Reminder of important clinical lesson

Growth monitoring still has a place in selected populations of children

M Hussain,¹ C M John,² K Mohamed,³ M Zbaeda,⁴ S M Ng,¹ S Chanderasekaran,¹ M Didi,¹ J C Blair¹¹Department of Paediatric Endocrinology, Alder Hey Children's Hospital, West Derby, Liverpool, UK;²Department of Paediatrics, Whiston Hospital, Prescot, Merseyside, UK;³Department of Paediatric Neurology, Alder Hey Children's Hospital, West Derby, Liverpool, UK;⁴Department of Paediatrics, Southport and Ormskirk Hospital, Ormskirk, UK

Correspondence to J C Blair, jo.blair@alderhey.nhs.uk

Summary

In 1998, a multiprofessional group developed a consensus on growth monitoring in the UK. While routine serial measurements were not recommended in healthy children, it is clear that there is a subset of children at increased risk of growth-modifying disease who may benefit from growth monitoring. This subset includes children with genetic disorders at increased risk of thyroid dysfunction. Symptoms and signs of thyroid dysfunction are non-specific in the early stages of disease and are easily mistaken for features of an underlying genetic disorder. In this article, we report the case of a 2.8-year-old girl with 18q deletion syndrome who was profoundly weak, hypotonic and poorly responsive at diagnosis of Grave's disease. She was tall and her bone age was 2 years advanced, indicating long-standing disease. Growth monitoring of this patient should have enabled earlier diagnosis and avoided a serious and potentially fatal episode.

BACKGROUND

This case is reported for three reasons:

1. To reinforce the previously reported association of autoimmune thyroid disease in patients with 18q deletion syndrome.
2. To report the life-threatening consequences of prolonged, unrecognised thyrotoxicosis in patients with conditions that render them more susceptible to the neurological complications of thyroid dysfunction.
3. To highlight the value of growth monitoring in the identification of children with thyroid disease.

CASE PRESENTATION

A white Caucasian girl who was known to have 18q deletion syndrome (break point at 18q22.2) presented at 2.8 years of age with a 48-h history of progressive weakness, ataxia, vomiting and drowsiness. There was a 1-year history of hyperphagia, diarrhoea, poor sleep and rapid growth and her parents described progressive prominence of the eyes over the preceding 4 weeks. On admission, the patient was poorly responsive and the Glasgow Coma Scale fluctuated between 8 and 10. She was profoundly hypotonic and hyporeflexic, and there were minimal anti-gravity movements (figure 1). The heart rate was 160 bpm and the skin was moist. Examination of the thyroid was normal. The patient's height was 96 cm (1.12 SD) and her target height was 162.2 cm (−0.25 SD) (figure 2). Her body mass index was 13.6 kg/m² (−2.45 SD).

INVESTIGATIONS

On biochemical assessment, the serum thyroid-stimulating hormone (TSH) was <0.03 mU/l (normal range (NR) 0.27–4.2 mU/l), FT4, 75 pmol/l (NR 12–22 pmol/l), free T3, 3.6 nmol/l (NR 1.4–2.8 nmol/l) and thyroid receptor antibodies, >405 mU/l (NR 9–14 mU/l). Plasma electrolytes,

C reactive protein, liver function tests, creatinine kinase and lactate dehydrogenase were normal. On ultrasound examination, the thyroid was uniformly enlarged with no nodules (isthmus 0.6 cm thick, right and left lobes 4×2×1.3 cm). Bone age x-ray was advanced by 2.6 years (5.4 years). Blood carbon dioxide levels were monitored closely in light of the profound hypotonia and risk of hypoventilation but remained within an acceptable range.

Such profound neurological manifestations of thyrotoxicosis in the presence of normal serum potassium have not been reported previously and for this reason the patient underwent extensive neurological assessment. MRI of the brain was normal except for delayed myelination consistent with a diagnosis of 18q deletion. Analysis of cerebrospinal fluid (CSF) showed normal glucose, protein and cell count. Electrophoresis of CSF demonstrated normal oligoclonal bands. All microbiology investigations, including bacterial and viral cultures, serology and PCR studies of blood and CSF were normal.

TREATMENT

Treatment with carbimazole (15 mg/day, 1.2 mg/kg/day) induced biochemical remission by day 14 of treatment (FT4, 12.1 pmol/l; TSH, <0.03; FT3, 2.4 nmol/l (NR 1.4–2.8 nmol/l)). Three years following presentation the patient is clinically and biochemically euthyroid on a 'block and replace' regimen, using carbimazole 15 mg daily (0.75 mg/kg/day) and thyroxine 50 µg/day.

