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Bone Marrow Oxalosis in a Two Year Old Child with Congenital Hypoplastic Kidneys – A Case Report

***Sundas Ali*[1]**
***Javera Tariq*[2]**
***Aliena Sohail*[3]**
***Humaira Rizwan*[4]**

[1-4]Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan.

Address for Correspondence
Dr. Sundas Ali
Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan.
sundasali243@gmail.com

Abstract

Oxalate deposition in different extra-renal tissues resulting in systemic involvement is called as systemic oxalosis. The urinary tract, including renal parenchyma, is the first deposition site followed by extra-renal organs, for instance, bone marrow. Bone marrow oxalosis is described by hepatosplenomegaly, deranged cell lines, i.e., cytopenias, leukoerythroblastosis, and calcium oxalate crystals in bone marrow biopsy. We are reporting a case of a 2 years old child with Chronic Kidney Disease and a history of congenital hypoplastic kidneys. The patient had mild pallor and features of renal osteodystrophy at the time of presentation. A bone marrow biopsy was performed that showed interstitial deposition of oxalate crystals and preserved trilineage hematopoietic constituents in the absence of peripheral cytopenias.

Keywords: Oxalosis, bone marrow, congenital hypoplastic kidneys, chronic renal failure, oxalate crystals, renal osteodystrophy.

Introduction

Oxalosis is a process of deposition of calcium oxalate crystals in different visceral organs resulting in bone marrow failure and recurring renal stones.[1] Hyperoxaluria is a condition with elevated serum levels of oxalate and resulting oxaluria. There is primary and secondary hyperoxaluria.[2] Primary hyperoxaluria is a rare congenital error with an approximate prevalence of 1 to 3 cases per million.[3] It is an inborn defect in the metabolic pathway of glyoxylate resulting in excessive oxalate production. Secondary hyperoxaluria is an acquired disease resulting from excessive intake of oxalate in diet, chronic hemodialysis, Crohn's disease, or bowel resection that must be ruled out before diagnosing primary hyperoxaluria. Oxalate, when integrated with calcium, has a high affinity to deposit in multiple organs. The first site of calcium oxalate deposition is tubulointerstitium of renal parenchyma, leading to acute and chronic tubulointerstitial nephritis and nephrolithiasis, renal failure. The deposition of crystals in kidneys is followed by bone marrow and other tissue deposits. Diffuse infiltration of bone marrow parenchyma by crystals results in pancytopenia and a leucoerythroblastic reaction.[2] Bone marrow oxalosis is defined by hepatomegaly, splenomegaly, cytopenia, leukoerythroblastosis, and calcium oxalate crystals that are birefringent under polarized microscopy and granulomatous structures in bone marrow biopsy.[4]

Herein, we report a case of hyperoxaluria diagnosed based on bone marrow biopsy in a 2-year-old male having congenital hypoplastic kidneys with grade III Chronic kidney disease.

Case Report

A 2-year-old male child, the resident of Sihala, a town in the suburbs of Islamabad city, known case of congenital hypoplastic kidneys with grade III Chronic kidney disease, presented to the pediatric OPD with pain and swelling of legs bilaterally for the past 3 months. He was unable to walk and also abandoned crawling about 4 months back. There was no history of fever, bleeding, and rash, any appetite, or weight changes. The child was on renal replacement medical management with tablet sodium bicarbonate, vitamin D supplements, and injection erythropoietin. He had never undergone hemodialysis. There was no significant family history of any congenital anomalies or hematological abnormalities. He was a consanguineous marriage product and had two siblings, a four-year-old sister and a six-year-old brother, both alive and healthy. There was no history of transfusion or drug allergies.

On physical examination, he was a sick looking child with mild pallor. There was no jaundice, koilonychia, leukonychia, clubbing, or lymphadenopathy. Mild hepatomegaly was noted, with liver measuring two fingers below the right costal margin. The spleen was not palpable. Prominence at wrist and ankle joints were noted, which were present since birth. The primary diagnosis was renal osteodystrophy.

