CASE REPORT

Hypopituitarism following cerebral oedema with diabetic ketoacidosis

K A Dunlop, D Woodman, D J Carson

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Clinical evidence of cerebral oedema occurs in approximately 1% of diabetic ketoacidosis episodes. Mortality from this serious complication is falling, but little is known of long term outcome. We describe hypopituitarism and executive dysfunction developing two years after cerebral oedema complicating diabetic ketoacidosis in a 12 year old with type 1 diabetes.

A white boy was diagnosed with type 1 diabetes at 2 years of age. Compliance with treatment was poor and hospital admissions were frequent. Transient left facial palsy and hemiparesis followed a hypoglycaemic episode at 7 years. At 12.9 years he was admitted with diabetic ketoacidosis (DKA)—arterial pH 7.1, plasma glucose 39.2 mmol/l. After six hours of intravenous fluids and insulin, the level of consciousness fell necessitating transfer to intensive care for ventilation. Episodes of hypertension and bradycardia occurred. Twenty hours later he developed unequal and dilated pupils and was treated with hyperventilation, intravenous mannitol, morphine, diazepam, and phenytoin. The pupillary responses normalised 45 minutes later and a computed tomography (CT) scan of the brain was normal. Electroencephalogram showed slow background activity with superimposed drug induced artefact, brisk responses to auditory and tactile stimuli, and no epileptiform focus. Consciousness was regained after 72 hours.

Extubation was unsuccessful because of laryngeal granulomatosis. A tracheostomy was performed. He left intensive care after 13 days; neurological examination was normal. Psychological and psychiatric assessments two and 11 days later respectively revealed attention difficulties and problems with topographical orientation and memory. He had urinary incontinence intermittently. One month later he went home. Diabetic control improved, with glycosylated haemoglobin (HbA1c) falling from 8.8% to 7.8% (non-diabetic range 3.0–5.3%) after six months, and insulin requirements from 1.1 units/kg/day to 0.8 units/kg/day.

Neuropsychological assessment utilising standardised psychometric tests, interviews, and accounts of his performance of everyday tasks revealed signs of dysexecutive syndrome, usually caused by damage to one or both frontal lobes of the brain. His abilities to plan and meaningfully organise material were affected and he was unable to read subtle social clues or to respond in socially appropriate ways.

Height velocity (Htvel) one year immediately before admission was 3.6 cm/year, and fell to 2.8 cm/year and 2.3 cm/year over the next two years (fig 1), during which time weight increased from the 50th to 97th centile, and genital development advanced from Tanner stage 1 to 3.

At 15.2 years insulin-like growth factor 1 (IGF-1) was 3 nmol/l, free thyroxine (FT4) 10.8 pmol/l, and thyroid stimulating hormone (TSH) 1.6 mU/l. Peak luteinising and follicle stimulating hormones were 20.3 U/l and 4.0 U/l

Figure 1 Patient's height record showing introduction of growth hormone and thyroxine treatments. The 3rd, 50th, and 97th centiles for height, with reference to data from Buckler-Tanner 1995, are depicted. rhGH, recombinant human growth hormone therapy commenced at age 15.4 years; T4, levothyroxine treatment commenced at 16.5 years.

respectively after stimulation with gonadotrophin releasing hormone. A testosterone primed insulin tolerance test (minimum plasma glucose 1.6 mmol/l) produced a peak serum cortisol of 722 nmol/l and growth hormone of 8.2 mU/l. TW2 bone age was 1.8 years behind chronological age.

Recombinant human growth hormone therapy was commenced at 15.4 years, a small increase in Htvel to 4.0 cm/year was achieved. At 16.5 years FT4 was 6.4 pmol/l and TSH

Abbreviations: CT, computed tomography; DKA, diabetic ketoacidosis; FT4, free thyroxine; Htvel, height velocity; IGF, insulin-like growth factor; TSH, thyroid stimulating hormone

1.4 mU/l. Levothyroxine sodium treatment was started. After seven months Htvel was 6.0 cm/year (fig 1). There were no changes in social or family circumstances at the onset of treatment to account for the change in height velocity. Genital development has continued to progress.

A magnetic resonance imaging scan of the head at 18.4 years of age showed no structural abnormality of the frontal lobes or hypothalamus/pituitary.

DISCUSSION

Little is known of long term outcome in the increasing number of survivors of cerebral oedema complicating DKA in childhood. A recent survey showed 25% mortality.¹ Of survivors 40% had serious neurological sequelae, motor problems being commonest. Learning difficulties also occurred but hypopituitarism was not reported.

The patient presented developed both hypothalamopituitary axis and frontal lobe damage despite a normal CT scan. It is known that neurological deterioration can precede radiologically visible cerebral oedema.² The evidence for growth hormone deficiency comprised a decreasing height velocity during a period of pubertal advancement, low growth hormone concentrations following hypoglycaemic stimulation (in contrast to high growth hormone concentrations commonly seen in type 1 diabetes), a low IGF-1 concentration, improved HbA1c concentration despite falling insulin requirements, and an acceleration in height velocity with treatment.

Intracerebral crises during the treatment of DKA have been reviewed by Rosenbloom.³ He found that over 50% treated early for neurological deterioration survived normal or mildly disabled (13 of 23) in contrast to only 3 of 46 treated late or not at all.

One child has been reported with hypothalamopituitary deficiency, residual right sided hemiplegia, and aphasia subsequent to confirmed cerebral oedema with DKA at age 4 years.⁴ CT scan three weeks later revealed resolution of the oedema but infarction of left temporal, thalamic, and hypothalamic areas. At 7 years old endocrine evaluation revealed isolated growth hormone deficiency which was felt to be a result of hypothalamic dysfunction.

Two children have been reported to develop hypothalamopituitary insufficiency following clinically suspected cerebral oedema and acute encephalopathy with DKA. One was 5 years old.⁵ CT scan 36 hours after neurological signs developed

revealed ischaemia in the posterior cerebral artery territory but no oedema. Visual impairment persisted 12 months later. From the second month onwards tertiary hypothyroidism, precocious puberty, and growth hormone and corticotrophin deficiencies were present, explained as following vascular hypothalamic damage. The second child, who was 15 years old, developed optic atrophy and deficiencies of TSH, gonadotrophic, adrenocorticotrophic, and antidiuretic hormones.⁶

Executive deficits often follow head injury with or without cerebral oedema. Our patient's hypopituitarism and cerebral impairment were probably linked to ischaemia of the hypothalamopituitary and frontal brain areas. We are not aware of other reports of these problems coexisting following cerebral oedema in DKA. Where cerebral oedema occurs it is important to recognise the possibility of hypothalamopituitary dysfunction as well as psychological problems in survivors.

Authors' affiliations

K A Dunlop, D Woodman, Royal Belfast Hospital for Sick Children, Northern Ireland, UK

D J Carson, Department of Child Health, Queens University, Belfast, Northern Ireland, UK

Correspondence to: Dr D J Carson, Department of Child Health, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ, Northern Ireland, UK; d.carson@qub.ac.uk

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