CASE REPORT

Unusual Manifestation of Acute Leukemia With Hematuria – A Case Report

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ABSTRACT

An 11-year-old boy with a family history of IgA nephropathy presented with hematuria, edema, hypertension, and oliguria. He had no hepatosplenomegaly or lymphadenopathy. Blood investigations revealed leukocytosis with normal renal function and urinalysis revealed gross hematuria. Because of the hematuria, he was suspected to have post-streptococcal glomerulonephritis, with potential diagnoses of IgA nephropathy and renal parenchymal disease. Additionally, lymphoproliferative disease involving the kidneys needed to be investigated due to leukocytosis. A full blood count revealed 49% of blast cells. Bone marrow studies confirmed B-cell acute lymphoblastic leukemia. Renal biopsy only demonstrated minor glomerular changes with acute tubular injury changes and granular cast. There were no features of leukemic infiltration. Immunofluorescence studies and electron microscopy findings showed no evidence of immune-mediated glomerulonephritis. After the commencement of chemotherapy, his leukemia achieved remission with hematuria resolution. His hypertension was controlled with antihypertensive drugs. This case report highlights a rare renal manifestation as the initial presentation of leukemia.
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Keywords: Acute lymphoblastic leukemia, Glomerulonephritis, Renal biopsy, Hematuria, Leukocytosis

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INTRODUCTION

The global incidence of acute lymphoblastic leukemia (ALL) is on the rise, and untreated cases result in early mortality. Common clinical manifestations of ALL include hepatosplenomegaly, pallor, fever, bruises, infections, fatigue, limb pain, and lymphadenopathy. Gross hematuria, the first presentation of leukemia in children, is rare (1). Diagnosing leukemia can be challenging when a child presents with atypical symptoms. A full blood count is the first line of investigation to diagnose leukemia, followed by a bone marrow study. Early diagnosis is associated with a high survival rate when the appropriate treatment is administered.

CASE REPORTS

An 11-year-old previously healthy boy reported headache, fever, gross hematuria, and peripheral edema associated with cough and a runny nose over the previous four days. He denied any musculoskeletal pain, loss of appetite, or weight loss. He had a significant family history of renal disease, with his sister diagnosed with IgA nephropathy and concurrent membranous nephropathy and his brother having idiopathic End-Stage Renal Failure. His past medical history was unremarkable, and there were no notable events, such as recurrent gross hematuria.

On examination, he was obese with a Body Mass Index (BMI) of 25, according to the World Health Organization (WHO) BMI Children Z-score chart. No pallor or bruising was observed. He had no hepatosplenomegaly, lymphadenopathy, rash, or testicular enlargement. He had oliguria and hypertension with a blood pressure reading of 134/84 mmHg, which was above the 95th

percentile on admission.

He was initially managed as a case of acute post-streptococcal glomerulonephritis, receiving intravenous Cefuroxime, fluid restriction, and oral Nifedipine 10 mg thrice daily. The differential diagnoses considered included IgA nephropathy and renal parenchymal disease. However, his full blood count revealed leukocytosis, raising suspicion of malignant cell infiltration into the kidneys. A Full Blood Picture revealed 49% of blast cells, and subsequent bone marrow examination confirmed the diagnosis of B-cell acute lymphoblastic leukemia (Figure 1). Other investigations (Table I) did not support the diagnosis of post-streptococcal glomerulonephritis as C3 and C4 levels were normal, and the anti-Streptolysin O titer was unremarkable. His urinalysis (Table I) showed proteinuria, microscopic hematuria, and a red blood cell count of more than 100 cells/µL. Renal ultrasound revealed normal findings, with the right kidney measuring 10.6 cm and the left kidney measuring 10.9 cm. There was no hydronephrosis, focal renal lesion, or mass observed, and the urinary bladder was unremarkable.

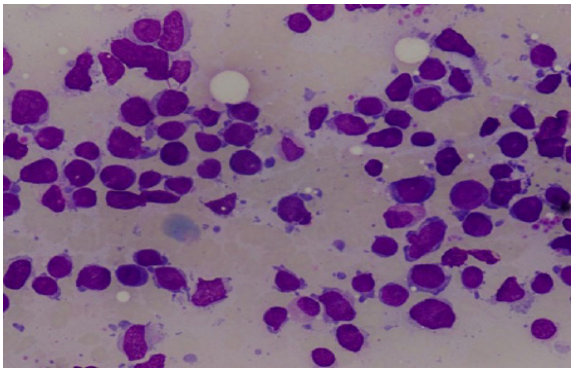

FIGURE 1: Hypercellular marrow with presence of homogenous population of blast cells. The blast cells are small to moderate in size, irregular nuclear outline,high nuclear to cytoplasmic ratio,scanty cytoplasm, fine chromatin pattern with inscopicuous nucleoli. Some of the blast show basophilic cytoplasm and cytoplasmic projection. Other haemopoeitic cells are suppressed.

