Acquired hypothyroidism in childhood and adolescence

- acquired hypothyroidism can be caused by both thyroid disease (primary hypothyroidism) and hypothalamic-pituitary disease (central hypothyroidism)

- furthermore, primary hypothyroidism may be either subclinical (elevated TSH and normal free T4) or overt (elevated TSH and low free T4)

Clinical presentation

- Declining growth velocity/short stature
- Abnormal pubertal development
- Altered school performance
- Other symptoms : sluggishness, lethargy, cold intolerance, constipation, dry skin, brittle hair, facial puffiness, and muscle aches and pains

Although hypothyroidism may cause weight gain, this is typically minimal and attributable to fluid retention rather than adiposity

If the cause is hypothalamic or pituitary disease, the child may have headaches, visual symptoms, or manifestations of other pituitary hormone deficiencies

Examination findings

- In primary hypothyroidism, the most common physical finding at presentation is a diffusely enlarged thyroid gland (goiter)

- Other abnormalities on physical examination may include: short stature; apparent overweight (more fluid retention than obesity); puffy facies with a dull, placid expression; bradycardia; pseudohypertrophy of the muscles; and delayed deep tendon reflexes

Laboratory abnormalities

In addition to characteristic findings on thyroid function testing, patients with primary hypothyroidism also may have:

- hyperlipidemia (most notably hypertriglyceridemia and low HDL), normocytic or macrocytic anemia, and hyponatremia

- Rarely, children may present with a myopathy and dramatically elevated serum creatine kinase levels, known as Kocher-Debre-Semelaigne syndrome

Imaging abnormalities

- Primary hypothyroidism may be associated with enlargement of the sella turcica, resulting from secondary hyperplasia of thyrotroph cells
- Occasionally, patients with severe hypothyroidism develop pericardial and pleural effusions, which may be presenting features
- As noted above, skeletal maturation (bone age) is delayed

ETIOLOGY

- *Autoimmune thyroiditis*

- The autoimmune process typically presents with a goiter, though the thyroid gland may be normal at diagnosis, or even atrophied in a minority
- If a goiter is present at diagnosis, it may persist, further enlarge, or regress over time
- Children with some chromosomal disorders or other autoimmune disorders are at increased risk for autoimmune thyroiditis : Down syndrome (trisomy 21), Turner syndrome, type 1 diabetes mellitus, celiac disease, and possibly Klinefelter syndrome

- *Disorders with transient hypothyroidism, developing after a short course of thyrotoxicosis*
- *Iodine deficiency*
- *Syndromes associated with acquired hypothyroidism :DiGeorge syndrome , Williams syndrome, Prader-Willi syndrome*
- *Late-onset congenital hypothyroidism*

- *Drugs* :

Antithyroid drugs ,Anticonvulsant drugs, Lithium , Immunomodulating or anticancer ,Iodine-rich ,Minocycline

- *Excess iodine ingestion*

- *Postablative*: Radioactive iodine therapy ,Thyroidectomy, Irradiation

- *Infiltrative diseases of the thyroid* :Cystinosis, Langerhans cell histiocytosis

- *Hemangiomas*
- *Thyroid hormone resistance*
- *Central hypothyroidism: Tumors, Meningoencephalitis, Head trauma, Irradiation*

DIAGNOSIS

Elevated TSH with low free T4 :overt primary hypothyroidism

- In children with mild elevations of serum TSH (5 to 10 mU/L), the test should be repeated before making treatment decisions

- In addition, some children with secondary (central) hypothyroidism may have a mild TSH elevation (although most patients with central hypothyroidism have normal or low TSH)

