CASE REPORTS

RICKETS DUE TO DISTAL RENAL TUBULAR ACIDOSIS– AN UNCOMMON PRESENTATION OF WILSON'S DISEASE

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Abstract

Rickets is a disease of bone mineralization of growth plate. Refractory rickets can be caused by distal (type 1) renal tubular acidosis (RTA). A number of conditions can result in distal RTA and Wilson's disease is an uncommon entity. Wilson's disease is a rare autosomal recessive disorder of copper metabolism with diverse presentations. We describe a case of refractory rickets due to distal RTA, caused by Wilson's disease. Diagnosis of Wilson's disease was confirmed with presence of Kayser–Fleischer (K–F) rings and high urinary copper. Further investigations revealed urinary acidification defect with hypercalciuria pointing towards distal RTA. He was treated with penicillamine & oral Zinc and significant clinical improvement was observed.

Key words: *Rickets, Wilson's disease, Renal Tubular Acidosis*

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Introduction

Wilson's disease is a rare autosomal recessive disorder of copper metabolism transmitted by mutant (*ATP7B*) gene on chromosome 13q14-21.[1] It may be asymptomatic for years until late adolescence. Heterozygous forms of this condition are generally without any symptoms. The reported frequency of heterozygous form of Wilson's disease is 1 in every 30,000 populations. Haematologic (haemolysis), neuropsychiatric manifestations, hepatitis or frank hepatic failure are the initial manifestations of Wilson's disease in most instances. Renal involvement in Wilson's disease may occur in the form of renal tubular defects (renal tubular acidosis type 1 and 2 and/or Fanconi's syndrome).[2] Intractable rickets is considered as a very rare feature of Wilson's disease, reported only by a few eastern authors. Rickets, by definition, is a clinicopathological entity of disrupting mineralization of growth plate that cause bone deformities and vulnerability to fracture. [3] The first reported case of Wilson's disease with rachitic presentation was in 1968 by Cavallino[4]. This is an extremely rare presenting feature of Wilson's disease.[5] Here we report a 22-year- old man presented with rickets due to distal RTA secondary to Wilson's disease.

Case report

A 22-year-old man, 1st issue of a non-consanguineous parent, presented with generalized muscle weakness and wasting with bone pain, stunted growth since childhood. At the age of 12 year, he noticed progressive bowing of his legs. There was no history suggestive of delayed milestones; developmental abnormalities. There was no history of chronic diarrhea or urinary complaints. He had history of adequate sun exposure. Family history was not

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contributory. He was diagnosed as rickets and treated with mega doses of vitamin-D in different tertiary care hospital on different occasion, without any improvement. One month back prior to his presentation on 12th December 2016, he noticed tremor on both hands. There was no history of jaundice or distension of abdomen.

His weight, height & BMI were 33 kg, 1.46 m and 15.5 kg/m^2 respectively. He had rickety rosary on chest wall (Fig-1) and generalized muscle wasting. There was bowing of both legs (Fig-2). His muscle tone was normal, muscle power was 4/5 in proximal groups and normal in distal groups, reflexes were normal. Gait was waddling in nature. Resting and action tremor of both hands were present. Kayser-Fleischer ring was present at the corneal margin of both eyes, confirmed by slit lamp examination. Other systemic findings were normal.

Investigations revealed Hb was13.9 gm/dl, WBC 4.5 x 10^3/iL, platelet count 160 x 10^3/iL, ESR 20 mm in 1st hour. His serum bilirubin was 14 ìmol/L, SGPT 25 U/L, albumin 42 gm/L, creatinine 1.2 mg/dL, creatine kinase 56 U/L (N 55-170 U/L), Na^+ 137 mmol/L, K^+ 4 mmol/L, Cl^- 109 mmol/L (N 95-107 mmol/ L), Ca^+8.2 mg/dL (N: 8.5-10.5mg/dl), Phosphate 2 mg/dL (N 2.4-4.3mg/dl), alkaline phosphatase 200 units/L (N 40-125 U/L). USG of whole abdomen was normal. X-ray of chest, hands, and pelvis showed generalized osteopenia, widening of anterior end of ribs, loser's zone in right 11th rib. Urine examination showed urine pH 7, glycosuria was present with normal corresponding blood glucose. ABG revealed pH 7.348 (N 7.35-7.45), PaO_2 108 mmHg, $PaCO_2$ 36 mmHg, and HCO_3 20 mEq/L (N 24-28 mEq/L) with anion gap of 12. Parathyroid hormone level was 53 pg/ml (N 16-75pg/ml) and 25-OH Vitamin D level was 15 ng/ml (N >20ng/ml), 24 hour urinary calcium excretion 474 mg/day (N 25-300 mg/day), serum ceruloplasmin was 30 mg/dl (N 20-60 mg/dl). Urinary copper excretion was 1359.5 ig/day. Acid load test reveals failure of acidification of urine.