OUTCOME AND FOLLOW-UP

Power significantly improved after 10 days and was normal by 2 months. The patient walked with support by day 22 and made dramatic developmental progress thereafter. She continues under regular review and 3 years after presentation her growth has slowed (height −0.52 SD, figure 2)

Figure 1 Appearance of a 2-year-old girl with 18q deletion syndrome at presentation of thyrotoxicosis illustrating hypotonic posture.

Figure 2 Growth trajectory and target height of a 2-year-old girl with 18q deletion syndrome at diagnosis and during treatment of thyrotoxicosis.

and bone age advance is less marked (bone age 7.4 years, chronological age 5.6 years). Her thyroid receptor antibody titres remain significantly elevated (174 U/l).

DISCUSSION

Autoimmune thyroid disease is reported to occur with increased prevalence in a number of chromosomal

syndromes including Down's, Turner, Di George, Noonan, Smith Magenis, and 1q terminal deletion syndromes and 18q deletion syndrome. Deletion of the long arm of chromosome 18 is one of the most common human aneusomies occurring in 1 in 40 000 live births. The syndrome is characterised by mental retardation, hypotonia, hearing impairment and foot deformities, although a wide spectrum

of physical, neurodevelopmental and biochemical features has been reported.¹ A large case series of children with 18q deletion syndrome reported a prevalence of autoimmune thyroid disease of 12% (six in 50).² In the majority of subjects thyroid hormone levels are low, but thyrotoxicosis has also been described.²⁻³ The clinical features of thyroid dysfunction can be readily attributed to the phenotype of an underlying genetic syndrome resulting in considerable delays in diagnosis. The phenotype may also predispose affected children to particularly severe complications of thyroid hormone deficiency or excess.

Children with 18q deletion syndrome are also short and the majority have a height more than 2 SD below the mean. The speed of growth is slow (more than 1 SD below the mean in the majority of children) and skeletal maturity is also delayed. Examination of the growth hormone (GH) insulin-like growth factor I (IGF-I) axis has demonstrated that most children with 18q deletion syndrome who are growing slowly have biochemical evidence of impaired secretion of GH or IGF-I.⁴ In light of these data, the pattern of growth of the girl reported in this paper was highly abnormal; her height was significantly above both the population mean and genetic target height and her skeletal maturity was considerably advanced. Early identification of these abnormalities of growth would have prompted consideration of a diagnosis of thyrotoxicosis enabling initiation of treatment before the acute illness. Hypotonia is also a dominant feature of the phenotype of children with 18q deletion syndrome and we speculate that this characteristic of the syndrome predisposed our patient to profound neurological complications of thyrotoxicosis.

Regular biochemical assessment of thyroid function is recommended in children with Down's syndrome and should also be considered in children with 18q deletion.

However, phlebotomy can be particularly challenging in children with learning difficulties and for children with 18q deletion syndrome would not aid identification of children with abnormalities of the GH-IGF-I axis. We report this case to highlight how growth monitoring in a highly selected group of children at risk of clinically silent growth-modifying disease can be valuable in identifying children requiring further investigation.

Learning points

- ▶ Autoimmune thyroid disease occurs with increased frequency in patients with 18q deletion.
- ▶ The phenotype of 18q deletion syndrome may render patients at increased risk of life-threatening neurological consequences of thyroid dysfunction.
- ▶ Growth monitoring is a valuable, non-invasive tool for the identification of thyroid dysfunction.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Cody JD**, Ghidoni PD, DuPont BR, *et al*. Congenital anomalies and anthropometry of 42 individuals with deletions of chromosome 18q. *Am J Med Genet* 1999;**85**:455–62.
2. **Schaub RL**, Hale DE, Rose SR, *et al*. The spectrum of thyroid abnormalities in individuals with 18q deletions. *J Clin Endocrinol Metab* 2005;**90**:2259–63.
3. **Tutunculer F**, Darendeliller F, Gunoz H, *et al*. 18q deletion syndrome associated with autoimmune thyroid disease presenting as hyperthyroidism. *J Pediatr Endocrinol Metab* 2005;**18**:419–20.
4. **Hale DE**, Cody JD, Baillargeon J, *et al*. The spectrum of growth abnormalities in children with 18q deletions. *J Clin Endocrinol Metab* 2000;**85**:4450–4.

This pdf has been created automatically from the final edited text and images.

Copyright 2011 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Hussain M, John CM, Mohamed K, Zbaeda M, Ng SM, Chandrasekaran S, Didi M, Blair JC. Growth monitoring still has a place in selected populations of children. *BMJ Case Reports* 2011;10.1136/bcr.01.2010.2640, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow