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Bilateral massive nephromegaly–A rare presentation of t-cell acute lymphoblastic leukemia

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ABSTRACT

Introduction: Renal infiltration by leukemia causing massive bilateral nephromegaly is an extremely rare presentation of T-cell acute lymphoblastic leukemia(T-ALL).
Case report: 18-month-old female toddler presented with fever and progressive abdominal distension of 4–6 weeks duration. Imaging revealed bilateral massively enlarged kidneys with normal excretion. Peripheral blood counts and smear examination was unremarkable and immunophenotypic evaluation of marrow was consistent with T-ALL. Chest imaging was unremarkable. She was started on modified Indian Childhood Collaborative Leukemia Group (ICiCLe) ALL protocol. Even with the best anti-tumor lysis syndrome (TLS) prophylaxis the child required two sessions of hemodialysis. An end-induction morphological remission & end-consolidation negative minimal residual disease (MRD) could be achieved.
Conclusion: Bilateral massive nephromegaly is an extremely rare presentation of T-ALL. This case emphasizes the unusual presentation, need for prompt remediation of TLS, and most importantly the use of early intensification with four drug anthracycline & dexamethasone-based therapy for the treatment of T-ALL in children.

1. Introduction

T-ALL accounts for 10–15% of cases of acute lymphoblastic leukemia/lymphoma and presents commonly as a mediastinal mass. Bilateral renal infiltration causing massive nephromegaly is an extremely rare presentation of T-ALL with about 10 cases in English language literature [1].

2. Case report

A 18-month-old female toddler presented with unremitting intermittent fever, progressive abdominal distension of 4–6 weeks duration, and clinical examination revealed significant pallor with large ballotable bilateral flank masses. Admission laboratory parameters were as hemoglobin of 6.5 g/dL (normal range, 11.5–13.5 g/dL), total leucocyte count of 23.9 $\times$ 10^9/L (normal range, 05–17 $\times$ 10^9/L) with normal differentials (no atypical cells in peripheral smear) and platelet count of 160 $\times$ 10^9/L (normal range, 150–450 $\times$ 10^9/L). Her blood biochemistry showed serum creatinine of 0.43 mg/dL (normal range, 0.17 to 0.42 mg/dL), blood urea 36 mg/dL (normal range, 16.8 to 48.5 mg/dL), serum lactate dehydrogenase (LDH) 1801 U/L (normal range, 125–220 U/L). X-ray chest was unremarkable. Contrast enhanced computerized tomography (CECT) of abdomen-pelvis revealed bilateral symmetrical homogenous enlargement of kidneys (right kidney: 12.5 $\times$ 7.2 cm and left kidney: 12.2 $\times$ 6.3 cm) with normal excretion and abdominal adenopathy [Fig. 1], suspecting renal lymphomatous infiltration with high disease burden prompt anti-tumor lysis syndrome prophylaxis (including rasburicase) was initiated. A diagnostic biopsy and staging bone marrow aspiration was planned, meanwhile her blood leucocyte counts dramatically increased to 83.2 $\times$ 10^9/L within 24-hours of admission with smear showing >25% lymphoid blasts and marrow flow-cytometry immunophenotyping confirmed diagnosis of T-ALL. CSF cytology was unremarkable. The decision for a diagnostic renal biopsy was abandoned, and was started on steroid prephase with hydration,

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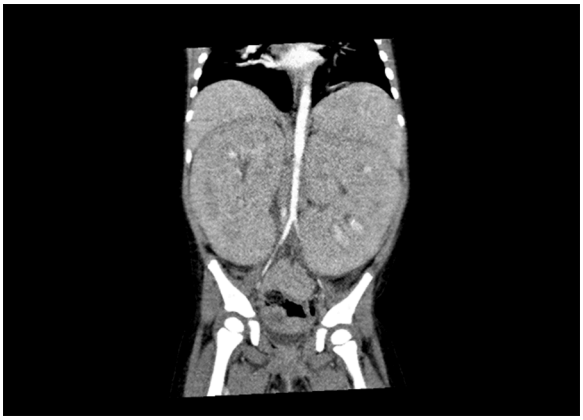

Fig. 1. CECT-Abdomen-Pelvis shows bilateral massively enlarged kidneys.

and with worsening serum electrolyte homeostasis and blood urea nitrogen levels, the child required two sessions of hemodialysis, later initiated on high-risk modified ICiCLe ALL protocol. A post-induction imaging showed significant reduction in the bilateral renal dimensions [Fig. 2], and an end-consolidation(3-months) negative minimal residual disease status has been achieved.

