

Congenital hypothyroidism with seizures: a case report

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Abstract

Congenital hypothyroidism (CH) is defined as thyroid hormone deficiency, present at birth. It is seen in 1:4,000 births and is caused by an anatomical defect, known as thyroid dysgenesis (underdevelopment or unusual location of the thyroid gland), by abnormal biosynthesis of the thyroid hormones (dysmorphogenesis), inborn errors of metabolism, genetic mutations or iodine deficiency. If untreated, severe neurological impairment develops. However, newborn screening programs have improved outcomes greatly, through early diagnosis and treatment. Clinical manifestations are often subtle at birth, due to the placental transfer of thyroxine (T_4), thus making diagnosis in the first few days of life difficult. Increased levels of thyroid stimulating hormone (TSH) and low levels of T_4 are confirmatory for this disorder.

We describe the case of a baby with CH who presented with neonatal seizures: a rare clinical presentation. Our case highlights the need to eliminate CH, as a cause of seizures, so that treatment can be initiated even more promptly to optimize neurological sequelae and outcome.

Keywords

Congenital hypothyroidism, seizures, neurological, amplitude-integrated electro-encephalography, BrainZ monitor, thyroxine.

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Background

The thyroid gland, one of the largest endocrine organs in the body, is situated just below the larynx and has two butterfly-shaped lobes, which contain follicles. These are its functional components. Thyrotropin-releasing hormone (TRH) is a hormone, produced by the hypothalamus, which stimulates the release of thyrotropin (thyroid-stimulating hormone or TSH) and prolactin from the anterior pituitary. TSH acts on the thyroid gland to produce thyroglobin, the precursor for the two thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). These hormones are responsible for regulation of metabolic processes as well as growth and energy use [1]. Although less abundant, the latter is the more potent and is the one that interacts with the target cell. Dietary iodine is required for thyroid hormone synthesis and it is a split by the tissues of one iodine atom that converts T_4 to T_3 . Another function of this gland is to produce calcitonin, which in conjunction with the parathyroid hormone preserves or releases calcium from the bones [1].

Introduction

Congenital hypothyroidism (CH) is defined as thyroid hormone deficiency present at birth [2]. It is seen in 1:4,000 births and is caused by an anatomical defect, known as thyroid dysgenesis (underdevelopment or unusual location of the thyroid gland), by abnormal biosynthesis of the thyroid hormones (dyshormogenesis), by inborn errors of metabolism, genetic mutations or iodine deficiency. Thyroid dysgenesis accounts for 80-85% of cases [3-5]. Raised thyroid stimulating hormone (TSH) levels and low levels of T_4 confirm this disorder. If CH remains untreated, severe neurological impairment develops [2]. Fortunately, newborn screening programs worldwide have improved outcomes greatly, through early diagnosis and treatment [5]. Clinical manifestations, which are often subtle at birth due to placental transfer of T_4 , include lethargy, sluggishness, hoarse cry, feeding problems, constipation, macroglossia, large fontanelle, umbilical hernia, hypotonia, delayed bone age, dry skin and hypothermia (Fig. 1) [5]. We describe the case of a neonate, born in 2012, who developed CH and presented with seizures, a phenomenon reported only twice before in the literature [6, 7]. A similar case has since been described by Sharma et al. (2014), whereby the rare association of CH and seizures was seen but also

included pseudo-Hirschprung's disease as part of the diagnosis [8].

