Unusual association of diseases/symptoms

A failing to thrive 18 month old with vitamin D deficiency rickets and *Helicobacter pylori* gastritisSulaiman S Bharwani,¹ Qudsia Shaukat,² Ghazala Balhaj,¹ Mouied Ashari³¹Department of Pediatrics, UAE University, Faculty of medicine, Al Ain, Abu Dhabi, United Arab Emirates;²Department of Pediatrics, Al Ain Hospital affiliate of Vienna Medical University, Al Ain, Abu Dhabi, United Arab Emirates;³Department of Pathology and Microbiology, Tawam Affiliate of Johns Hopkins Hospital, Al Ain, Abu Dhabi, United Arab Emirates**Correspondence to** Dr Sulaiman S Bharwani, sulaiman.bharwani@gmail.com**Summary**

A 14-month-old girl presented with the recurring bouts of vomiting and diarrhoea and failure to thrive. At 7 months of age, the baby was found to be exclusively breast fed and her blood tests revealed low calcium, low phosphorous and markedly elevated alkaline phosphatase. She was started on vitamin D and calcium supplements. Five months later, she came in with lower-limb bowing, irritability, vomiting and loose stools. The laboratory studies revealed very low serum hydroxyvitamin D, and high serum dihydroxyvitamin D. Vitamin D dose was doubled. Ten weeks later, her growth velocity had fallen and she continued to have intermittent loose stools. The oesophagogastroduodenoscopy was done and the biopsies showed *Helicobacter pylori* gastritis and mild duodenitis. After eradication of *H pylori*, there was a dramatic improvement in her growth and activity and upon 6 months follow-up there was no clinical or radiologic evidence of rickets.

BACKGROUND

Many regions of the world share a higher dual burden of *H pylori* infection and vitamin D deficiency (serum hydroxyvitamin D <30 nmol/l or <10 ng/ml).^{1 2} In addition, vitamin D has in recent years attracted a lot of attention due to its immune modulating properties³ and its insufficiency (serum hydroxyvitamin D =30 to 75 nmol/l or 10–30 ng/ml) has been shown to be associated with a wide range of conditions like cardiovascular disease, diabetes, hypertension and cancer.^{4–7} The North-African and Middle-East regions are no exceptions.^{2 8 9}

Current estimates in developed countries put the prevalence of vitamin D insufficiency in the general population to be between 60% and 80%.^{10 11} In the United Arab Emirates, the high prevalence among women of the childbearing age puts the infants at particularly high risk for rickets.¹² Infants who are exclusively breast fed beyond 6 months of age with little or no sun exposure often develop rickets in the region.¹³ Children on vegetarian diets have been shown to have nutritional deficiencies, and in some cases rickets due to vitamin deficiency.¹⁴

Table 1 Column A, B, C and D denote laboratory investigations and results at the patient's age of 7 months, 12 months, 14.5 months and 18 months, respectively

Diagnostic test	A (7 months)	B (12 months)	C (14.5 months)	D (18 months)	Normal values (range)
Serum calcium					
mmol/l	2.1	2.2	2.45	2.38	2.23–2.58
mg/dl	8.7	8.9	9.6	9.5	8.9–10.3
Serum phosphorus					
mmol/l	0.5	0.8	1.7	–	0.7–1.4
mg/dl	1.6	2.7	5.2	–	2.4–4.6
Serum alkaline phosphatase (iu/l)	1717	1037	545	325	42–121
Serum 1,25(OH) ₂ vitamin D					
nmol/l	–	11	–	–	50–200
ng/ml	–	3	–	–	20–60
Serum 1,25(OH) ₂ vitamin D					
pmol/l	–	222	–	–	43–148
pg/ml	–	85	–	–	25–45
Parathyroid hormone (PTH) (pmol/l)	–	16.5	–	–	1.3–9.3
Serum creatinine (μmol/l)	–	–	14.3	–	35–88
Blood urea nitrogen (mmol/l)	–	–	1.2	–	2.9–9.3
Serum haemoglobin (g/l)	–	–	111	–	115–155
Urine calcium/creatinine (Uca/Ucr ratio)	–	0.08	–	–	0.10–0.094

Abnormal values are in bold.

–Not available.

1,25(OH)₂ vitamin D, 1,25-hydroxyvitamin D.

Figure 1 Growth chart-trajectory depicting growth velocity disturbance and recovery over a 12-months period. The arrow indicates the point of initiation of the treatment for *Helicobacter pylori* infection.

CASE PRESENTATION

This report describes a 14-month-old girl who was referred to a primary care clinic due to her failing to thrive and the recurring bouts of vomiting and diarrhoea. The referring doctor had initially seen this patient when she was 7-month-old and was moderately dehydrated due to what appeared to be a viral gastroenteritis. Incidentally, the blood tests revealed low serum calcium, low serum phosphorus and markedly elevated alkaline phosphatase (table 1 column A).

