Hypercacleaemia is an uncommon problem in infancy. It may be a manifestation of Williams' syndrome, vitamin D or calcium excess, as well as disorders associated with reduced bone formation, such as hypophosphatasa, or increased bone resorption, such as malignancy. Occasionally it may reflect an abnormality of the calcium sensing receptor (hypocalciuric hypercalcaemia) with an associated altered "set point". Primary hyperparathyroidism is extremely rare (hypocalciuric hypercalcaemia) with an associated altered "set point". We present a case of spinal muscular atrophy type 2 where the initial presentation was with hypercalcaemia and constipation. Recognised causes of hypercalcaemia in infancy were excluded and we suspect that the raised calcium reflects altered bone turnover secondary to the underlying neuromuscular disease.

CASE REPORT

A 10 month old girl presented with a long standing history of constipation. She was born at 41 weeks gestation following an unremarkable pregnancy. She passed meconium within the first 24 hours but became constipated shortly afterwards and for many months was only opening her bowels every 10–14 days. She was referred to the local hospital and was awaiting review by the paediatric surgeons with a view to awaiting review by the paediatric surgeons with a view to performing a rectal biopsy, when she was found to have spinal muscular atrophy type 2. We suspect that the hypercalcaemia with hypercalciuria observed in this case reflects altered bone turnover secondary to the underlying neuromuscular disease.

Both parents had alkaline phosphatase levels well within the normal range (typically low normal in heterozygote carriers of hypophosphatasa) and normal calcium concentrations (typically raised in hypocalciuric hypercalcaemia). The patient's investigations are summarised in table 1. She was commenced on a low calcium diet, comprising less than 90 mg calcium daily as well as chlorothiazide (25 mg/kg) to reduce urinary calcium excretion. Her calcium fell into the normal range (fig 1) and her alkaline phosphatase increased to 143 IU/l. Her urine calcium creatinine ratio also fell to more normal values.

She was started on lactulose and sodium picosulphate because of her constipation and maintained a daily to alternate day bowel habit on this regimen. Our patient remained hypotonic despite normalisation of calcium levels, and at subsequent assessments she was noted to be hyporeflexic with muscle wasting proximally in her upper limbs and proximally and distally in her lower limbs. At this stage she was noted to have developed a frog-like posture when supine, although she could still sit unaided. Other components of her development apart from motor function remained hypotonic despite normalisation of calcium levels, and at subsequent assessments she was noted to be hyporeflexic with muscle wasting proximally in her upper limbs and proximally and distally in her lower limbs. At this stage she was noted to have developed a frog-like posture when supine, although she could still sit unaided. Other components of her development apart from motor function were normal and there were no feeding difficulties and no concerns about recurrent or severe respiratory tract infections. Creatine phosphokinase was checked on two separate occasions and was normal (69 and 54 U/l), but in view of the clinical picture she was referred to the local muscle clinic. Molecular genetic testing revealed a homozygous deletion of SMN1 exons 7 and 8, which, in the context of the clinical picture, confirmed a diagnosis of spinal muscular atrophy type 2. Her current management includes regular physiotherapy with her dietary calcium intake titrated according to her blood and urine biochemistry.

DISCUSSION

This is the first time to our knowledge that an infant has developed hypercalcaemia and associated symptoms because of an underlying neuromuscular disorder. This is unlikely to be a chance association and the hypercalcaemia with hypercalciuria and nephrocalcinosis in this child probably reflects altered bone turnover as a consequence of reduced muscle tone and activity.

Hypercalcaemia is described in adolescents with neuropathy and immobilisation can also result in this biochemical picture. Patients with abnormal bone structure and function may be particularly susceptible. We suspect that a "shift" in the balance between dietary intake, bone formation, and bone breakdown away from the norm was responsible for the biochemical picture that we observed with a relatively high calcium intake for a skeleton that was not growing and developing in the normal manner. Hypercalcaemia is a rare
Hypercalcaemia in infancy 385

Figure 1  Total plasma calcium concentrations and urine calcium/creatinine ratio plotted against age (weeks). The unbroken arrow illustrates when a low calcium diet was introduced and the broken arrow when chlorothiazide was commenced.

Hypercalcaemia in infancy illustrates when a low calcium diet was introduced and the broken arrow plotted against age (weeks). The unbroken arrow illustrates when a low calcium diet was introduced and the broken arrow when chlorothiazide was commenced.

The spinal muscular atrophies are a clinically and genetically heterogeneous group of disorders. They are characterised by degeneration of the spinal cord anterior horn cells and associated muscular atrophy and weakness. The subcategorisation of childhood proximal spinal muscular atrophy, which is caused by deletions of the SMN1 gene on chromosome 5, relies on the achievement or not of specific motor milestones. Children with type 1 spinal muscular atrophy typically present very early with hypotonia and never achieve the ability to sit independently. These children typically die of the complications of respiratory impairment by the age of 2 years. Spinal muscular atrophy type 2 is milder—children sit independently, often having normal motor milestones in the first 6–8 months, but subsequently do not walk unaided. While these children may be susceptible to complications such as chest infections and feeding difficulties, with appropriate management, survival into adulthood is likely. In type 3 spinal muscular atrophy, children do achieve the ability to walk independently; the spectrum of severity in this type of spinal muscular atrophy is very broad indeed.

ACKNOWLEDGEMENTS
We would like to thank Professor Michael Whyte for his helpful comments about this patient prior to diagnosis.

REFERENCES
Hypercalcaemia in infancy; a presenting feature of spinal muscular atrophy

K Khawaja, W T Houlsby, S Watson, K Bushby and T Cheetham

Arch Dis Child 2004 89: 384-385
doi: 10.1136/adc.2003.028225

Updated information and services can be found at:
http://adc.bmj.com/content/89/4/384

These include:

References
This article cites 9 articles, 2 of which you can access for free at:
http://adc.bmj.com/content/89/4/384#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Calcium and bone (78)
- Metabolic disorders (761)
- Motor neurone disease (10)
- Neuromuscular disease (166)
- Drugs: CNS (not psychiatric) (497)
- Constipation (60)
- Diet (325)
- Renal medicine (273)
- Urology (446)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/