Acute Lymphatic Leukemia Masquerading as Recurrent Acute Kidney Injury – A Case Report

Abstract

Acute kidney injury (AKI) is an uncommon presenting feature in acute lymphatic leukemia (ALL). We report an unusual case of a 15-year-old girl who has experienced multiple episodes of AKI over an 8 month period with unremarkable WBC counts. She now returned with constitutional symptoms and rapidly progressive renal failure with bulky kidneys, proteinuria, and sterile pyuria. A renal biopsy revealed diffuse interstitial infiltration with CD3 positive, TdT positive, and CD20 negative lymphoblasts, suggestive of acute T cell leukemia. Bone marrow studies and flow cytometry later confirmed the diagnosis of T cell ALL. Unfortunately, she succumbed to an intracranial bleed during the intensive phase of chemotherapy. In addition to the atypical presentation of ALL, this case highlights the importance of timely renal biopsy in cases of AKI, where the cause is unclear.

Keywords: *Acute kidney injury, Recurrent AKI, Acute lymphatic leukemia, Renal biopsy*

Introduction

Acute kidney injury (AKI) as the initial presentation of acute lymphocytic leukemia (ALL) is uncommon, though reported earlier.[1–4] We describe an unusual presentation of T-cell ALL presenting with recurrent episodes of AKI.

Case Report

A 15-year-old girl visited our hospital in June 2021 with fever and fatigue for 3 days. She was pale with cushingoid facies, mild pedal edema, and stable vital parameters. A 2x2 cm left axillary lymph node was palpable. Her systemic examination was otherwise unremarkable.

Her past medical history was remarkable, having been hospitalized thrice elsewhere in the previous 8 months with fever and AKI [Table 1].

She initially presented in November 2020 with fever, vomiting, anemia, azotemia, and bland urine. Ultrasound showed bulky kidneys without obstruction. Peripheral smear showed dimorphic anemia. Antinuclear antibody (ANA) was negative and C3 complement was normal. AKI resolved spontaneously. Serum creatinine improved to 0.9 mg/dL.

In February 2021, she developed fever, fatigue, vomiting, and breathlessness. Evaluation revealed advanced renal failure, transaminitis, severe anemia, and leukopenia. Hematologic workup was not done. She recovered with dialytic support, blood transfusions, empiric steroids, and antibiotics. Her cultures were negative. Serum creatinine improved to 0.76 mg/dL.

She presented next in May 2021 with fever, vomiting, altered sensorium, severe renal failure, and anemia. She improved again with temporary dialytic support and steroid dose enhancement. Serum creatinine declined to 1.6 mg/dl.

On her current admission, she had leucocytosis, azotemia [Table 2], albuminuria and pyuria. Serum calcium and uric acid levels were normal. Serum complement levels, ANA, ANA profile, and ANCA serology were unremarkable. Ultrasound showed bulky kidneys with increased echogenicity. Blood and urine cultures were sterile.

She underwent hemodialysis on Days 2 and 4 and a renal biopsy was performed on Day 5. She was given empiric pulse methylprednisolone (125 mg) on day 6 and 7 for rapidly progressive renal failure. On day 7, the renal biopsy was provisionally reported as diffuse interstitial infiltration with atypical lymphoid cells, suggestive of leukemia.

On day 8, WBC counts increased to 33,100/mm^3 and uric acid to 45 mg/dL. Further doses of methylprednisolone were withheld. She remained normocalcemic with hypophosphatemia of 2.5 mg/dL which later reduced to 1 mg/dL. The LDH level was elevated at 1314 U/L. Peripheral smear showed 11% blasts and a bone marrow study was performed. Hyperuricemia was managed with parenteral Rasburicase and prolonged dialysis sessions. Thereafter, she remained off dialysis though stable azotemia persisted.

Her renal biopsy [Figure 1] finally showed diffuse interstitial infiltration by atypical monomorphic lymphoid cells positive for CD3 and terminal deoxynucleotidyl transferase (TdT) and negative for CD20 by immunohistochemistry, suggestive of T-cell-ALL. Peripheral smear, bone marrow examination, and flow cytometry reports were consistent with acute T-cell ALL [Figure 2].

She was transferred to pediatric oncology services for further care. She succumbed to an intracranial bleed during the induction phase of ALL treatment.

