

Effect of thyroxine on elevated creatinine levels in central hypothyroidism

This report describes the case of a newborn male infant with elevated creatinine levels, initially attributed to renal failure. Further investigation revealed panhypopituitarism secondary to an ectopic posterior pituitary. The creatinine levels returned to normal following treatment with thyroxine. The diagnosis and possible pathogenesis are discussed.

Adnan Zafar¹

BSc, MBBS, MRCPCH
Neonatology Registrar
adnan157@doctors.org.uk

Sundaram Janakiraman¹

MRCPCH, MBBS
Consultant Neonatologist

Jawad Sultan Raja²

MBBS
Senior House Officer

¹University Hospital of North Tees,
Stockton on Tees

²Tees, Esk and Wear Valleys NHS
Foundation Trust

A newborn male infant, who was born at term with a birth weight of 3kg and a head circumference of 32cm, was admitted to the neonatal unit at almost eight hours of age with severe hypoglycaemia and a cyanotic episode. On admission to the unit:

- A clinical examination revealed a floppy and peripherally cyanosed baby with an oxygen saturation of 85-88%
- Echocardiography did not reveal abnormality
- A systemic examination was unremarkable, with no dysmorphic features and normal male external genitalia
- The infant was hypoglycaemic; a venous sample showed a blood glucose level of 0.3mmol/L (a normal level is >2.5mmol/L). The infant was given a dextrose bolus and needed a 12.5% dextrose infusion to maintain blood sugar
- First line metabolic investigations revealed:

- a raised blood ammonia level of 163µmol/L (normal, <50µmol/L)
- a lactate level of 0.7mmol/L (normal, <2.5mmol/L).

Complete screening for inborn errors of metabolism was unremarkable but screening for hypoglycaemia yielded the following results:

- Growth hormone level, 3.5ng/mL (normal range, 15-20ng/mL)
 - 17-hydroxyprogesterone (17-OHP) level, 18.8nmol/L (normal, <5nmol/L). Note, in children with congenital adrenal hyperplasia, 17-OHP values are >100nmol/L
 - Serum insulin level, 2.4mU/L (normal range, 1.6-10.9mU/L)
 - Low serum adrenocorticotrophic hormone (ACTH, <5ng/L)
- The infant was started on antibiotics for

suspected sepsis soon after admission. His creatinine level started becoming abnormal on day 2, ranging between 74-230µmol/L (normal, <50µmol/L). This was initially attributed to renal failure as right-sided renal pelvic dilation was seen on antenatal scans.

Oral feeds were introduced on the third day of life; however the infant deteriorated and developed hyponatraemia (low blood sodium), hyperammonaemia and direct hyperbilirubinaemia with sustained elevated creatinine levels. His potassium value remained within the normal range. A very low random cortisol level (31nmol/L) indicated adrenal insufficiency and, as a result, he was treated with hydrocortisone.

A cranial ultrasound examination did not reveal any pathology but abdominal ultrasound confirmed the right-sided renal pelvic dilation with no dramatic increase in size compared to the antenatal measurements.

Following hydrocortisone initiation, the infant's sodium, glucose and urea levels started to normalise but the serum creatinine level remained elevated. A screening for hypopituitarism was performed; thyroid stimulating hormone (TSH) levels were variable:

On day 4:

- TSH = 1.24mIU/L (normal range for a full term newborn, 1.3-16mIU/L)
- Free thyroxine (FT4) = 10pmol/L 11-33pmol/L)

On day 11:

- TSH = 2.50mIU/L
- FT4 = 8pmol/L

Following discussion with a paediatric endocrinologist, the infant was started on thyroxine on day 11. By this time he was clinically stable and fit to undergo a

Keywords

central congenital hypothyroidism; creatinine; hypopituitarism; ectopic posterior pituitary

Key points

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1. This case considers an infant with congenital hypopituitarism.
2. Elevated creatinine in central hypothyroidism is a known phenomenon however its reversal with thyroxine has not been previously seen.
3. It is postulated that lack of thyroxine in central hypothyroidism may cause elevated creatinine levels.

magnetic resonance imaging (MRI) scan that revealed panhypopituitarism secondary to an ectopic posterior pituitary. After starting thyroxine, the creatinine level started to fall and within two days of starting treatment, it was within the normal range.

Discussion

This report describes the case of a newborn male infant with elevated creatinine levels, initially attributed to renal failure, but later revealed as panhypopituitarism secondary to an ectopic posterior pituitary.

Babies born with congenital hypopituitarism can present in a variety of ways¹, the most common presentations are acute adrenal crisis, hypogonadism, failure to thrive and rarely SIADH (syndrome of inappropriate antidiuretic hormone secretion).

Hypopituitarism – a lack of one or more pituitary hormones – can affect all hormones of the anterior and posterior pituitary, in which case the term panhypopituitarism applies. A lack of the pituitary hormone TSH, leads to insufficient stimulation of the thyroid gland and thyroid hormone deficiency – central hypothyroidism (compared to primary hypothyroidism, which is caused by inadequate function of the gland itself). Thyroid hormone replacement is a vital part of management of panhypopituitarism because hypothyroidism can have multi-systemic effects. The infant was referred to a paediatric endocrinologist for long-term management of his condition.

In the setting of hypopituitarism, elevated creatinine levels along with hyponatraemia can be mistaken for adrenal

insufficiency or renal failure secondary to antidiuretic hormone deficiency. The infant's elevated creatinine level was considered to be either the result of pre-renal failure or from an obstruction that could have caused renal pelvic dilation on antenatal scans. Despite treatment with hydrocortisone for presumed adrenal insufficiency, the creatinine level continued to be elevated. The infant's sodium levels and other renal parameters settled by this time. It was only after starting thyroxine that his creatinine level normalised.

Elevated creatinine levels in hypothyroid infants and reversal with thyroxine is known for primary hypothyroidism but has not been previously reported for central hypothyroidism in children. In one study, hypothyroid infants with primary thyroid disorder aged up to one month were divided into mild/moderate and severely hypothyroid groups according to their TSH and T4 levels². In both groups, creatinine levels reversed after treatment with thyroxine.

Basement membrane thickening in the kidneys has been seen in hypothyroid individuals³. This could cause physiological changes, which include decreased renal plasma flow and decreased glomerular filtration rate (GFR). Decreased GFR in turn results in elevated creatinine levels. In a study on an adult population, this decreased GFR was reversible with thyroxine replacement⁴, although a recent study in a paediatric population was inconclusive⁵.

One explanation for the improvement of creatinine levels with thyroxine is its action on the renin-angiotensin system. Low renin levels are seen in hypothyroidism

and thyroid hormone treatment is thought to be associated with an increased angiotensin receptor density in the kidneys. This could account for improved filtration and secretion and hence improvement in the creatinine level. In the infant presented in this case, urea and sodium levels normalised after starting hydrocortisone therapy but there was no change in creatinine – the creatinine level returned to normal only after starting thyroxine therapy.

Conclusion

An elevated creatinine level is a known phenomenon in central hypothyroidism however its reversal with thyroxine has not been previously reported.

Reversibility of creatinine levels with thyroxine is compelling evidence for an association of elevated creatinine with central congenital hypothyroidism.

References

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