She weighed 7 kg at the time so she was started on 0.4 µg of vitamin D (0.05 µg/kg/day) and 300 mg/day calcium gluconate. The parents were instructed on introducing the child to a vitamin D-enriched diet. The patient presented 5 months later with lower-limb bowing, irritability, vomiting and diarrhoea. The stool culture was sent and reported no growth. The laboratory studies were repeated

and reported low serum phosphorus, normal calcium and elevated serum alkaline phosphatase (table 1 column B). 1,25-Hydroxyvitamin D level was markedly diminished at 11 nmol/l (normal 50–200 nmol/l) and serum 1,25-dihydroxyvitamin D (1,25-OH D₃) level was elevated to 222 pmol/l (normal 43–148 pmol/l) and parathyroid hormone level was raised to 16.5 pmol/l (normal 1.3–9.3 pmol/l). Radiographs showed irregular fraying and widening of the distal metaphyses of the long bones. At that time she was 12 months old, weighed 8.4 kg (fifteenth percentile) and measured 72 cm (twenty-fifth percentile) in length. She was mildly dehydrated but was tolerating oral rehydration solution. Her vitamin D dose was doubled to 0.1 µg/kg/day and she remained on the calcium supplements. Ten weeks later she continued to have intermittent loose stools and occasional vomiting and the serum alkaline phosphatase remained elevated (table 1 column C). On this occasion as

Figure 2 Stomach biopsy (Warthin–Starry stain) with *Helicobacter pylori* bacteria.

Figure 3 Duodenal biopsy (H&E stain) with mild chronic inflammation and normal villi.

in the previous one, a stool specimen was sent for culture and was reported growing normal commensals. The stool microscopy showed no ova or parasite. The patient was treated with metronidazole 5 mg/kg/dose three times a day for 7 days for suspected bacterial overgrowth, however,

she continued to lose weight and her growth velocity had fallen (figure 1). The patient underwent endoscopy and the stomach biopsies showed *H pylori* associated gastritis (figure 2) and mild chronic inflammation in the duodenal biopsy. The villi were described to be within normal limits

and there were no significant intraepithelial lymphocytes (figure 3). The patient was put on the triple therapy (amoxicillin, clarithromycin and omeprazole) regimen to treat *H pylori* infection. The parents were advised to continue the oral vitamin D and calcium supplements. She returned to follow-up, 3 months later as an active playful toddler who was growing well (figure 1). The *H pylori* eradication was confirmed by ELISA-based antigen test on a stool specimen. 6 months later she had no more radiologic features of rickets and her serum alkaline phosphatase levels were steadily heading toward normal (table 1 column D).

INVESTIGATIONS

- ▶ Long bones radiographs were consistent with the findings of rickets
- ▶ Serum biochemistry and vitamin D assays confirmed vitamin D deficiency
- ▶ Growth chart plotting showed a drop in growth velocity
- ▶ Stomach biopsies diagnosed *H pylori* gastritis
- ▶ Stool antigen test confirmed eradication of *H pylori* after the therapy.

DIFFERENTIAL DIAGNOSIS

- ▶ Vitamin D deficiency rickets exacerbated by *H pylori* infection
- ▶ Vitamin D deficiency rickets secondary to inadequate diet or frequent gut losses.

TREATMENT

- ▶ Eliminating *H pylori* infection with triple therapy regimen (amoxicillin, clarithromycin and omeprazole)
- ▶ Assuring compliance with appropriate dosing of oral 1,25 OH D₃, and calcium gluconate
- ▶ Encouraging vitamin D-enriched diet.

OUTCOME AND FOLLOW-UP

- ▶ Remarkable clinical and radiologic recovery
- ▶ Significant biochemical improvement.

DISCUSSION

There is evidence to suggest that vitamin D negatively regulates the chronic inflammation in *H pylori* gastritis and that the deficiency of vitamin D can facilitate T helper cells aggression in subjects with chronic *H pylori* infection, thereby increasing the severity of gastric mucosal injury.¹⁵ Both *H pylori* gastritis and vitamin D deficiency are independent risk factors for growth disturbances^{16 17} and the patient in the case being darker skinned carried an additional risk factor¹⁸. What were evident from the start were the patient's diagnosis and the treatment plan. What is difficult to prove is the hypothesis that the hypovitaminosis D in this patient led to the exacerbation of *H pylori* gastritis. The latter further diminished the vitamin D absorption and increased the requirement, thus creating a vicious cycle which was broken only after the eradication of *H pylori* infection. More observational studies are needed to establish the causality in this relationship. Coeliac disease was excluded in our patient with the intestinal biopsy which is the gold-standard in diagnosing the condition. Bacterial overgrowth and giardiasis were suspected, although not

proven, and with oral metronidazole intake a few weeks prior to the endoscopy and biopsy, they were less likely to have played a role in our patient's findings.

This case highlights the importance of diagnosing and treating *H pylori* gastritis in children with growth failure and vitamin D deficiency, especially when the appropriate oral vitamin D supplements fail to improve the clinical and or biochemical picture. The delay in managing such cases can carry a high medical and societal cost accounting for multiple hospital visits, frequent tests and parental work interruptions and perhaps residual rachitic sequelae in the patients.¹⁸

Learning points

- ▶ Vitamin D deficiency in children can occur in places with adequate sunshine.
- ▶ Prolonged exclusive breastfeeding without vitamin D supplement causes rickets.
- ▶ *H pylori* gastritis can exacerbate vitamin D rickets either directly by diminishing absorption of oral vitamin D or indirectly by losses in vomitus and diarrhoea.
- ▶ Serial plotting of growth charts and serum alkaline phosphatase values are valuable in following the course of rickets.
- ▶ Treating *H pylori* infection may be beneficial in improving the vitamin D status.

Competing interests None.

Patient consent Obtained.

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