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CASE REPORT

Fanconi Syndrome: A Rare Initial Presentation of Acute Lymphoblastic Leukemia

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Abstract A-14-year old boy, presented with a short history of excessive thirst and increased urine output. Clinical examination showed pallor, generalized lymphadenopathy and hepatosplenomegaly. For evaluation of his polyuric state he underwent routine laboratory investigations, including renal function test, acid-base studies, urine analysis. Blood tests suggested hypokalemia, hypouricemia, hypocalcemia and hyperchloremia with normal liver and kidney function tests. The arterial blood gas analysis was suggestive of normal anion gap metabolic acidosis. Urine analysis was suggestive of hyperuricosuria, hypercalciuria and glycosuria with a positive urine anion gap. His hemogram showed pancytopenia with differential count showing 88% blasts. Bone marrow examination and flow-cytometry confirmed the diagnosis of B cell acute lymphoblastic leukemia. Hence this case was atypical and very interesting in the sense that the Fanconi syndrome is very rare to be an initial presenting feature of acute lymphoblastic leukemia. The patient was started on oral as well intravenous supplementation with potassium, bicarbonate, calcium and phosphorus. Simultaneously, as per the modified BFM -90 protocol (four drug based regimen-Prednisolone, vincristine, daunorubicin, cyclophosphamide along with L-asparaginase), he was started on induction protocol. By the end of 3rd week of induction therapy, his urine output started normalizing and finally settled at the end of induction therapy. At present he is in the maintenance phase of chemotherapy.

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Introduction

The syndrome of proximal tubular dysfunction resulting in renal loss of amino acids, glucose, bicarbonate, phosphate, calcium, uric acid and other organic compounds is referred to as Fanconi syndrome. The etiology of this condition may be inherited or acquired secondary to other disorders or drugs, severe electrolyte imbalances may complicate management of other related conditions especially that of concomitant malignant disorders. The association of Fanconi syndrome with acute lymphoblastic leukemia is exceedingly rare. In this case report, we depict the course and management of a young male with the concomitant Fanconi syndrome and acute lymphoblastic leukemia.

Case Summary

A-14-year-old boy presented with a history of excessive thirst and increased urine output of 6–7 L/day. On examination, he had bilateral cervical, axillary lymphadenopathy, marked pallor and hepatosplenomegaly. Baseline metabolic profile revealed hypokalemia, hypouricemia, hypocalcemia and hyperchloremia with normal liver and kidney function tests. The arterial blood gas analysis was suggestive of normal anion gap metabolic acidosis. In urine analysis, there was evidence of hyperuricosuria, hypercalciuria and glycosuria with a positive urine anion gap. The calculated creatinine clearance was normal (111 ml/min). These metabolic alterations were highly suggestive of proximal renal tubular dysfunction. His complete blood count showed a white blood cell count of

3.0×10^9/L with 88 % blasts, hemoglobin 68 g/L and platelet count 76.0×10^9/L. Bone marrow examination showed hypercellular marrow spaces with sheets of abundant immature cells replacing all three hematopoietic elements. On flowcytometry, blast cells were positive for CD19, CD 10, CD 20, CD 79a confirming the diagnosis of B (CALLA) cell acute lymphoblastic leukemia. Bilateral enlargement of the kidney (Right -13 cm, Left-12.5 cm) was noticed on ultrasonography. A possibility of leukemic infiltration of the renal parenchyma was kept, however kidney biopsy was deferred in view of thrombocytopenia. The patient was started on oral as well intravenous supplementation with potassium, bicarbonate, calcium and phosphorus. His daily fluid requirement (oral, plus intravenous) was calculated according to urine output and central venous pressure monitoring. Simultaneously, he was started on induction therapy as per the modified BFM-90 protocol (four drug based regimen- Prednisolone, vincristine, daunorubicin, cyclophosphamide along with L-asparaginase). His hospital stay was complicated by febrile neutropenia and fungal pansinusitis for which he underwent endoscopic debridement. Histopathology was suggestive of mucormycosis and hence was treated with liposomal amphotericin B (3 mg/kg/day). He successfully completed induction chemotherapy and post-induction bone marrow was in remission. By the end of induction chemotherapy, his electrolyte supplementations were gradually reduced in accordance with normalization of his urine output and metabolic parameters (Table 1). At present, the patient continues to be on regular follow up and has proceeded to the maintenance phase of chemotherapy.