On laboratory workup, complete blood count showed a Total Leucocyte Count of 11.5 $x10^9$/l, hemoglobin of 11.1 g/dl, platelet count of 310 x 10^9/l, MCV 76.2 fl, MCH 23.2 pg, MCHC 30.5 g/dl, RDW-CV 15.8%. Differential Leucocyte Count showed 70% lymphocytes, 20% neutrophils, 7% monocytes and 3% eosinophils. The peripheral film showed a hypochromic, microcytic blood picture with anisocytosis and pencil cells. Reticulocyte count was 1.4%. CRP was negative. Biochemical profile showed serum Lactate Dehydrogenase 18 U/L (140-280 U/L), serum Parathyroid Hormone levels 24 pg/ml (normal 5.7-34 pg/ml), serum triglycerides 446 mg/dl (normal 40-160 mg/dl), bilirubin 0.3 mg/dl (normal 0.1-1.2 mg/dl), ALT 14 U/l (4-42 U/L), serum alkaline phosphatase 327 U/L (normal up to 135 U/L), serum phosphorus 4.8 mg/dl (normal 4-7 mg/dl), serum calcium 9.7 mg/dl (normal 8.5-10.5 mg/dl). Serum electrolytes were within normal limits. Urine Routine Examination showed clear urine with a high pH of 8, proteinuria, presence of ketones, and no evidence of crystals, casts, or bacteria. Renal function tests were highly deranged with Blood Urea Nitrogen (BUN) of 111 mg/dl (normal 7-20 mg/dl), creatinine of 3.8 mg/dl (0.8-1.2 mg/dl) and uric acid of 8.6 mg/dl (normal 2.5-5.5 mg/dl). No evidence of renal calculi was seen on imaging studies. X-ray right forearm was done, which showed findings suggestive of hematological or metabolic disorder. Bone marrow aspiration and biopsy were performed to exclude any underlying pathology. Aspiration was hemodiluted. Trephine biopsy showed hypercellularity with a random distribution of erythroid, myeloid, and megakaryocytic series cells [Figure 1]. However, it was observed that there were radially arranged crystals of calcium oxalate in some intertrabecular regions of trephine sections with foreign body giant cell reaction around them, giving a sunburst appearance. [Figure 2-3] A final diagnosis of bone marrow oxalosis was given based on the specific morphology of crystalline deposits and renal derangement.

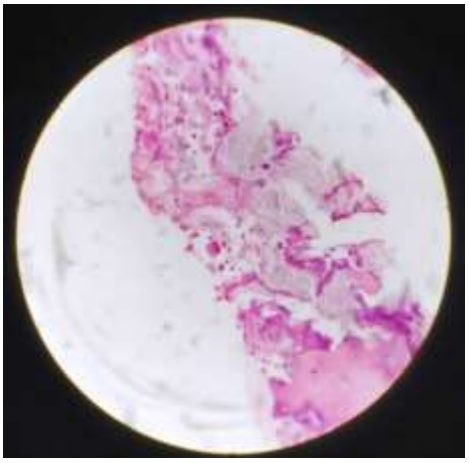

Figure 1. Calcium Oxalate crystals on bone marrow trephine section (H&E400X)

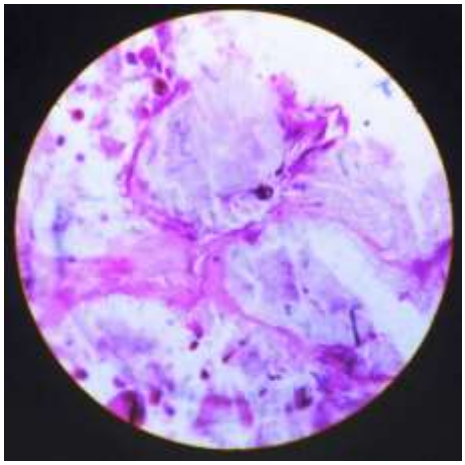

Figure 2. Calcium Oxalate crystals on bone marrow trephine section (H&E 1000X)

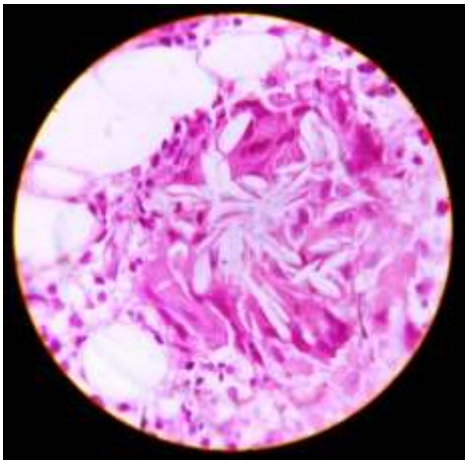

Figure 3. Calcium Oxalate crystals on bone marrow trephine section (H&E 1000X)

