Thyroid Imaging in Infants

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KEYWORDS

• Hypothyroidism • Congenital • Newborn • Radioisotope imaging • Ultrasound

KEY POINTS

- Congenital hypothyroidism (CH) is the most common preventable cause of mental retardation.
- It is important to know the cause of each patient's thyroid dysfunction to foresee the course of therapy and outcomes.
- Imaging methods, such as ultrasound (US) and thyroid scan (TS), help determine the anatomy and function of the thyroid gland.
- Although TS is considered superior in detecting ectopic thyroid tissue, US is able to detect the presence of thyroid tissue not otherwise visualized in 15% of patients.

INTRODUCTION

Thyroid hormone is critical for normal growth and brain development. Untreated hypothyroidism in infancy is the leading cause of intellectual impairment worldwide.[1] Timing of treatment initiation is crucial to protect normal development and growth. Neonatal hypothyroidism screening was initially developed in Quebec in 1972 with the availability of a highly sensitive and specific radioimmunoassay adaptable to measuring thyroid hormone level on dried filter paper specimens. Initial newborn screening data published in August of 1978 reported the frequency of primary hypothyroidism as 1 in 4254 births. In 1992, CH was estimated to occur in 1 in 3000 to 4000 live births[2,3] and recently, rates ranging from 1:1400 to 1:2800 have been reported by screening programs in many countries, including the United States, Canada, Greece, Italy, and New Zealand.[1,4–8]

The authors have nothing to disclose.

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Endocrinol Metab Clin N Am 45 (2016) 255–266
http://dx.doi.org/10.1016/j.ecl.2016.02.005 **endo.theclinics.com**
0889-8529/16/$ – see front matter

In addition to permanent CH, newborn thyroid screening programs detect transient CH, which occurs in 5% to 10% of infants. These babies have low or normal thyroxine (T4) levels with variably elevated serum thyrotropin concentrations. Most common causes of transient CH in North America include transplacentally derived thyrotropin receptor-blocking maternal autoantibodies (1%–2%) and goitrogenic agents.[9]

The increasing incidence of CH is mostly explained by changes in screening programs. Thyrotropin cutoffs have been decreased to improve sensitivity, changed from greater than 20 μU/mL to greater than 7 μU/mL to 15 μU/mL.[10,11] Increased screening of patients at higher risk of CH has also contributed to the rise in incidence. Premature, very-low-birth-weight infants, weighing less than 1500 g, have a CH incidence of 1:153 to 1:250.[1,11–14] These babies have an immature hypothalamic-pituitary-thyroid axis and as a result are predisposed to development of transient primary hypothyroidism and the syndrome of transient hypothyroxinemia of prematurity.[9] Such infants may have a delayed thyrotropin surge at delivery and low circulating triiodothyronine (T3), T4, and free T4 (FT4).[15] Preterm newborns presenting with persistent thyrotropin values greater than 10 μU/mL develop permanent CH more frequently compared with term newborns.[7,11] Other factors, including medications (dopamine, steroids, and iodine) and blood transfusions, may contribute to thyroid dysfunction. Although hypothyroidism in very-low-birth-weight infants may be transient, permanent CH can be masked by a delayed rise in thyrotropin in these patients and rescreening is recommended.[16] In addition, risk factors for thyroid impairment include the presence of twin gestation, in vitro fertilization, respiratory distress, and other postnatal complications of prematurity.[15]

The cause of CH implied from diagnostic visualization studies can have significant implications on genetic counseling, prognosis, and treatment.[17] CH can result from thyroid dysgenesis, dyshormonogenesis, pituitary/hypothalamic hypothyroidism, or autoimmunity.[18,19] Although thyroid dysgenesis and dyshormonogenesis are considered to have an established pathophysiology, the diagnoses of transient and mild hypothyroidism are somewhat controversial.[20,21] It is necessary to make the distinction between transient and permanent hypothyroidism, because this has implications for long-term clinical management. Differentiation is usually made by a 30-day trial without LT4 treatment at 3 years of age, when cessation of LT4 is not thought to result in severe neurologic damage. Mild CH (MCH) is defined as thyrotropin less than 25 μU/mL and normal T4 and T3 levels.[20] Only 25% to 40% of MCH patients recover normal thyroid function at re-evaluation of the thyroid axis, when Levothyroxine (LT4) therapy is discontinued at 3 years.[22,23] In the remainder, MCH persists. It is possible that a significant number of behavioral and neurologic disorders recognized later in life resulting in poor school performance may be caused by unrecognized forms of neonatal CH.[5]

Labeling a patient with thyroid agenesis or ectopy and, by inference, permanent hypothyroidism means that the patient needs lifelong LT4 therapy and a trial off LT4 can be avoided if a definitive diagnosis of thyroid agenesis or thyroid ectopy has been made.[24]

Thyroid dysgenesis describes infants with ectopic, completely absent (agenesis), partially absent (hypoplasia) or morphologically abnormal glands (hemiagenesis).[9,25] Dysgenesis is the most common cause of CH, accounting for 85% of all cases; 2% to 3% of thyroid dysgenesis cases are familial and associated with mutations in the homeobox genes TTF1 (NKF2.1), TTF2 (FOXE1), and PAX8.[9] For more information on the genetics of thyroid gland development, please see Stoupa A, Kariyawasam D, Carré A, et al: Update of Thyroid Developmental Genes, in this issue.

In dyshormonogenesis, the gland is frequently present in the usual anatomic location but has impaired function.[25] Infants with dyshormonogenesis comprise 10% to 15% of newborns with CH. The defects include decreased iodine trapping, defective