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Teenager with Severe Bowing of Limbs

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Abstract

Bowing of long bones may be secondary to several aetiologies. Among the causes for bowing of long bones include congenital and acquired form of rickets, skeletal dysplasia, osteogenesis imperfecta and renal tubular acidosis (RTA).

Keywords: Bowing long bones; Rickets; RTA; Skeletal dysplasia

Introduction

Bowing of long bones may be secondary to several aetiologies1. Among the causes for bowing of long bones include congenital and acquired form of rickets, skeletal dysplasia, osteogenesis imperfecta and renal tubular acidosis (RTA). The purpose of this case report is to highlight the general approach to severe bowing of long bones in particular, the differences between primary and secondary form of RTA

History

15-year old Malay boy, the youngest of 4 siblings was admitted in orthopaedic ward for a closed fracture of the right humerus and the right femur following motor vehicle accident. He was referred to paediatric endocrine for further evaluation as the boy had multiple bowing of upper and lower limbs with signs of rickets such as flaring of wrist and rickety rosary of the chest.

His parents were second cousins. He was born full term with birth weight of 3.1 kg. Antenatally was uneventful and there was no problems in the immediate neonatal period. However he had delayed developmental milestones especially in gross motor in which he started to walk at the age of 18 months. In addition to that his mother noted him to be smaller compared to other siblings. He was a fussy eater and had a poor appetite. He was first admitted at about one year of age due to vomiting and dehydration but the family defaulted further follow up.

The patient denied about history of recurrence fracture, no recurrence vomiting, polyuria, fever, fits and no chronic diarrheal. Clinically, he was short (height 91.0 cm; less than 3rd percentile) and thin, (weight 15.0 kg; less than 3rd percentile). He had slight frontal bossing, sparse hair and poor dentition. His scleras were not bluish and there was no dentinogenesis imperfecta. There were multiple bowing of all long bones of the upper and lower limbs with flaring of wrists and rickety rosary. His upper body segment was 44.0 cm, lower segment on the right and left was 48.0 cm and 47.0 cm respectively. His upper and lower segment ratio was about 1.0. He was prepubertal and his testicular volumes were only 2.0 ml. Reviews of other systems examinations were unremarkable.

Discussion

This teenager had multiple clinical signs which were bowing of long bones, signs of rickets, severe failure to thrive and delayed puberty. In addition to that he had poor oral intake because of poor appetite but he denied to have chronic diarrhoeal and polyuria. With those clinical clues, he most probably had serious underlying chronic medical conditions which could be either renal or gastrointestinal diseases [1]. Signs such as bowing of long bones, rickets and absence of chronic diarrhoeal made gastrointestinal diseases such as inflammatory bowel syndromes not very likely. Failure to thrive and delayed puberty are not very specific as those problems could occur in any long standing medical conditions [2]. He most likely had a tubular loss such as renal tubular acidosis with presence of bone signs, failure to thrive and delayed puberty. Poor appetite could be secondary to chronic metabolic acidosis in RTA [3].

The supporting evidences for RTA were hyperchloraemic metabolic acidosis with normal anion gap and persistence hypokalemia [4]. This boy had persistence metabolic acidosis ranging from pH of 7.20-7.25, blood AG of 12, low potassium that ranged from 2.2-2.7 mmol/L and plasma chloride as high as 120. In RTA, metabolic acidosis is because of loss of bicarbonates in proximal tubular defect or lack of acid production by the distal tubule [5]. Anion gap represents the difference of unmeasured anions and cations in the plasma. The normal value of the blood anion gap is 10-12 mEq/L [6]. Accumulation of organic acids as in diabetic ketoacidosis are characteristically associated with metabolic acidosis and an increased anion gap. Normal plasma anion gap in the presence of metabolic acidosis and hyperchloraemia suggests increased urinary bicarbonate loss in proximal RTA, gastrointestinal loss of bicarbonate associated with diarrhea and impaired excretion of H^+ ions in distal RTA [7].

