CASE REPORT

Hypercalcaemia in infancy; a presenting feature of spinal muscular atrophy

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

A 10 month old girl presented with a history of constipation from early life. She was found to be hypercalcaemic with hypercalciuria and nephrocalcinosis. Her mild motor delay and hypotonia were thought to be linked to chronic hypercalcaemia, but when these features failed to improve despite normocalcaemia on a low calcium diet the possibility of neuromuscular disease was explored in more detail. She was subsequently 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 reduced muscular activity.

Hypercalcaemia 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 hypophosphatasia, 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 in infancy. 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.

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
problem in infancy and childhood and we took care to exclude other causes of this biochemical picture in this age group.

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.

Our patient had a low alkaline phosphatase level at presentation, which rose as circulating calcium concentrations fell on a low calcium diet. Hypercalcaemia can suppress PTH and inhibit bone formation and we were keen to encourage passive and active muscular activity as a means of enhancing bone accretion as the calcium fell. The subsequent rise in alkaline phosphatase is likely to reflect the beneficial impact of normocalcaemia and active and passive movement on bone formation.

Children with spinal muscular atrophy or congenital muscular dystrophy are frequently hypotonic in the first months of life, and this may be associated with constipation that is attributed to their underlying muscle weakness. We do not know the extent to which hypercalcaemia occurs in other young children with neuromuscular disease, although it is possible that inter-individual differences in bone metabolism might contribute to susceptibility. We believe that this as an area worthy of further study.

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