Discussion

Renal tubular acidosis is a rare complication of hematolymphoid malignancies. It has been described in the context of plasma cell dyscrasias such as multiple myeloma and other monoclonal gammopathies [1, 2]. The pathogenic mechanism described in these situations is related to damage to the tubular epithelial cells by monoclonal light chain deposition. Similar mechanisms have also been described in acquired Fanconi's syndrome related to monoclonal light chain deposition and amyloidosis in chronic lymphocytic leukemia [3]. Control of the underlying disorder may ameliorate the tubular dysfunction, especially in plasma cell disorders. Drugs used in the management of hematological malignancies and viral illnesses may also be responsible for the development of renal tubular dysfunction. Commonly implicated agents include cisplatin, ifosfamide, carbonic anhydrase inhibitors, valproate and tenofovir [4]. Our patient did not receive any of these agents. However, there are potential drugs like steroids, high dose methotrexate and trimethoprim–sulfamethoxazole used during treatment of acute lymphoblastic leukemia (ALL) which can cause renal tubular dysfunction and lactic acidosis [5]. Hyperuricemia, hyperkalemia and hyperphosphatemia can be seen in acute leukemias in the setting of high tumor burden. Cases have been reported in which patients of acute leukemia had presenting features of renal tubular dysfunction—renal tubular acidosis, lactic acidosis or ketoacidosis [6–8]. Recently Vanmassenhove et al. reported a series of eight lymphoma patients who had concurrent Fanconi syndrome [9]. Ahuja et al. reported case of three siblings of Fanconi

Table 1 Depiction of laboratory parameters with normal range and patient values at presentation and after 4 weeks of chemotherapy (Modified Bfm-90 Protocol)

Values (units)	Normal range	Values at presentation	Interpretation	Values at the time of discharge
Potassium (mEq/L)	3.5–5	2.8	Hypokalaemia	3.7
Uric acid (mg/dl)	2.6–7.2	0.98	Hypouricemia	2.65
Calcium (mg/dL)	8.6–10.2	6.9	Hypocalcaemia	10.0
Phosphorus (mg/dL)	2.5–4.5	1.8	Hypophosphatemia	4.1
Chloride(mEq/L)	98–106	121	Hyperchloremia	96
Blood Ph(mmol/L)	7.35–7.45	7.241	Acidosis	7.4
Bicarbonate(mmol/L)	22–24	5.1	Hypobicarbonatemia	21.1
Plasma anion gap	8–16	11.9	Normal anion gap	15
Urinary anion gap (mEq/L)	0–10	31	Positive anion gap	24
Urine Ph (mmol/L)	4.5–8	6.0	Alkaline	
24 h urine uric acid(mg/TV)	250–750	1,750	Hyperuricosuria	525
24 h urine phosphate(mg/TV)	400–1,300	1,972	Hyperphosphaturia	643
24 h urine calcium(mg/TV)	100–300	414.8	Hypercalciuria	405
Urine spot glucose	Absent	4+	Glycosuria	–

syndrome who later developed acute leukemia [10]. Proposed mechanisms for the development of lactic/ketoacidosis include overproduction of lactate by cancer cells, reduced renal and hepatic clearance secondary to disease infiltration and cell apoptosis secondary to hypoxia [11]. The mechanisms of disease in our case might be related to tumor cell infiltration of the renal parenchyma as evidenced by increased kidney size, although the same could not be proved in the absence of histopathological confirmation. Rapid restoration of renal tubular function following the initiation of chemotherapy also suggests that the disorder was related to the malignant infiltration. Unusual presentations of acute lymphoblastic leukemia may complicate and delay diagnosis and management. There should be a high index of suspicion to detect this reversible and acquired metabolic syndrome in patients of leukemia having renomegaly for guiding appropriate supportive therapy during chemotherapy.

Conclusion

Hematological malignancies are amongst very rare causes of the renal dysfunction syndrome. Causes like tumor lysis, chemotherapy related and opportunistic infections are amongst the commoner conditions causing renal dysfunction. However, rarely as described in our case, leukemic infiltrates can cause renal dysfunction per se with varied manifestations. Early suspicion and aggressive treatment are the crux as patients are not likely to improve unless the chemotherapy is given.

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