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Tumor Genesis Syndrome in a Paediatric Patient with Burkitt Lymphoma of Abdomen

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Case Report

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Abstract: Electrolyte disturbances are common in patients with hematological malignancies and are mostly due to tumour lysis syndrome. Tumour genesis syndrome although uncommon occurs when rapid cell proliferation and DNA synthesis deplete extracellular phosphate. These ominous electrolytes disturbances may indicate rapid tumour genesis and require urgent treatment intervention to halt the crises of rapid leukemic cell proliferation. A 4 -year-old boy diagnosed with Burkitts lymphoma of abdomen developed severe hypophosphatemia prior to treatment initiation followed by acute renal failure requiring hemodialysis on treatment initiation. With appropriate timely supportive care child recovered and eventually completed the planned chemotherapy schedule and is under follow up now.
Keywords: Tumour Genesis Syndrome; Burkitt lymphoma.

INTRODUCTION

Electrolyte disturbances are common in patients with hematological malignancies and are mostly due to tumour lysis syndrome. Tumour genesis syndrome although uncommon occurs when rapid cell proliferation and DNA synthesis deplete extracellular phosphate. These ominous electrolytes disturbances may indicate rapid tumour genesis and require urgent treatment intervention to halt the crises of rapid leukemic cell proliferation. Here we describe a child with Burkitt Lymphoma of Abdomen who developed severe hypophosphatemia prior to treatment initiation followed by development of tumour lysis syndrome on treatment initiation.

CASE REPORT

A 4 year old boy presented with intermittent lower abdominal pain and progressive abdominal distension of 1 week duration. He began to have fever with sore throat that did not respond to antipyretics and antibiotics. He was admitted in view of increasing abdominal distension and breathlessness. Physical examination revealed a sick, tachypneic child with a temperature of 39 °C, blood pressure of 90/60 mmHg and heart rate of 125 bpm. There was no significant pallor or lymphadenopathy. Child was in respiratory distress with an oxygen saturation of 96% while receiving 1 L/min nasal oxygen. Cardiovascular examination was normal. There was an ill-defined, mobile non–tender mass in the right hypochondrium. There was no hepatosplenomegaly.

The hemoglobin was 9.6 gm/dl, platelet count 6,72,000/cmm, white blood cell count 9,200/cmm, with a normal differential count and peripheral smear. Erythrocyte sedimentation rate was 25 mm/1st hr. Blood urea was 33mg/dl, serum creatinine was 0.6 mg/dl and uric acid was 15.9 mg/dl (Normal range 2.5-8.5mg/dl). The serum concentrations of sodium was 143 mEq/L, potassium 4.6 mEq/L,calcium 8.5 mg/dl and serum phosphorus was 1.8 mg/dl (Normal range 2.5-4.5mg/dl). Serum lactate dehydrogenase was 6604 U/L. Liver function tests were within normal limits. There was no central nervous system or bone marrow infiltration. The chest radiograph was normal. Contrast enhanced CT Abdomen showed focal transmural thickening of ascending colon, mesentry and peritoneum with multiple enlarged preaortic, paraaotric and retroperitoneal lymph nodes with minimal ascites. Bilateral grade II hydroureteronephrosis was present. Ultrasound guided biopsy from abdominal mass with immunohistochemistry yielded the diagnosis Burkitts lymphoma. In view of the hyperuricemia, pre-chemotherapy hyperhydration with potassium free fluid at the rate of 3L/m2 and urate oxidase (Rasburicase) at 0.2 mg/kg/ single dose was given along with meticulous urine output monitoring. Child was started on reduction phase with prednisolone alone, hypophosphatemia further worsened (serum phosphorus 0.5-0.8 mg/dl) and child also developed hypokalemia 2.4-3 mEq/L(3.4-5.1mEq/L).All other biochemical parameters were within normal limits and the urine output was maintained. Intravenous chemotherapy that

included cyclophosphamide (300mg/m2) and vincristine 1mg/m2 was given on December 10 followed by clinical and laboratory evidence of tumour lysis syndrome within 24 hours. After 24 hrs of chemotherapy the laboratory parameters were B urea - 232 mg/dl, serum creatinine 1.7 mg/dl, uric acid -2.7 mg/dl, S. potassium -3.8 mEq/dl, S Calcium -3.6 mg/dl and serum phosphorous was 19 mg/dl. Child developed symptomatic hypocalcemia which required intravenous Calcium gluconate) supplementation. On the third day after chemotherapy the child developed anuria along with acute kidney injury. He underwent four cycles of hemodialysis and subsequently the renal parameters normalized. Child also developed hypertension requiring multiple antihypertensive, which could eventually be gradually tapered and stopped after six months. Child completed the planned chemotherapy for Stage III, Group B Burkitt lymphoma as per FAB LMB 96 and is kept under follow up and remains disease free four years after diagnosis.