Discussion

Leukemic infiltration of the kidney is usually subclinical and often an autopsy finding.[1] AKI due to leukemic infiltration in ALL is uncommon (<1%),[1] though previously reported.[2,3,4]

Our case is unique for its presentation with recurrent episodes of AKI over an extended period. The absence of overt leukemic manifestations, spontaneous resolution of AKI on her first presentation, and response to steroids on subsequent occasions possibly hindered an earlier

Table 1: Lab parameters on previous hospitalizations November 2020, February 2021, and May 2021

	First hospitalization			Follow-up	Second hospitalization			Follow-up	Third hospitalization				Follow-up
	18/11/20	21/11/20	23/11/20	30/11/20	3/2/21	10/2/21	14/2/21	26/2/21	30/4/21	1/5/21	8/5/21	14/5/21	25/5/21
Hb (mg/dL)	8.1			8.4	6.7	7.4	7.5	8.6	9.6				9.2
WBC (/mm^3)	5500			6800	2980				12410				
DLC	P70L24M5			P62L28M5	P80L13M1				P66L22M10				
Platelets (*10^3/mm^3)	285			373									
Urea (mg/dL)	93				210	104	65	28	165	192	156	73	31
Creat (mg/dL)	5.8	3.1	1.9	0.9	8.3	3.4	1.7	0.76	7.8	10.8	4.2	2.4	1.6
Na (meq/L)	140			141	121	129	133	141	136	140	129	139	139
K (meq/L)	6.2	4.5	3.9	3.5	4.9	2.6	3.0	3.3	4.2	4.7	2.1	3.3	4.1
Ca (mg/dL)	8.9			9.3	7.0				9.7				
P (mg/dL)	5.9			2.3					13.5				
Bilirubin (mg/dL)					1.9/1.7				0.34				
AST/ALT (IU/L)					134/176				10/12				
ALP (IU/L)					1839				129				
TP/A/G (g/dL)					7/3.5/3.5				7.5/3.5				

Hb: Hemoglobin, WBC: White blood cell count, DLC: Differential leucocyte count, P: Polymorphs, L: Lymphocytes, M: Monocytes, Creat: creatinine, Na: sodium, K: potassium, Ca: calcium, P: phosphorus, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, TP: Total protein, A: albumin, G: globulin.

Table 2: Lab parameters on current presentation June 2021

	5/6/21	7/6/21	13/6/21	14/6/21	15/6/21	16/6/21	19/6/21
Hb (mg/dL)	10.1	9.4	8.8	8.6	8.2	8.1	7.9
WBC (/mm^3)	21800	11700	31200	33600	33100	36000	28400
DLC	P58L30M12	P85L13M2	P69/L21/M10	P64L22M14	P77L17M6	P75L20M5	P63L30M7
Platelets (*10^3/mm^3)	151	170	179	178		163	150
ESR (1st hour)	100						
Urea (mg/dL)	158						
Creat(mg/dL)	5.59	6.52	5.44	4.93	4.28	4.52	5.78
Na (meq/L)	140						139
K (meq/L)	4.55	5.18	3.46	3.39	3.56	3.69	3.29
Ca (mg/dL)	8.3		9.2	9.2	8.7		
P (mg/dL)			2.5	1.5	1.0	1.5	
Uric acid (mg/dL)		4.3	45.8	18	24.9	12.2	9.3
Mg (meq/L)			1.74				
Bilirubin (mg/dL)		0.18					
AST/ALT (IU/L)		18/112					
ALP (IU/L)		213					
TP/A/G (g/dL)		6.2/3.4/2.8					
LDH (IU/L)			1314				
Urine examination							
Albumin	++						
Pus Cells/HPF	numerous						
RBC/HPF	0-1						
PC ratio	3.98						

Hb: Hemoglobin, WBC: White blood cell count, DLC: Differential leucocyte count, P: Polymorphs, L: Lymphocytes, M: Monocytes, ESR: Erythrocyte sedimentation rate, Creat: creatinine, Na: sodium, K: potassium, Ca: calcium, P: phosphorus, Mg: magnesium, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, TP: Total protein, A: albumin, G: globulin, LDH: Lactate dehydrogenase, RBC: Red blood cells, HPF-High power field, PC ratio: Protein creatinine ratio.