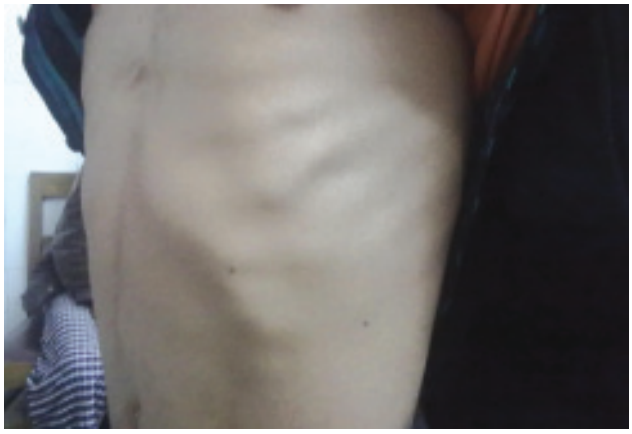

Fig-1: *Shows rickety rosary in chest wall.*

So he was diagnosed as a case of Wilson's disease with rickets due to distal renal tubular acidosis (type 1). He was given zinc acetate (50mg tds), D-penicillamine (250mg bid), oral calcium and 1, 25 OH vitamin D. On subsequent follow up his muscle weakness and tremor was significantly improved.

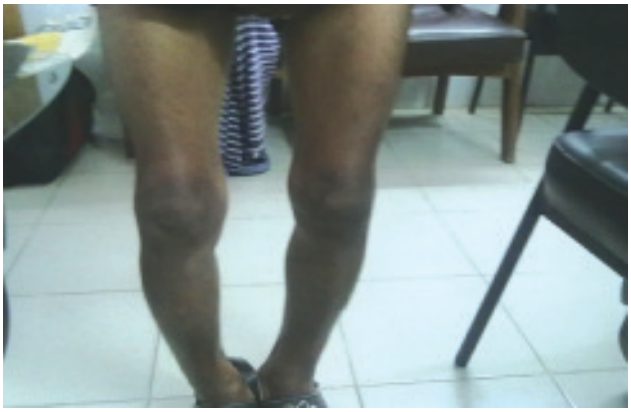

Fig- 2: *Shows bowing of both legs.*

Discussion

Clinical Wilson's disease is a relatively rare condition and it must be considered in any young patient with neuro-psychiatric problems, haemolysis, and liver disease with or without intractable rickets. Nutritional rickets/ osteomalacia is relatively common phenomena in developing countries. Most cases of rickets are diagnosed by typical musculoskeletal problems and bone deformities along with laboratory findings including low serum calcium and phosphorus level, raised serum alkaline phosphatase and decreased serum 25 (OH) D3 and 24 hours urine calcium excretion. In our case 24 hour urinary calcium excretion was increased due to distal RTA in contrary to nutritional rickets, where it is usually decreased.

In distal RTA, there is failure of excretion of hydrogen ion from the distal renal tubule, which results in decreased urinary excretion of ammonium causing metabolic acidosis. As a buffer against metabolic acidosis bony resorption increases and metabolic transformation of calcium phosphate to hydroxyapatite is interrupted, result in hyper-phosphaturia, hypercalciuria, and disturbed 1, 25 (OH) D3 production. This man presented with rickets and had features of CNS involvement for only one month, without any symptoms and signs related to hepatic & hematological involvement. In our case, we ruled out hypoparathyroidism and confirmed that primary

cause is metabolic acidosis and the contributing factor is vitamin D deficiency.

Most cases of Wilson's disease and rickets are reported from India and China; probably addressing the racial and nutritional backgrounds as contributing factors. Zinc acetate, conventional D-penicillamine and trientine therapy are novel therapies for Wilson's disease. There are some reports of efficacy of captopril in controlling Wilson's disease[6].

Conclusion

In case of intractable rickets, a careful search for underlying treatable conditions such as Wilson's disease should be considered. The main aim of this case report is to present one of the rare causes of rickets which can be diagnosed easily and treated very cheaply.

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