Urine pH is an estimate of the number of free H^+ ions in the urine. The presence of alkaline urine during metabolic acidosis suggests defective renal acidification, as in distal RTA. Urine anion gap provides an estimate of urinary ammonium (NH_4^+) excretion gap. Under normal circumstances, urine anion gap is positive due to the presence of dissolved anions such as sulfates and phosphates. Metabolic acidosis is associated with a compensatory rise in NH_4^+ production, resulting in a negative urine anion gap. Patients with RTA typically show impaired renal NH_4^+ excretion and a positive urine anion gap [8]. The boy had urine pH of 8 and a positive urine anion gap of 23 [9]. He also had bilateral medullary nephrocalcinosis from the ultrasound of his kidneys (Figure 1). His laboratory work ups were consistent with distal type of RTA [9].

The bone work ups were done as he had multiple bowing of long bones and signs of rickets (Figures 2-5). He had low to normal plasma calcium; 1.9-2.2 mmol/L, low phosphate that ranged from 0.75-0.99 mmol/L, high alkaline phosphatase 345-478 IU/L, high intact parathyroid hormone 8.0-15.0 pmol/L. His 25(OH) Vit D was normal; 78.7 nmol/L but he had a high active vitamin D level; 482 pmol/L.

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Further analysis of urinary electrolytes showed that he had urinary phosphate loss which was 80.6%. His tubular reabsorption of phosphate was only 19.4% and his TMP/GFR was 0.1 mmol/L (1.0-1.65) (Table 1) [10].

The bone work ups showed that he had calciopenic, phosphopenic forms of rickets. High parathyroid hormone can be due to low calcium or low vitamin D level but as the boy had a normal storage of vitamin D thus he had secondary hyperparathyroidism related to low calcium. Low phosphate or phosphopenic form of ricket does not cause secondary hyperparathyroidism.

The primary mechanism that leads to low calcium and phosphate in the first place should be explored. Among the causes of the rickets include congenital and acquired form of rickets such as nutritional ricket, hypoparathyroidism, pseudohypoparathyroidism, vitamin D deficiency, vitamin D dependent ricket type 1, type 2 or vitamin D resistant ricket and RTA [11]. Untreated primary form of ricket could result in secondary form of RTA due to loss of bicarbonate as a consequence of secondary hyperparathyroidism [12]. Primary kidney tubular diseases or RTA could also manifest as ricket because of impairment in the synthesis of active vitamin D [13]. This teenager had very long standing medical problems as he only turned again to the medical attention at the age of 15 years old. Could his problems arise

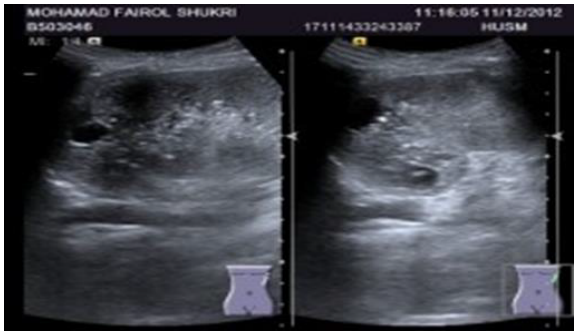

Figure 1: Bilateral nephrocalcinosis.

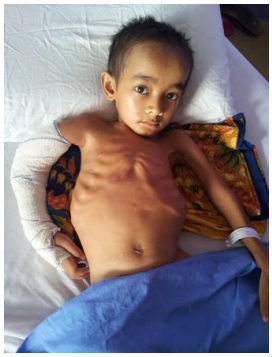

Figure 2: Rickety rosary of chest.

Figure 3: Flaring of wrist.

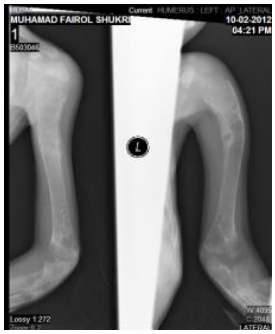

Figure 4: Bowing of upper limbs and old fractures.