Elevated TSH with normal free T4 : subclinical hypothyroidism

- As mild TSH elevations (5 to 10 mU/L) may normalize on repeat testing
- Mild elevation of serum TSH concentration (ie, 5 to 10 mU/L) occurs in 10 to 23 percent of obese children, associated with normal or slightly elevated free T3 and normal T4 values
- Elevated serum leptin, present in children with obesity, stimulates increased transcription of the thyrotropin-releasing hormone (TRH) gene
- In patients with no evidence of autoimmune thyroiditis (normal TPOAb and TgAb), persistently elevated TSH may be caused by mutations in the TSH receptor gene
- Occasionally, are caused by confounders that affect assay measurement of TSH, such as heterophile antibodies or macro-TSH

Normal or low serum TSH with low free T4 : central hypothyroidism

- Similar results may be found with nonthyroidal illness syndrome

- A few children with central hypothyroidism have slightly high serum TSH concentrations because they secrete immunoreactive but biologically inactive TSH

TREATMENT AND PROGNOSIS

Levothyroxine dose — Initial doses:

- Age 1 to 3 years – 4 to 6 mcg/kg
- Age 3 to 10 years – 3 to 5 mcg/kg
- Age 10 to 16 years – 2 to 4 mcg/kg

most clinicians would treat until growth and puberty are complete, and then reevaluate thyroid function

Alternatively, the replacement dose can be calculated as a function of body surface area, in which case, the dose at any age is approximately 100 mcg/m2/day

- In children with longstanding hypothyroidism, rapid correction of hypothyroidism may be associated with untoward effects, in particular on behavior and an increased risk of pseudotumor cerebri

- In these cases, we recommend a slower up-titration to full dosing, for example one-quarter of the estimated full dose for four to six weeks, then advancing by a one-quarter dose increase every four to six weeks, such that full dosing is achieved by 12 to 16 weeks

For patients with subclinical hypothyroidism, treatment decisions often depend on the degree of thyroid-stimulating hormone (TSH) elevation:

- For those with TSH levels >10 mU/L, there is general agreement to treat

- There is some controversy about the need to treat children with mild subclinical hypothyroidism, characterized by TSH elevations between 6 and 10 mU/L:

- If there are clinical features likely to be associated with hypothyroidism, such as a decreasing height velocity
- presence of a goiter
- positive antithyroid antibodies
- metabolic complications such as dyslipidemia

Monitoring and dose adjustment

- For children with acquired primary hypothyroidism, serum TSH and free T4 should be checked 4 to 6 weeks after initiation of treatment and after any dose change and then every 6 to 12 months

- The levothyroxine dose is adjusted to maintain TSH and free T4 (or T4) in the normal reference range , based on experience, recommended target TSH in the lower one-half and free T4 in the upper one-half of the reference range

- For children with central hypothyroidism, only measurement of serum free T4 or T4 is generally required for dose monitoring

Adverse effects

Treatment with levothyroxine is generally well tolerated and has minimal adverse effects:

- Patients with longstanding hypothyroidism are at risk for developing pseudotumor cerebri shortly after initiation of levothyroxine treatment

- Children with more chronic (or severe) hypothyroidism also are at higher risk of temporary poorer school achievement and hyperactivity at initiation of treatment

- The potential consequences of overtreatment vary with age: Infants with open cranial sutures may develop craniosynostosis, and older children may develop adverse behavior changes and lower school performance

- Treatment does not lead to substantial changes in weight or body mass index for most children

- Both hypothyroidism and overtreatment can affect bone mineral density

Course

- Once levothyroxine therapy is started, it probably is best to continue treatment until growth and pubertal development are complete

- At that time, if there is a question of permanency of hypothyroidism (for example, in children with subclinical hypothyroidism), it can be addressed by discontinuing levothyroxine and measuring serum TSH one month later

- Hypothyroidism caused by autoimmune thyroiditis is not invariably permanent; some children treated for several years have persistently normal thyroid function after levothyroxine treatment is discontinued

Height outcomes

- Children whose hypothyroidism is diagnosed and promptly treated prior to puberty typically have good catch-up growth and normal adult height outcomes
- For children who are diagnosed and treated just before or during puberty, and who have longstanding chronic hypothyroidism, adult height may be diminished; the height deficit ranges from 8 to 14 cm