Table I: Investigations

Test	Result	Range
Total white count (x10⁹/L)	37	7 – 11
Hemoglobin (g/dL)	13.3	12 – 15
Platelet (x10⁹/L)	342	150 – 400
Prothrombin time (seconds)	14.8	12.6 – 15.7
INR	1.44	1 – 1.5
activated Partial Thromboplastin Time (seconds)	31.8	30 – 45
Urea (mmol/L)	6	1.8 – 7.1
Sodium (mmol/L)	142	135 – 145
Potassium (mmol/L)	4.0	3.5 – 5.0
Creatinine (µmol/L)	51	61 – 114
Serum Calcium (mmol/L)	2.36	2.15 – 2.55
Phosphate (mmol/L)	1.12	0.87 – 1.45

CONTINUE

Table I: Investigations (cont.)

Test	Result	Range
Magnesium (mmol/L)	0.79	0.73 – 1.06
Uric Acid (µmol/L)	581	210 – 420
Alkaline phosphatase (U/L)	248	122 – 469
Alanine transaminase (U/L)	24	10 – 50
Aspartate transaminase (U/L)	42	10 – 50
Serum albumin (g/L)	46	38 – 54
Total bilirubin (µmol/L)	4.1	< 25
C3 (g/L)	1.63	0.66 – 1.30
C4 (g/L)	0.25	0.20 – 0.60
Antinuclear Antibody	Negative	-
Urinalysis result		
Red blood cells (cells/µL)	>100	
Pus cells (cells/µL)	<10	
Epithelial cells (cells/µL)	<10	
Protein (g/L)	1.31	
Ketone	negative	
Nitrite	negative	

He was started on UKALL 2011 Regimen C chemotherapy after the diagnosis of leukemia was confirmed. He developed thrombocytopenia as a result of bone marrow suppression due to chemotherapy. A renal biopsy was required to exclude IgA nephropathy or leukemic infiltration of the kidneys due to persistent hematuria. The biopsy was performed after three weeks of chemotherapy when his thrombocytopenia had resolved. At the time of the renal biopsy, he received Dexamethasone, Vincristine, Daunorubicin, and Asparaginase. The renal biopsy revealed minor glomerular changes, acute tubular injury, and granular casts (Figure 2a & 2b). Mild tubular atrophy and interstitial fibrosis were present, with occasional lymphocytic infiltrates observed. Immunofluorescence studies showed unremarkable findings. Electron microscopy revealed focal lamellations within a glomerular basement membrane of normal thickness, excluding thin basement membrane disease.

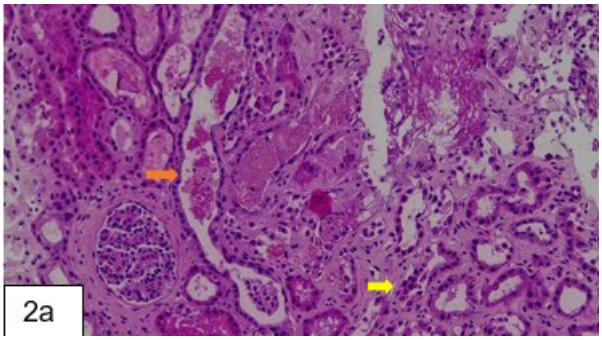

FIGURE 2a: Figure 2a illustrates features of acute tubular injury (yellow arrow). Several tubules are dilated and lined with flattened epithelium, with some areas showing regenerative epithelial changes. Additionally, focal regions display single-cell necrosis, loss of the brush border, and desquamation of the tubular lining. Granular casts and red blood cell casts are also visible in the tubules (orange arrow), 100x H&E.

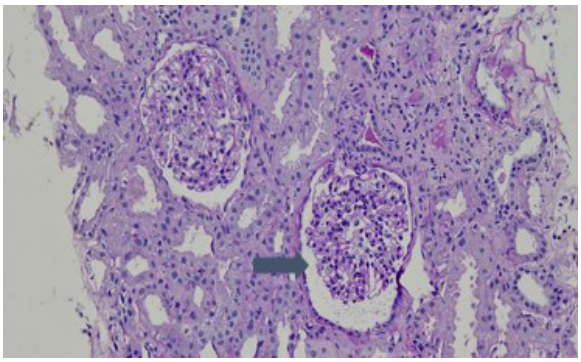

FIGURE 2b: Minor glomerular changes with focal and mild expansion of mesangial matrix accompanied by mild increase in mesangial cells cellularity (green arrow), 200x PAS.