Presentation of our case

The male infant was delivered at 41⁺² weeks gestation, by emergency caesarean section for failure to progress. Apgar scores were 8 at 1 minute and 9 at 5 minutes. The neonate was admitted to our unit at day 4 with abdominal distension and umbilical flare. Investigations revealed no obstruction or sepsis. His mother had been treated throughout her pregnancy with thyroxine for a mildly elevated TSH level (4.1 mU/L). On day 7, the baby had apnoeic spells intermittently for a period of 12 hours, with bradycardia and desaturations noted on his monitor. These episodes ceased spontaneously. However, he then had periods of sharply defined respiratory movement followed by sucking, lip smacking, eye rolling and then a smile. Two very brief periods of seizure activity thereafter were captured on amplitude-integrated electro-encephalography (aEEG) by means of a BrainZ monitor (Fig. 2). Electrolytes and blood glucose levels were normal during this episode. Anti-convulsant therapy was not required. His neonatal screen result was suggestive of CH, with confirmation on thyroid function tests (TFTs) (TSH > 500 mU/L and T_4 < 3.2 pmol/L). Oral thyroxine was introduced at 15 micro-grams/kg daily until blood levels had stabilized. Ultrasound of his thyroid gland showed it to be small and irregular. Magnetic Resonance Imaging (MRI) and electro-encephalogram (EEG) were carried out in the first week of life and the results were normal. However, he referred bilaterally on routine hearing screening. On further audiology assessment, congenital deafness was confirmed. Pendred syndrome, a genetic disorder, characterized by sensori-neural loss with CH, inner ear abnormalities and goitre was considered [5]. However, this was ruled out due to his normal ear findings, timing of deafness and the genetic nature of this disease. He was discharged home at 2 weeks of age, thriving well. Bilateral hearing aids were fitted with good progress demonstrated at follow-up reviews, with all growth and developmental milestones being met appropriately.

Discussion

A number of prenatal and neonatal conditions, such as intra-uterine ischaemia, congenital viral infections, cardio-respiratory compromise and