Discussion

Deposition of oxalate in various extra-renal tissues leading to a systemic involvement is named as systemic oxalosis. Bone marrow forms one of the major compartments of this insoluble oxalate pool. The additional organs involved comprise soft tissue, heart, nerves, joints, skin, retina, and other visceral lesions.[5]

Oxalosis can be primary (inherited) or secondary. Primary hyperoxaluria type 1 (PH1) is the most common and also considered as the severe form of PH. It accounts for nearly 80% of the cases of PH and is caused by a defect in the Vitamin B6 dependent hepatic peroxisomal enzyme - Alanine Glyoxalate Aminotransferase (AGT). The function of this enzyme is that it catalyzes the transamination of L-alanine and glyoxalate to pyruvate and glycine. The enzyme defect has been ascribed to a mutation in the AGXT gene located on the chromosome. The causes of Secondary Hyperoxaluria are an increase in dietary and intestinal absorption (enteric hyperoxaluria), excessive intake of oxalate precursors, and alteration in gut microflora.

Addressing hyperoxaluria at the right time is essential because it has the potential to cause devastating consequences that can present as early as infancy or in the sixth decade of life. One such concern includes the development of End-Stage Renal Disease (ESRD), which can be a reason for significant morbidity and mortality. Elevated plasma oxalate levels lead to oxalate deposition in various organ systems. Systemic oxalosis should be prevented, but unfortunately, the diagnosis is often delayed in more than 40% of patients. In a survey by Hoppe et al., 30 % of patients had already reached ESRD when the diagnosis was made. In some cases, the diagnosis was concluded only when the disease reappeared following renal transplant. Hyperoxaluria is a challenging disease requiring appropriate treatment and a high index of suspicion. Most important of all is a timely diagnosis, which can be of great value.[6]

PH is a group of rarely found autosomal-recessive inherited disorders, out of which PH1 is the most frequent form. The approximate prevalence of the disease ranges from 1 to 3 per million population and an evaluated frequency rate of 1: 100,000 live births/year has been observed in Europe. Rates are reported to be higher in inbreeding populations. PH is reported for <1% of pediatric ESRD patients from the United States of America, Japan and the United Kingdom. However, due to consanguineous marriages, especially in third world countries, it is not surprising to know that PH exists very commonly. The scarcity of registries in the developing countries results in the origin of epidemiological facts and figures from prominent referral setups.[7]

Progression to ESRD overtime occurs mainly because of progressive renal parenchyma inflammation and interstitial fibrosis due to nephrocalcinosis and recurrent urolithiasis. This causes renal impairment and needs timely consideration.[7, 8]

Our case was 2 years old child who was diagnosed as Chronic Kidney Disease in the background of congenital hypoplastic kidneys. He presented with mild pallor and features of renal osteodystrophy. Bone Marrow biopsy revealed deposition of oxalate crystals interstitially, and since trilineage hematopoietic elements were preserved, peripheral cytopenias were not observed. Sharma et al. presented two cases of 12 and 28 years of advanced renal failure due to recurrent renal stones and cytopenias, in whom the diagnosis of oxalosis was made on BM biopsy.[1] However, our case had no evidence of renal calculi.

A definitive diagnosis of primary hyperoxaluria is made by genetic studies, and if genetic studies prove inconclusive, giving no additional details, then a liver biopsy is undertaken to establish a diagnosis.[9]

Early diagnosis and appropriate conservative treatment are required to prevent the possible complications resulting from cytopenias if full-blown marrow failure ensues. The treatment of choice for systemic oxalosis is a kidney transplant or combined liver and kidney transplantation.[10]

Conclusion

Bone Marrow oxalosis is a rare finding. Physicians are recommended to consider this as a differential diagnosis in patients with renal failure and metabolic abnormalities, especially in childhood. Moreover, parents of primary oxalosis must be offered genetic counseling, especially where consanguineous marriages are prevalent. Prompt diagnosis and related conservative treatment are essential to avoid the expected complications resulting from cytopenias.

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