After one month of chemotherapy, his leukemia went into remission, and his hematuria resolved. However, his hypertension needed to be controlled with oral Felodipine 10 mg once daily and oral Atenolol 25 mg twice daily.

DISCUSSION

The typical presentations of acute leukemia include fever, easy bruises, pallor, hepatosplenomegaly, lymphadenopathy, and musculoskeletal manifestations. Renal manifestations such as hematuria, proteinuria, and hypertension are rarely seen in acute leukemia. However, this patient's full blood count revealed leukocytosis, which prompted further investigations that confirmed the diagnosis of leukemia—B-cell ALL.

Hematuria in acute leukemia can have multiple causes, including thrombocytopenia, coagulopathy, and leukemic infiltration of the kidneys. Concomitant sepsis or urinary tract infection can contribute to hematuria. Acute tubular injury due to tumor lysis syndrome must not be overlooked as a potential cause. Relevant investigations are important to determine the causes of hematuria.

Apart from the diagnosis of leukemia, the managing team also encountered a diagnostic dilemma regarding his kidney condition, whether it was a renal manifestation of acute leukemia or acute leukemia with concomitant IgA nephropathy, given his contributive family history. The team prioritized the treatment of leukemia, and due to chemotherapy-induced thrombocytopenia, the renal biopsy was performed three weeks after chemotherapy initiation. There is also a possibility that the immunosuppressants administered may have caused renal abnormalities, leading to hematuria in this patient, along with evidence of acute tubular injury on microscopic examination. The kidney biopsy enabled us to exclude IgA nephropathy, as immunofluorescence microscopy for IgA yielded negative results.

Acute Kidney Injury (AKI) is defined as an acute reversible deterioration of kidney function evidenced by elevated creatinine levels and/or reduced urine output. The incidence of acute kidney injury (AKI) in children with ALL is approximately 15.4% (2). In fact, AKI is more common in acute myeloid leukemia than in ALL. Correlating clinically, this patient had reduced urine output with normal renal function suggestive of AKI. A kidney biopsy in this patient showed features of acute tubular injury, which is a key contributor to AKI pathogenesis. Other causes of AKI in patients with leukemia are multifactorial, including volume depletion, leukemic infiltration into the renal parenchyma, consequences of nephrotoxic drug effect, glomerular disorder, obstructive uropathy, septicemia due to the compromised immune system, tumor lysis syndrome, and renal vascular disorder (3). Recognizing that acute tubular injury plays a crucial role in AKI pathogenesis helps to elucidate the complexities of kidney complications in leukemia patients.

This patient's acute tubular injury may also have been caused by intrinsic factors such as leukemic infiltration. The negative findings on renal biopsy help in excluding leukaemic infitration, however as the biopsy only performed after the chemotherapy this possibility cannot be totally rule out. Leukemic infiltration can lead to tubular compression and microvasculature disruption, causing AKI (3). The incidence of kidney infiltration among ALL was approximately 54% (3). With the commencement of treatment, the condition can be reversed with improved kidney function. The exact mechanism of hematuria is not well understood as acute tubular necrosis alone without glomerulopathy rarely presents with gross hematuria.

Acute tubular necrosis secondary to lysosome-induced is one of the common causes of intrinsic AKI in leukemia. The lysosome is freely filtered by the glomerulus and reabsorbed by the proximal tubule. Clonal expansion in leukemia results in increased lysosomal production. Elevated urinary lysosome levels cause direct tubular damage leading to kaliuresis and proteinuria. Proximal tubular injury causing reduce reabsorption resulting in nephritic-range proteinuria and pseudonephrotic syndrome (3). Treating the disease will lower lysosomal levels and enhance kidney function in cases of acute kidney injury.

As illustrated in this case, his kidney issues were resolved with chemotherapy. However, he will require long-term follow-up to monitor his renal function and blood pressure and determine the reversibility of this condition.

CONCLUSION

Renal manifestations of acute leukemia are rare. Meticulous examination and thorough investigation are crucial to ensure the correct diagnosis. Early and appropriate treatment ensures a favorable prognosis.

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