3. Discussion

T-ALL accounts for about 15% of the cases of acute leukemia and commonly presents as a mediastinal mass, with liver, lymph nodes, spleen and testis being the common extramedullary sites involved. Bilateral renal infiltration causing massive nephromegaly is a rare occurrence of T-ALL [1].

Acute renal failure (ARF) in acute leukaemia is generally due to direct leukemic infiltration, nephrotoxic drugs, sepsis, radiation nephropathy and most importantly TLS and uric acid nephropathy [1]. Sherief et al. reports of a 13-month-old female infant presenting with bicytopenia and massive nephromegaly and bone marrow aspiration revealed infiltration by blasts of biphenotypic lineage, and could achieve end-induction remission, but unfortunately succumbed to sepsis in consolidation. Escobar et al. reported the case of a 6-year-old girl presenting with uremia and bilateral massive nephromegaly due to infiltration by T-ALL cells albeit normal blood counts, similarly P.H.Asdahl et al. reports a case of 10-year-old boy presenting with visual disturbances, bilateral renal enlargement with infiltration by T-ALL, who developed ARF and has remained in remission for three years post-therapy [1-3].

Sherief et al. and P.H.Asdahl et al. portend the significance of prephase with steroids in conjunction with hydration in cases with high risk of TLS, our patient was started on prednisolone with hydration and rasburicase to minimize risk of TLS, but eventually required 2-cycles of hemodialysis [1,3]and in most cases of leukemic renal infiltration causing uraemia, the patients have required hemodialysis, but no late renal complication or stigmata noted after completion of chemotherapy [3].

Early intensification of therapy with 4-drug anthracycline based induction consisting of dexamethasone, pegylated-aspargase, vincristine and daunorubicin along with triple intrathecal chemotherapy followed by augmented Berlin-Frankfurt-Munster(aBFM) like cyclophosphamide-based consolidation has been found to dramatically improve outcomes in T-ALL, with rates comparable to B-ALL [4].

T-ALL has vastly different biological kinetics *vis a vis* B-ALL and prognostic significance of renal leukemic infiltration is till obscure, with Hann et al. predicting worse outcomes in patient with increasing renal size and biochemical disturbance, while recent studies have disputed the prognostic significance of renal infiltration in patients treated with intensive-regimens. [5, 6]

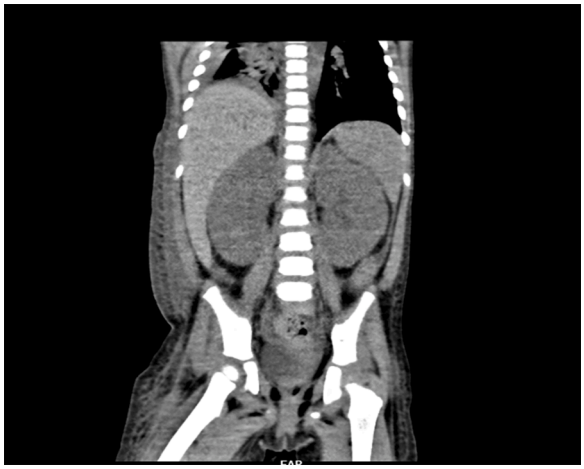

Fig. 2. CECT Abdomen-Pelvis(Post-induction) shows significant reduction of size of the kidneys.

Historically marred by worse outcomes combined with the lag in the development of clinically approved monoclonal antibodies or CAR-T cell therapy, recent improvements in our understanding of the disease biology along with introduction of intensive chemotherapy regimen from accrued data from multiple international trial groups has resulted in significant improvement in outcomes in children [4].

4. Conclusion

Renal infiltration by acute leukemia is an important differential in a child presenting with bilaterally enlarged kidneys *cum aut sine* features of renal functional abnormalities, the need for prompt and often preemptive measures anticipating tumor lysis syndrome and most importantly early intensification with four-drug T-ALL-focused protocols can significantly improve outcomes in children.

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Declaration of Competing Interest

None declared.

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