Congenital hypothyroidism

Key facts

- Congenital hypothyroidism (CH) occurs because of defects in the pituitary or thyroid gland, or thyroid hormones, resulting in an absent or underdeveloped thyroid gland (dysgenesis), or a thyroid that cannot make thyroid hormone (dyshormonogenesis).
- It is common for certain subtypes of CH, such as dyshormonogenesis, to be genetically inherited.
- CH affects between 1 in 2,000 and 1 in 3,000 newborns.
- CH is more prevalent in females, affecting more than twice as many as males.
- The condition can be associated with irreversible neurological problems and poor growth if it is not detected and treated early. Prompt diagnosis and treatment results in normal growth and development in most cases.

Clinical features

Due to the presence of maternal thyroid hormones, infants are often clinically normal at birth. They can, however, present with a **wide range of symptoms** including:

- feeding difficulties;
- hypothyroid symptoms, such as lethargy and constipation;
- delayed mental development;
- learning difficulties; and
- poor co-ordination.

Common signs of the condition include:

- large fontanelles;
- myxoedema - with coarse features, a large head, and oedema of the genitalia and extremities;
- nasal obstruction;
- macroglossia;
- jaundice - prolongation of the physiological jaundice;
- umbilical hernia;
- hypotonia;
- cardiomegaly;
- pericardial effusion - usually asymptomatic;
- failure of fusion of distal femoral epiphyses;
- short stature, hypertelorism, depressed bridge of nose, narrow palpebral fissures and swollen eyelids in the growing child;
- presence of a goitre (more likely with dyshormonogenesis, thyroid hormone resistance and transient hypothyroidism); and
- other congenital defects present in 5% of cases, for example, atrial septal defects or ventricular septal defects.

Thyroid gland defects (dysgenesis)

- Accounts for 75% of all cases of CH.
- Occurs because of a missing, ectopic or poorly developed thyroid gland.
- Between 2% and 5% of cases are inherited, therefore the chances of another sibling being affected are low.

Disorders of thyroid hormone metabolism (dyshormonogenesis)

- Accounts for 10% of all cases of CH.
- Examples of this condition include thyroid stimulating hormone (TSH) unresponsiveness and defects in thyroglobulin structure.
- These conditions are usually inherited, and so there is a risk that any future siblings may also be affected.

Hypothalamic or pituitary dysfunction

- Accounts for 5% of all cases of CH.
- Pituitary hypothyroidism usually occurs with other disorders of pituitary dysfunction, for example, lack of growth hormone.
- Hypothalamic causes include tumours, ischaemic damage or congenital defects.

Transient hypothyroidism

- Accounts for 10% of all cases of CH.
- It is usually related to either maternal medications (for example, carbimazole) or to maternal antibodies. In maternal thyroid disease, immunoglobulin G (IgG) auto-antibodies can cross the placenta and block thyroid function in utero; this improves after delivery.

Diagnosis

- As part of the UK newborn screening programme, all babies born in the UK are screened using the pinprick test, which is analysed for TSH.
- A high TSH is suggestive of congenital hypothyroidism; these patients are then referred to paediatric endocrinology or a paediatrician with a specialist interest in CH.
- Infants may have an ultrasound scan of the thyroid gland, or thyroid radionuclide scanning.
- Thyroid auto-antibodies are measured.
- False positive results usually occur due to thyroglobulin deficiency and illness.
- In a small proportion of cases, thyroid hormone resistance may not be picked up by newborn screening because TSH levels can be normal.

Genetic basis and genetic testing

- Most cases of congenital hypothyroidism are sporadic, which means they occur in people with no history of the disorder in their family.
- Thyroid dysgenesis is inherited in 2-5% of cases. Two of the genes involved are *PAX8* and *TSHR*. Casual variants in these genes usually have an autosomal dominant pattern of inheritance.
- Thyroid dyshormonogenesis occurs due to variants in one of several genes involved in the production of thyroid hormones. These genes include *DUOX2*, *SLC5A5*, *TG*, *TPO* and *TSHB*. Variants in these genes have an autosomal recessive inheritance pattern.

Clinical management

- Treatment aims to detect the disease early and replace the thyroid hormone, to prevent development of irreversible neurological disability.
- Thyroxine hormone replacement with L-thyroxine is given once daily and titrated to TFTs (thyroid function tests, including TSH and T4).
- TFTs need to be monitored on a regular basis. The frequency of blood tests can be reduced after the first two years of life, once adequate replacement is achieved.
- T4 should ideally be kept in the upper half of the normal range.
- Transient congenital hypothyroidism does not need to be treated unless the low T4 and raised TSH persist beyond two weeks. Treatment is usually terminated after three to five months.

Direction to further reading, guidelines and patient groups

- British Thyroid Foundation: www.btf-thyroid.org
- American Thyroid Association: www.thyroid.org
- Screening laboratory handbook
- NHS newborn blood spot screening programme

This information is intended for educational use and was current in September 2019. For clinical management, it is recommended that local guidelines and protocols are used.

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