis syndrome is an oncological emergency with significant morbidity and mortality. It most commonly occurs either spontaneously or following cytotoxic chemotherapy in hematological malignancies with great tumor burden, such as lymphoblastic leukemia, acute myeloid leukemia, and Burkitt lymphoma [1]. It also occurs in other bulky tumors with high sensitivity to chemotherapies [1,2]. The incidence of TLS with multiple myeloma has been increasingly reported both spontaneously [3,4], and following treatment with new agents such as Bortezomib [5-7], and Pomalidomide in refractory cases [8].

TLS is a result of tumor cells rapidly releasing their intracellular contents into the extracellular space, overwhelming homeostatic mechanisms. This abrupt and quick process is the pathogenesis for hyperphosphatemia in TLS, then in turn is exacerbated by AKI. The hyperphosphatemia then causes hypocalcemia by binding the calcium, forming phosphate-calcium crystals which precipitate in the renal parenchyma causing the AKI that is usually observed [9].

Cairo-Bishop suggest a criteria to aid the diagnosis of TLS. It mandates laboratory sequela of two or more abnormal serum findings including: Uric acid level >8mg/dl, potassium level >6meq/L, phosphorus lever >4.5mmol/dl, and/or calcium level <7mg/dl, either 3 days before, or 7 days after chemotherapy. And features suggestive of clinical TLS which fulfills the laboratory conditions and one or more of the following: acute kidney injury expressed as serum creatinine >1.5x upper limit of normal, developing cardiac arrhythmia or sudden death or onset of seizures [10].

Our patient had an atypical presentation of hypercalcemia in context of TLS which was, to our knowledge, never described in patients with multiple myeloma. It was however, documented once in a patient with diffuse large B cell lymphoma on chemotherapy [11]. Hypercalcemia in multiple myeloma is a common paraneoplastic syndrome [12]. It has been ascribed to dysregulation of osteoblasts

and osteoclasts, in which bone absorption increases and bone construction decreases leading to uncoupled bone remodeling. In turn, the pathogenesis of myeloma bone disease and consequent bone pain, pathologic fractures and hypercalcemia ensue [13].

In accordance to previous reports examining risk factors for development of TLS in multiple myeloma patients, our patient had a high disease burden which was reported to pose an increased chance of TLS following Bortezomib therapy in several studies [14-17]. Further risk with features such as an elevated pretreatment serum uric acid level, preexisting renal damage, tumor infiltration of the kidney, and advanced age were also significant [1]. Others suggest unfavorable cytogenetics and light chain disease as high risk features [18]. In our case and most recorded cases, typically patients developed symptoms suggestive of the complication very early in the course of treatment with Bortezomib, and thought to be at highest risk during the first cycle of therapy [6,14-17]. As such, high index of suspicion in such patients, close monitoring, and considering preventative measures should be done especially during early phases of treatment to ensure timely and efficient management with improved outcomes.

## Conclusion

In summary, high risk multiple myeloma patients for TLS should be monitored closely. Presence of hypercalcemia and lack of the full metabolic picture of TLS should not derail the recognition and early management of TLS as it is a life-threatening condition.

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