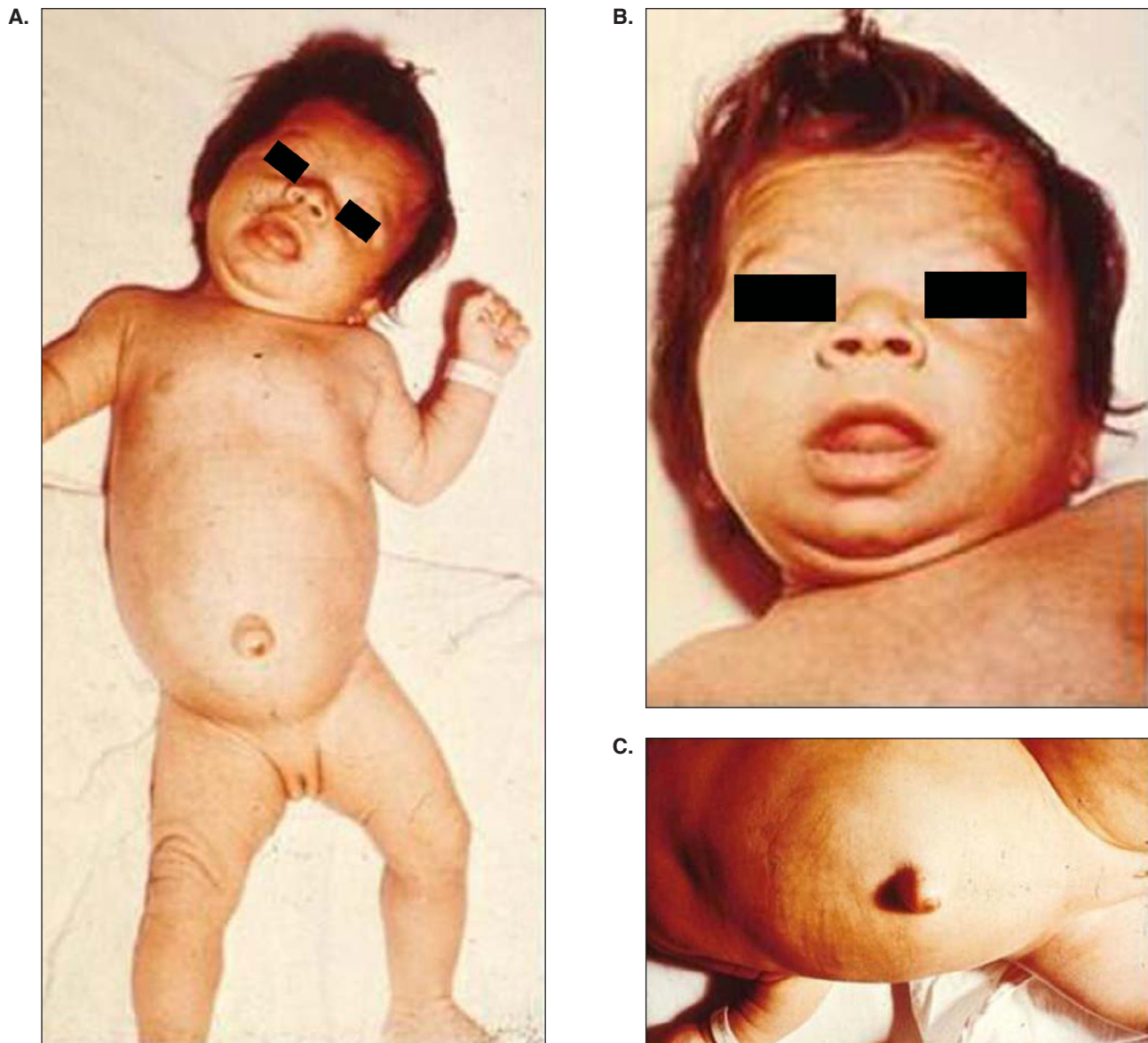


Figure 1. Neonate with features of hypothyroidism: dry skin, macroglossia, abdominal distension, umbilical hernia and hypotonia (A, B, C).

intra-cranial haemorrhage, can be associated with convulsions, as can a variety of postnatal conditions [6]. However, CH had never been linked to seizures in babies previously, until Aly et al. described one such case [6]. Their term male infant was born to a diet controlled gestational diabetic mother, on anti-depressant therapy, who had been treated previously for hypothyroidism. She received one dose of ampicillin for positive group B streptococcus status, prior to delivering by emergency caesarean section for thick meconium stained liquor, a non-reassuring fetal heart rate and failure to progress. Her baby required respiratory support briefly and chest radiograph was normal. At day 6, he had seizures with a

coarse inspiratory stridor. The seizures were unresponsive to anticonvulsant therapy initially. However, when controlled, his medication was ceased. He was diagnosed with CH and was treated with thyroxine. His neurological evaluation was normal at 6 months of age.

The second case, in 2009, involved a mother with autoimmune hypothyroid disease, who was non-compliant with treatment [7]. She delivered a female term infant, who required positive pressure ventilation for poor respiratory effort at birth and was also treated for sepsis. On day 2, she developed seizures, which lasted an hour, despite administration of anticonvulsants. A lidocaine infusion eventually contained them.

