

Short reports

Congenital hypothyroidism missed on screening

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SUMMARY Three patients with congenital hypothyroidism missed on routine screening due to normal low thyrotrophin concentrations in the neonatal period presented in later childhood. Clinicians should remain aware of hypothyroidism as a cause of morbidity in early childhood despite a national screening programme.

Screening for congenital hypothyroidism started in Northern Ireland in January 1980. Over the last five complete years 137 612 infants have been screened and 33 patients diagnosed hypothyroid. The annual incidence of one in 4170 live births is similar to the experience in other European centres.¹ During the same period, three patients with normal screening tests taken between seven and 10 days after birth were diagnosed clinically hypothyroid at 7-33 months of age. These patients were born in 1981 when the screening policy was to measure whole blood thyroxine concentrations in duplicate on all samples and follow up the lowest 20% with an estimation of whole blood thyrotrophin concentrations in duplicate. Patients with thyrotrophin concentrations ≥ 25 mU/l were recalled for examination and further investigation. The screening method was subsequently changed to measuring thyrotrophin concentrations alone on all patients, a practice followed by most centres in the United Kingdom, as it is generally agreed that thyrotrophin screening will identify more patients with hypothyroidism than

thyroxine screening.² However, the following case reports of patients missed on neonatal screening have important implications when a raised thyrotrophin concentration is used as the only indication for recall.

Case reports

The initial neonatal screening results are summarised in Table 1. All three patients had thyroxine concentrations in the lowest 20% range, so thyrotrophin estimations were performed in duplicate from the same whole blood sample. As the thyrotrophin concentration was not raised no further action was taken.

All three patients, born at term by normal delivery, had symptoms from early infancy consistent with hypothyroidism, most notably prolonged jaundice, feeding difficulty, and lethargy. Diagnosis was delayed until 7-33 months of age, by which time obvious hypothyroid facies, short stature, delayed developmental milestones, and delayed bone age were present. Thyroxine replacement therapy was started with dramatic clinical improvement in each case.

When patients were over 3 years old they were assessed by standard intelligence tests. After withdrawing thyroxine for a short period a radioisotope scan (¹²³I) was performed. These results are summarised in Table 2. None of the patients had circulating thyroid antibodies, and their mothers had no evidence of thyroid or autoimmune disease.

Table 1 Neonatal screening results and age at clinical presentation

Case No	Sex	Age (days)	Thyroxine (nmol/l)	Thyrotrophin (mU/l)	Age at diagnosis (months)	Bone age at diagnosis (Greulich and Pyle)
1	M	7	41	<25	7	38 weeks' gestation
2	F	8	38	<25	33	6 months
3	M	10	53	<25	33	6 months

Conversion: SI to traditional units—Thyroxine: 1 nmol/l = 77.7 µg/100 ml.

Table 2 *Results of intelligence tests and effects of thyroxine withdrawal*

Case No	Age (years)	Stanford Binet intelligence scale	Duration of thyroxine withdrawal (days)	Serum thyroxine (nmol/l)	Serum thyrotrophin (mU/l)	¹²³ I Scan
1	3.6	89	24	16	87	Athyreosis
2	3.3	95	37	11	380	Hypoplastic
3	3.3	100	37	15	390	Ectopic

Conversion: SI to traditional units—Thyroxine: 1 nmol/l ≈ 77.7 µg/100 ml.

Discussion

Three patients with congenital hypothyroidism are presented who were not diagnosed by routine neonatal thyrotrophin screening despite symptoms consistent with that diagnosis from birth. The most severely affected patient both clinically and on intelligence testing on follow up was found on subsequent investigation to have no functioning thyroid tissue on radioisotope scan. The two patients both diagnosed at 33 months of age with hypoplastic or ectopic glands showed dramatic physical and intellectual improvement with thyroxine replacement therapy. This more prolonged presentation with less morbidity is consistent with some endogenous thyroxine production during the critical period of brain growth in infancy and agrees with a previous report of higher intelligence quotients in patients diagnosed at 2 years compared with those diagnosed between 6 and 9 months of age.³

Why were low thyroxine concentrations on screening not associated with rises in thyrotrophin concentrations in the neonatal period? All screening procedures are subject to human and laboratory error, which are difficult to exclude retrospectively.⁴ Unfortunately, the original samples were not available for retesting as four tests of thyroid function (thyroxine and thyrotrophin in duplicate) had been performed on the original dried blood spots. The sample still remaining had been autoclaved as a routine procedure to denature haemoglobin before phenylalanine screening and was therefore unsuitable for repeat estimation of thyrotrophin concentration. All samples, however, were measured in duplicate by reliable assays. No patient was preterm or breast fed, and no mother had evidence of thyroid disease. A normal increase in thyrotrophin concentrations was shown after withdrawal of treat-

ment at 3 years of age. The probability remains that these patients had an abnormally slow rise in thyrotrophin concentrations after birth. Similar patients have been described and the suggestion made that the cause may be immaturity of the hypothalamic-pituitary-thyroid axis.⁵

The present hypothyroid screening policy, using thyrotrophin alone, adopted throughout most centres in Europe will not detect these patients unless a second screening test is routinely repeated after a few weeks. Alternatively, thyroxine concentrations could also be measured routinely on all samples and low thyroxine results followed or investigated. Either procedure would greatly increase the time and expense of screening and so is unlikely to be undertaken routinely. It is important therefore, that clinicians continue to remain aware of hypothyroidism as a potential cause of illness in infants despite a national screening programme.

References

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