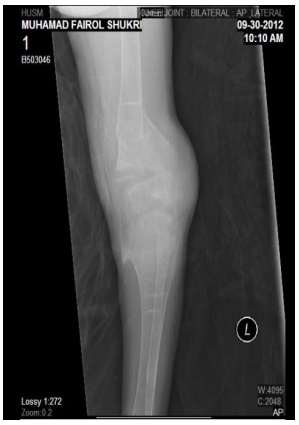

Figure 5: Bowing of lower limb and old fractures.

Lab.parameters	Baseline (reference range)	One month after treatment	Four month after treatment
Calcium (mmol/L)	1.91	2.04	2.23
Phosphate (mmol/L)	0.49	1.20	1.19
Potassium (mmol/L)	2.2	2.1	4.8
Sodium (mmol/L)			
Alkaline phosphatase (U/L)	325	286	328
iPTH (pmol/L)	15.4 (1.6-6.9)		
pH/HCO_3/BE	7.20/9.0/-18.0		7.34/21.0/-4.0
25(OH)Vit D3 (nmol/L)	78.7 (50-160)		
1,25$(OH)_2$Vit D3 (pmol/L)	482 (50-160)		
Fractional Excretion Calcium	0.29%		
Fractional Excretion phosphate	80.0%		37%
Tubular Reabsorption Phosphate	19.0%		63.0%
TMP P/GFR (mmol/L)	0.1 (1.15-2.44)		
Urine pH	5.0		
Plasma anion gap			
Urine anion gap	23.9		
LH (IU/L)	<0.1		
FSH (IU/L)	0.5		
Testosterone (nmol/L)	0.4		
Free T4 (pmol/L)	11.5		
TSH (m IU/L)	0.5		

Table 1: Summary of biochemical workups.

form untreated primary ricket or as a results of long standing RTA with ricket as a complication.

We thought, the boy had primary distal RTA as the background problem (Table 2). As he did not receive proper medical care, this results in chronic metabolic acidosis and impairment of active vitamin D synthesis by the kidney. Impaired synthesis of vitamin D contributes to low calcium and secondary hyperparathyroidism. High parathyroid hormone leads to a rise in the 1, 25$(OH)_2$ Vit D as in this case [14].

Furthermore the baseline ALP level is not markedly high as seen in most cases of primary ricket.

High level of 1,25$(OH)_2$ Vit D is also seen in type 2 vitamin D dependent ricket or vitamin D resistant ricket which is due to mutation in the vitamin D receptor causing problem in the binding of vitamin D to its receptor. Most of the patient would have alopecia which was absent in this patient. Only the molecular study could give a definite answer to this differential diagnosis [15].

Phosphate wasting is due to secondary hyperparathyroidism and this leads to worsening of bowing of bones.

The management is to correct metabolic acidosis, potassium replacement and suppression of secondary hyperparathyroidism. The boy received potassium citrate solution and rocalcitriol to correct his biochemical disorders. In addition to that he received gradual nutritional rehabilitation. After few months of the treatment, he had a normal blood gas, potassium level and the tubular reabsorption of phosphate was improved to 63%. He also had put on his weight as his appetite improved (Figure 6).

Distal RTA can be autosomal dominant or autosomal recessive. Autosomal recessive distal RTA has an earlier onset that is usually in the first months of life. It can progress into nephrocalcinosis and sensorineural hearing loss. Autosomal dominant distal RTA is less severe and appears later during adolescence or adulthood and may or may be complicated by nephrocalcinosis [16].

Common genes for autosomal recessive distal RTA are ATP6V1B1, ATP6V0A4 and SLC4A1, which encode subunits a4 and B1 of V-ATPase and the AE1 bicarbonate/chloride exchanger respectively. However, autosomal dominant distal RTA is only related to mutations in AE1. Proper genetic workup and counselling are very important in this family as the boy had features consistent with autosomal recessive type of distal RTA [17].

