

Congenital anomalies associated with hypothyroidism

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SUMMARY Seven of the 34 infants identified through the Welsh Hypothyroid Screening Programme have additional congenital abnormalities. Two infants have a previously undescribed syndrome, two have chromosomal abnormalities, two have congenital heart disease, and one has a myelomeningocele. Congenital hypothyroidism often seems to be associated with other congenital abnormalities.

Methods

All infants born in Wales since 1981 have been screened for congenital hypothyroidism through the Wales Congenital Hypothyroid Screening Programme.

Blood is taken from infants by heel stab at 6 days of age onto standard filter paper cards, which are then mailed to the newborn screening laboratory at the University Hospital of Wales. Half the sample is used for phenylketonuria testing and the remainder for thyrotropin assay by the regional radioimmunoassay service.

When a sample in which the thyrotropin concentration exceeds 20 mU/l is identified a serum sample from the infant is requested; estimation of thyrotropin and free thyroxine concentrations is performed. If the thyrotropin concentration exceeds 20 mU/l on the second sample the child is examined by a paediatrician and a thyroid scan and *x* ray film of one of the lower femoral epiphyses are requested before thyroid hormone replacement therapy is started. The results, together with information concerning the health of the parents, the pregnancy, and the drug history, are recorded on a standard form, which is returned to University Hospital.

Results

Altogether, 123 200 infants have been screened for hypothyroidism since the programme began, of whom 43 infants have been recalled for further investigation. Thirty four infants had persistent primary hypothyroidism (incidence 1:3600), and nine had transient hypothyroidism (incidence 1:13 600).

Thyroid scans were obtained in 19 infants. Of these, 10 were athyreotic; four had ectopic thyroid tissue, two had increased uptake, and three had normal scans.

Seven infants (20%) with persistent primary hypothyroidism had associated extrathyroid abnormalities (Table). For comparison, the latest available incidence of congenital abnormalities in the general population in South Glamorgan for 1979–1981 was 3.9%. (Cardiff Birth Survey, 1979–81. Department of Medical Statistics, University Hospital of Wales.)

Two infants (cases 1 and 2) were brothers. They exhibited spiky hair, unilateral cleft lip and palate, bilateral choanal atresia, hypoplastic epiglottis and larynx, and long tortuous eyelashes. Neither infant had detectable thyroid tissues on I¹³² scan.

Two infants (cases 3 and 4) had chromosomal abnormalities. Case 3 had one extra chromosome 9 in which the distal end of the long arm had been deleted (47,XY + 9 del (q 32)). The child had microcephaly, large anterior fontanelle, low set ears, a large nose with a prominent columella extending below the ala, retrognathia, clinodactyly of the fifth finger, rocker bottom feet, micropenis, and prominent cutis marmorata in infancy. Two siblings, the mother, a maternal uncle, and the maternal grandmother had a balanced translocation between chromosomes 2 and 9 (t(2,9)q 37; q 32). There were no other abnormal family members. Case 4 had Down's syndrome; the chromosomal constitution was 47,XX + 21.

Two infants (cases 5 and 6) had congenital heart defects. Case 5 had a small ventriculoseptal defect, which closed spontaneously before 6 months of age

Table *Congenital abnormalities in seven hypothyroid infants*

Case No	Sex	Abnormality	Scan result
1	M	Spiky hair syndrome	Athyroid
2	M	Spiky hair syndrome	Athyroid
3	M	Trisomy 9	No scan
4	F	Trisomy 21	No scan
5	M	Ventriculoseptal	No scan
6	F	Patent ductus	Athyroid
7	M	Lumbosacral myelomeningocele	Normal scan

and did not require medical or surgical intervention. Case 6 had a patent ductus arteriosus. She developed signs of cardiac failure and was treated medically. At 6 months of age she developed pneumonia and subsequently died.

Case 7 had a large lumbosacral myelomeningocele and hydrocephalus.

Discussion

The incidence of transient and persistent hypothyroidism in Wales is similar to that reported from other centres.¹ Most centres have concentrated on congenital abnormalities of the thyroid gland. Extrathyroid abnormalities have occasionally been mentioned,² but no attempt has been made to ascertain the incidence of such abnormalities in a population of hypothyroid infants. In this series 20% of the infants with persistent congenital hypothyroidism also had extrathyroid congenital abnormalities.

Cases 1 and 2 seem to have a previously unidentified syndrome of which hypothyroidism is an integral part. They will be described in greater detail elsewhere.

Congenital hypothyroidism in Down's syndrome is well recognised; an incidence of 1:128 has been reported.³

Two children with chromosomal constitutions similar to case 3 have been described.⁴ The postmortem findings in one of the children noted the presence of 'primitive follicles' in the thyroid gland, but no details of thyroid function are available.

Two infants in the series had congenital heart disease (cases 5 and 6). Congenital heart disease is a common malformation with an incidence of 1% in the general population. In one large study of defects associated with congenital heart disease, congenital endocrine abnormalities were found in 1% of patients.⁵ Although no details of the endocrine abnormalities were given, it would be surprising if congenital hypothyroidism were not among the

abnormalities as it is the most common congenital endocrine defect.

An increased incidence of congenital hypothyroidism in neural tube defects has not been described, and it is possible that case 7 represents a chance association in view of the high frequency of neural tube defects in the region.

In conclusion, our study has shown two important points. Firstly, in a relatively small series of infants identified with congenital hypothyroidism there is an increased incidence of extrathyroid abnormalities. Secondly, three children with congenital abnormalities in this series were already physically or mentally handicapped and without routine screening hypothyroidism might not have been considered in view of the other problems. Prompt treatment has avoided adding a further handicap.

It will be interesting to see if centres with more experience of screening have also noted an increased incidence of congenital abnormalities in infants with congenital hypothyroidism.

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