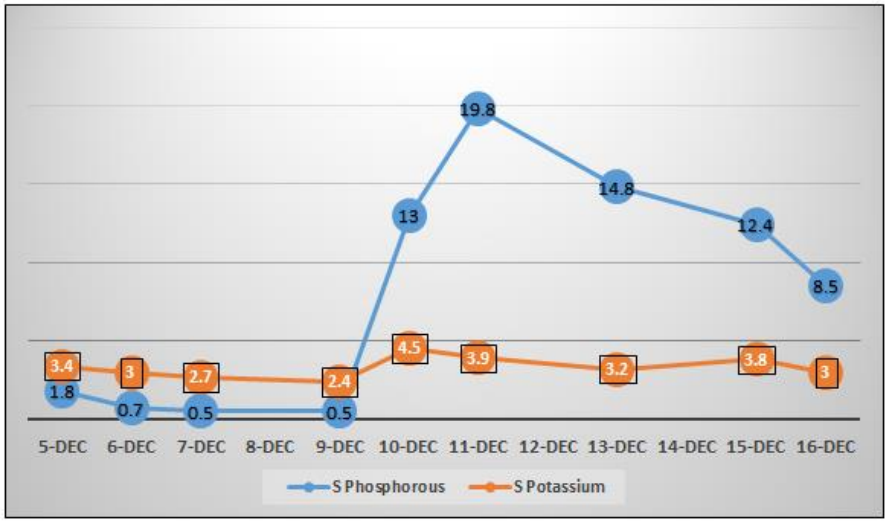

Fig-1: Graph showing trend of the changes in serum phosphorous and serum potassium levels at presentation and after initiation of cytoreductive chemotherapy on December 10

DISCUSSION

Various electrolyte disturbances have been reported in patients with hematological malignancies due to combinations of apoptosis, rapid proliferations of malignant cells, organ infiltration, poor nutritional intake and complications of chemotherapy. Tumour lysis syndrome, characterized by hyperkalemia, hyperphosphatemia, hyperuricemia and hypocalcemia is the frequently found electrolyte disturbance. Tumour genesis syndrome although uncommon occurs when rapid cell proliferation and DNA synthesis deplete extracellular phosphate.

Severe hypophosphatemia is a life-threatening emergency and has been reported in patients with acute leukaemia with relapses [1], at the time of blastic transformation in chronic myeloid leukaemia[2] and during haematopoietic reconstitution after allogenic peripheral stem cell transplantation [3]. These patients may present with acute respiratory failure, muscle weakness, acute congestive heart failure, torsade de pointes and tetany which require acute intensive care and urgent correction of electrolyte disturbances [4].

The causes of hypophosphatemia in hematological malignancy are multifactorial including abnormal cellular metabolism, renal wasting, poor nutritional phosphate intake, and complication of cytotoxic drugs [3, 5].Transcellular uptake of phosphate by rapid proliferating tumour cells remains one of the most important causes for hypophosphatemia in leukemic patients. Severe hypophosphatemia at presentation may be an indicator of ongoing aggressive tumor genesis. During tumor genesis there is an increased rate of uninhibited aerobic glycolysis by the blast cells causing rapid transcellular uptake of phosphate which might cause a sudden acutely life-threatening decrease in serum phosphate [6]. Hence, the importance of giving special attention to the severe hypophosphatemia at initial presentation, the need to urgently initiate chemotherapy at the earliest and to anticipate tumor lysis syndrome immediately upon starting chemotherapy. Rapid switch from severe hypophosphatemia to hyperphosphatemia after initiating chemotherapy (Figure 1) indicates the change from blast proliferation to tumor lysis [7].This dramatic shift in phosphate balance could be life-threatening and close monitoring, and appropriate management of the serum phosphate concentration is crucial. Hypokalemia has been attributed to lysozymuria-induced renal tubular injury, influx of potassium into metabolically active cells, and hypomagnesemia. Severe malnutrition has been reported as an important risk factor for the development of hypokalemia because of limited potassium reserve. [8].Hypokalemia in this patient

might have also been contributed by the anti-hyperkalemic measures initiated at diagnosis.

Our patient with Burkitt lymphoma abdomen presented with severe hypophosphatemia and hypokalemia attributable to aggressive tumor genesis which rapidly switched over to tumor lysis syndrome with severe hyperphosphatemia, symptomatic hypocalcemia, and acute kidney injury after initiating cytoreductive chemotherapy. Patient required hemodialysis to normalize the renal parameters and the dyselectrolytemias. Child also developed hypertension requiring multiple antihypertensives, which were gradually tapered and stopped. Patient eventually completed the planned chemotherapy and is under follow up.

CONCLUSION

This case report illustrates an uncommon presentation of severe hypophosphatemia and hypokalemia in a child with Burkitt lymphoma of the abdomen. Tumor genesis syndrome is a less recognized or less reported phenomenon and might be an indirect indicator of aggressiveness of the tumor. Early recognition of these electrolyte abnormalities and the possibility of subsequent development of tumor lysis syndrome should alert the oncologist for initiating the necessary life- saving urgent interventions.

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