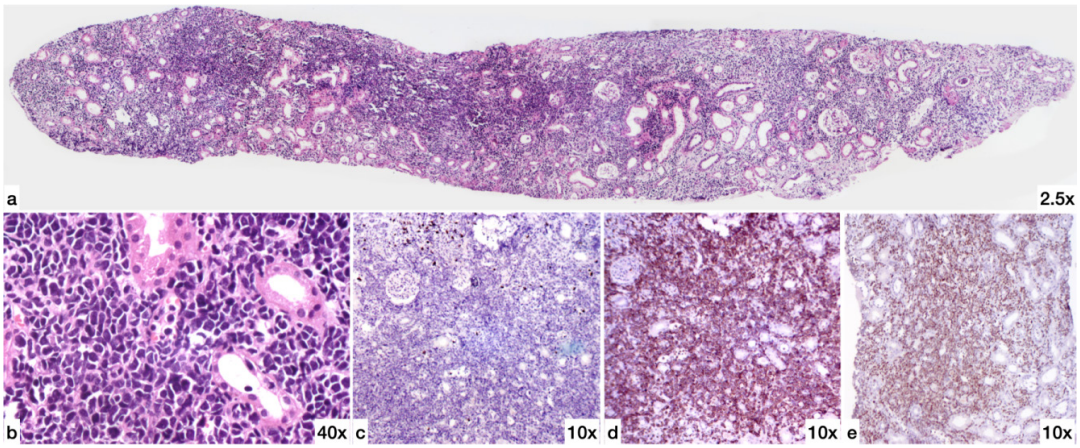

Figure 1: Renal Biopsy (a) H&E (2.5X magnification): One core of renal tissue showing interstitium diffusely infiltrated by atypical small round blue cells. (b) H&E High power (40X magnification) showing the atypical cells to be monomorphic lymphoid cells with scant amount of cytoplasm and irregular large hyperchromatic nucleus. The cells are 2.5 to 3 times size of small mature lymphocytes and have irregular nuclear contours. (c) CD20 (10X magnification)The atypical lymphoid cells are negative for CD20. (d) CD3 (10X magnification) The atypical lymphoid cells are strongly positive for CD3. (e) TdT (10X magnification) The atypical lymphoid cells are positive for terminal deoxynucleotidyl transferase (TdT). H&E: Hematoxylin & Eosin.

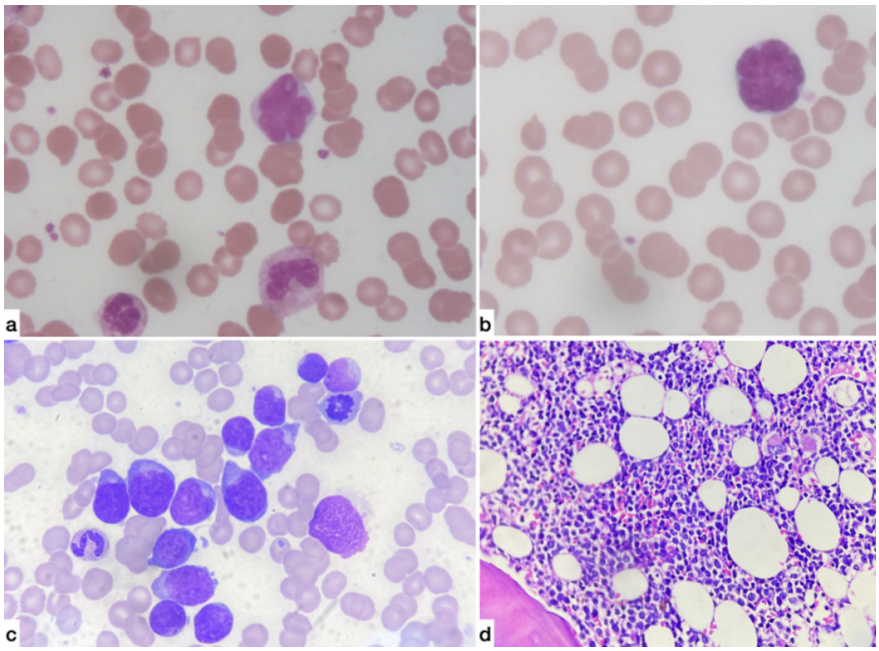

Figure 2: (a & b) Peripheral smear (100X magnification): Atypical cells having 2.5 to three times the size of small mature lymphocytes with scant to moderate cytoplasm, highly irregular nuclear membranes and opened out chromatin with many showing prominent nucleoli. (c) Bone marrow Aspirate (100X magnification): Blasts with scant to moderate bluish cytoplasm and irregular opened out nucleus with 1-2 prominent nucleoli. (d) Bone marrow Trephine (40X magnification): Shows sheets of atypical monomorphic lymphoid cells irregular nuclear contours and prominent nucleoli.

diagnosis. Initial presentation of ALL with AKI and normal WBC counts, although uncommon, has been reported.[5,6] Arguably, abnormal cells may have been missed by automated counters but could have been detected by an earlier peripheral smear.

During this admission, at the outset, there was no evidence of usual causes of AKI in ALL like tumor lysis, hyperuricemia, volume depletion, sepsis, or obstruction. Biopsy findings confirmed that her AKI was entirely due to leukemic infiltration of the kidneys. Her kidneys were consistently bulky on imaging, strongly suggesting that the previous AKI episodes were also attributable to leukemic kidney infiltration. An earlier kidney biopsy would have expedited the diagnosis.

Administering pulse steroids unravelled very high WBC counts and severe hyperuricemia with high LDH levels, indicating tumor lysis syndrome. Concurrent hypophosphatemia was likely due to the incorporation of phosphorus into rapidly growing tumor cells.[2,7] Therefore, caution is warranted when prescribing empiric pulse steroids when the cause of AKI is uncertain.

AKI at initial presentation usually indicates a worse prognosis for ALL.[2,8] Our patient succumbed during the induction phase of ALL treatment.

Conclusion

Our case highlights an unusual presentation of ALL with recurrent episodes of AKI. A kidney biopsy was crucial in confirming the diagnosis, especially in the absence of clear indicators of a hematological malignancy. This emphasizes the importance of timely kidney biopsy when the etiology of AKI is unclear.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

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