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Letter to the Editor

Erroneous diagnosis of rickets

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Rickets is the clinical consequence of defective bone mineralization in children (Table 1). The clinical features of rickets include bone pain and deformities, muscle weakness, and profound sweating (1, 2). Findings include biochemical (Table 1) and radiographic abnormalities (metaphyseal cupping) (1, 2). The diagnosis of rickets is based on personal history, physical examination, and biochemical testing, and is confirmed with radiographs (1, 2). We report three children who were initially erroneously diagnosed as having rickets.

Patient No.1 was a 10-year old boy with an uneventful personal history. Owing to having flat feet, the boy was examined by an orthopedist because who noticed a very mild chest asymmetry and stated "severe vitamin D-deficiency with bone deformities." The boy was referred to the pediatric bone clinic for high doses of vitamin D. There he had normal serum calcium (S-Ca 2.36 mmol/L), serum phosphate (S-P 1.51 mmol/L), alkaline phosphatase (S-ALP 3.99 μkat/L), parathyroid hormone (S-PTH 1.42 pmol/L) levels, together with normal calciuria and phosphaturia. The wrist X-ray was normal. Rickets was ruled out and high doses of vitamin D were deemed unnecessary.

Patient No.2 was a 6-month-old boy with and uneventful history receiving regular antirachitic prophylaxis (500 IU cholecalciferol/day). The parents noticed somewhat increased sweating and a pediatric practitioner ordered a serum evaluation of bone alkaline phosphatase (S-bALP) and vitamin D concentration (S-25-OH-D). The S-bALP was elevated in comparison with adult reference values, which is quite normal in the growing skeleton. Vitamin D concentration was below the reference range (40 nmol/L; normal 75-125 nmol/L). The child was diagnosed as having vitamin D-deficient rickets and received 5 000 IU of cholecalciferol/day orally for one week and was referred to the pediatric bone clinic. There, the S-Ca, S-P, total S-ALP, PTH, phosphaturia and calciuria were all normal, as was the wrist X-ray. The diagnosis of rickets was ruled out, together with other possible causes of hyperhidrosis and the patient returned to his regular daily dosage of 500 IU of cholecalciferol.

Patient No.3 was an 8-months-old boy with a normal personal history who was thriving and receiving regular antirachitic prophylaxis. The parents noticed he had a yellowish skin color and visited their pediatrician who ordered liver function tests: S-bilirubin, aspartate aminotransferase (S-AST), alanine aminotransferase (S-ALT), and S-ALP. The S-bilirubin, AST, ALT were all normal, but the S-ALP was significantly elevated (80 μkat/L; normal 2.5-9.5 μkat/L). Wrist X-ray, S-Ca, P, and PTH were not assessed. The diagnosis of vitamin D-deficient rickets was established and the infant received an intramuscular dose 300 000 IU of vitamin D2. After three weeks, the S-ALP dropped to 50 μkat/L and the boy was referred to the pediatric bone clinic as "non-healing vitamin D-deficient rickets." There, the S- Ca, P, PTH, phosphaturia, and calciuria were all normal. The S-ALP was 30 μkat/L. Wrist X-ray was also normal, with no signs of florid or healing rickets. A detailed personal history revealed that child was exclusively receiving carrots in vegetable soup. This resulted in hypercarotenemia, the real cause of his "jaundice" (5). The final diagnoses were transient hyperphosphatasemia of infancy (THI) and hypercarotenemia (3-5). The boy's diet was adjusted to current recommendations and he also returned to the regular daily dosage of 500 IU of cholecalciferol.

In conclusion, when considering rickets, findings must be evaluated thoroughly and should not be viewed separately. Non-indicated high doses of vitamin D could result in hypercalcemia and soft tissue calcifications.

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Table 1. Differential diagnosis of rickets

Diagnosis	Cause	S-Ca	S-P	S-ALP	S-PTH	U-Ca	U-P	S-25(OH)D	S-1,25(OH)$_2$D
Nutritional/ vitamin D-deficient rickets	Vitamin D/ calcium deficiency/ lack of sunlight/ malabsorption	normal to low	low	high	high	low	high	low	low to normal
Vitamin D-dependent type I rickets (autosomal recessive)	Enzyme deficiency 25(OH)D-1α-hydroxylase	low	low	high	high	low	high	high	very low
Vitamin D-dependent type II rickets (autosomal recessive)	End-organ resistance to calcitriol (receptor disorder)	low	low	high	high	low	high	low to normal	high
Hypophosphatemic X-linked rickets	Hypophosphatemia due to FGF 23 excess	normal	low	high	normal	low to normal	high	normal	low
Hypophosphatemic rickets (autosomal recessive)	Hypophosphatemia due to FGF 23 excess	normal	low	high	normal	normal	high	normal	low to normal
Hypophosphatemic rickets with hypercalciuria (autosomal recessive)	Hypophosphatemia due to tubular sodium-phosphate cotransporter defect	normal	low	high	low	high	high	normal	high
Tumor-induced rickets/ osteomalacia	Hypophosphatemia due to FGF 23 excess	normal	low	high	normal	normal to high	high	normal	low
Transient hyperphosphatasemia of infancy (THI)	Unknown; probably impaired ALP clearance	normal	normal	very high	normal	normal	normal	normal	normal

ALP: alkaline phosphatase; FGF23: fibroblast growth factor 23; S-ALP: serum activity of alkaline phosphatase; S-Ca: serum level of calcium; S-P: serum level of phosphate; S-PTH: serum level of parathyroid hormone; S-1.25(OH)2D: serum level of vitamin S-1.25(OH)2D (calcitriol); S-25(OH)D: serum level of vitamin 25(OH)D (calcidiol); U-Ca: urinary excretion of calcium; U-P: urinary excretion of phosphate

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