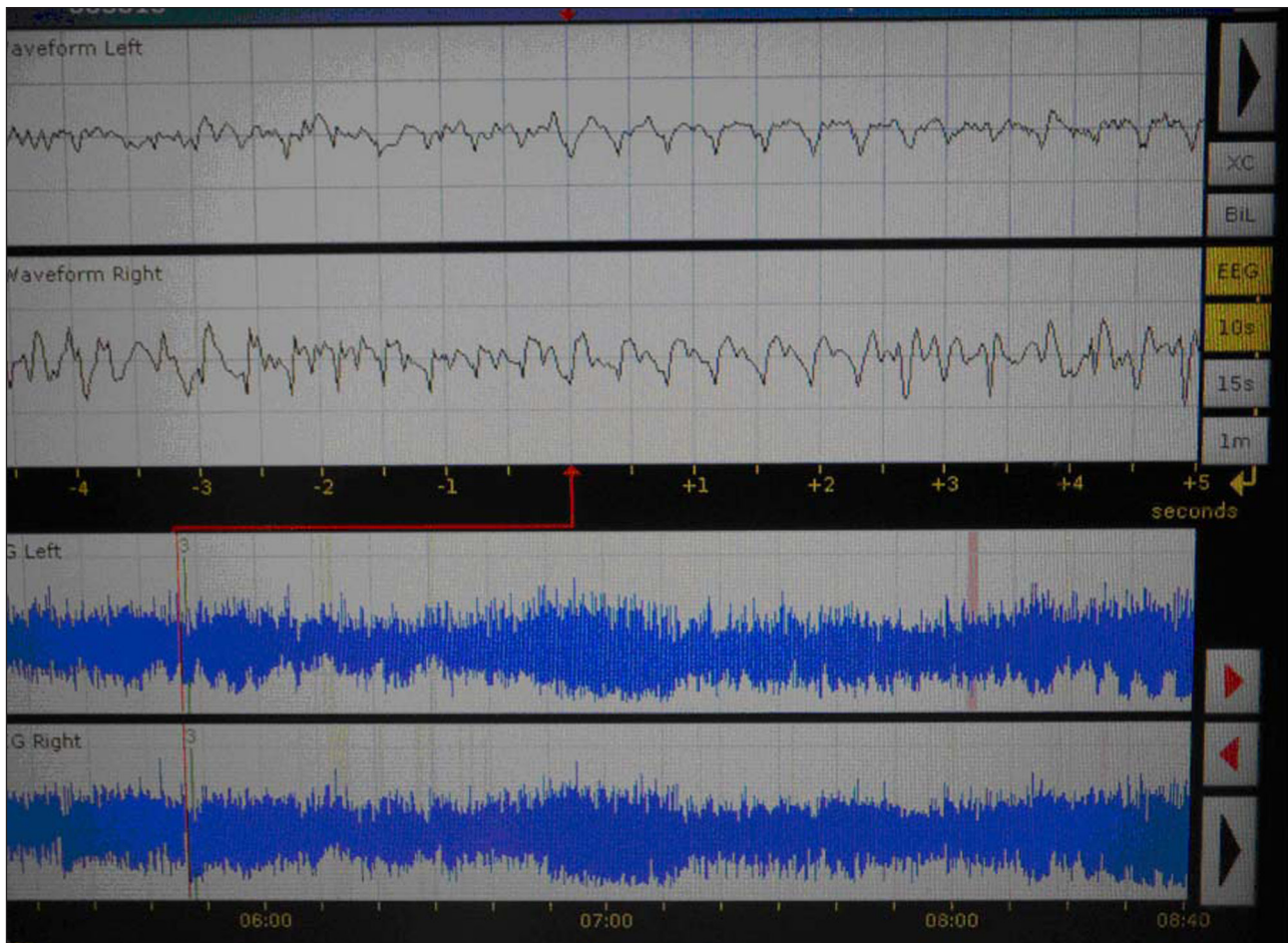


Figure 2. Rhythmic discharges are seen on the raw electro-encephalogram (EEG), indicating seizure activity.

Investigations to rule out other causes of seizures were normal, as were both MRI and EEG. TFTs, however, confirmed the diagnosis of CH. This mother had low thyroxine levels and therefore, not surprisingly, her baby showed evidence of developmental delays.

A paucity of literature exists with regard to neonatal seizures in association with CH. However, several animal studies have demonstrated a strong possible link, with neural cells being found at aberrant locations [6]. A Spanish study by Navarro et al., in 2015, demonstrated altered behaviour in hypothyroid rat pups, with abnormalities of both the hippocampus and somatosensory cortex [9]. The results of these studies indicate a possible pathophysiological basis for seizures.

Conclusion

Just as with the other cases described, our case provides evidence that CH can present with seizures in the neonatal period. Our “take-home

message” would be to consider performing TFTs as part of the investigative process for neonatal convulsions. Hence, treatment for hypothyroidism can be commenced even before neonatal screening test results are available. This would give an earlier edge to maximizing the baby’s neurological sequelae and outcome.

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Ethics

Ethics approval has been obtained through our hospital ethics committee.

Declaration of interest

There have been no conflicts of interest in writing the article, with no funding required.

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