Clinical/Lab parameters	Primary RTA	Untreated rickets with secondary RTA
Clinical signs of rickets	present	present
Calcium/phosphate	variable	variable
High ALP	Mild to moderate	Very high
IPTH	high	high
25(OH)Vit D	normal	Low with nutritional form
1,25$(OH)_2$Vit D	High with secondary hyperparathyroidism	variable
Metabolic acidosis	yes	Yes (late stage due to secondary hyperparathyroidism)
Medullary nephrocalcinosis	present	absent

Table 2: Differences between primary RTA and untreated rickets with secondary RTA.

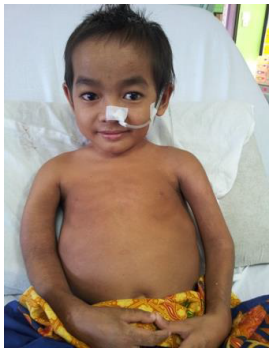

Figure 6: Post treatment.

Conclusion

Proper workups are very important to distinguish between different causes of bowing of long bones as the treatment is different. Both primary RTA and long standing untreated rickets may result in metabolic acidosis and may be missed if the clinician is not aware of those two conditions.

References

1. Chan JC, Scheinman JI, Roth KS (2001) Consultation with the specialist: renal tubular acidosis. Pediatr Rev 22: 277-287.
2. Bagga A, Bajpai A, Gulati S, Singh A (2001) Distal renal tubular acidosis with severe bony deformities and multiple fractures. Indian Pediatr 38: 1301-1305.
3. Rocher LL, Tannen RL (1986) The clinical spectrum of renal tubular acidosis. Annu Rev Med 37: 319-331.
4. Bouzidi H, Daudon M, Najjar MF (2009) Primary distal renal tubular acidosis. Ann Biol Clin (Paris) 67: 135-140.
5. Ring T, Frische S, Nielsen S (2005) Clinical review: Renal tubular acidosis--a physicochemical approach. Crit Care 9: 573-580.
6. Pereira PC, Miranda DM, Oliveira EA, Silva AC (2009) Molecular pathophysiology of renal tubular acidosis. Curr Genomics 10: 51-59.
7. Laing CM, Unwin RJ (2006) Renal tubular acidosis. J Nephrol 19(9): S46-52.
8. Rodríguez-Soriano J, Vallo A (1990) Renal tubular acidosis. Pediatr Nephrol 4: 268-275.
9. Batlle D, Moorthi KM, Schlueter W, Kurtzman N (2006) Distal renal tubular acidosis and the potassium enigma. Semin Nephrol 26: 471-478.
10. Nicoletta JA, Schwartz GJ (2004) Distal renal tubular acidosis. Curr Opin Pediatr 16: 194-198.
11. Kossoy AF, Weir MR (1986) Renal tubular acidosis in infancy: a clinical approach to diagnosis and treatment. South Med J 79: 1256-1258.
12. Derakhshan A, Basiratnia M, Fallahzadeh MH, Hosseini-Al-Hashemi G (2007) A neglected case of renal tubular acidosis. Saudi J Kidney Dis Transpl 18: 585-589.
13. Lucas GN, Seneviratne TR (1998) Distal renal tubular acidosis with rickets and nephrocalcinosis. Ceylon Med J 43: 168-169.
14. Igarashi T, Sekine Y, Kawato H, Kamoshita S, Saigusa Y (1992) Transient neonatal distal renal tubular acidosis with secondary hyperparathyroidism. Pediatr Nephrol 6: 267-269.
15. Pumarino H, Contreras P, Vivanco X, Abodovsky N, Campino C (1982) [Vitamin D-dependent rickets and renal tubular acidosis. Clinical and metabolic effects of 25-dihydroxyvitamin D]. Rev Med Chil 110: 1213-1218.
16. Escobar L, Mejía N, Gil H, Santos F (2013) Distal renal tubular acidosis: a hereditary disease with an inadequate urinary H^+ excretion. Nefrologia 33: 289-296.
17. Miura K, Sekine T, Takahashi K, Takita J, Harita Y, et al. (2013) Mutational analyses of the ATP6V1B1 and ATP6V0A4 genes in patients with primary distal renal tubular acidosis. Nephrol Dial Transplant 28: 2123-2130.