The Essential Role of Thyroid Scintigraphy and High Resolution Ultrasound for The Etiological Diagnosis of Congenital Hypothyroidism

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ABSTRACT

Congenital hypothyroidism (CH) is the most common congenital endocrine disorder and is a common, preventable cause of mental retardation and growth failure if thyroid hormone replacement is ensured at the proper time and dose. It is well documented that without L-thyroxine replacement from early life, CH causes irreversible neuro-developmental impairment. The three main causes of congenital hypothyroidism are: a) dysembryogenesis, i.e., thyroid dysgenesis, b) dyshormonogenesis and c) transient hypothyroidism. Thyroid dysgenesis includes agenesis and/or the complete absence of the thyroid gland.The diagnosis of CH through new born screening (NBS) program in Bangladesh has greatly contributed to the start of treatment within an adequate time frame since 1999 but the etiological diagnosis is usually delayed until the age of 3 years.

This reported case of a 13 years old teenage girl emphasized the importance to find the etiology of her CH diagnosed on day 10 after her birth. The importance of assessing biochemical status of thyroid along with high resolution neck ultrasound (HRUS) and 99mTc-thyroid scintigraphy could change the entire scenario and ensure proper treatment of CH in a place far away from the capital city.

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INTRODUCTION

Congenital hypothyroidism (CH) is a condition that results from inadequate thyroid hormone production at birth. The three main causes of congenital hypothyroidism are dysembryogenesis, dyshormonogenesis, and transient hypothyroidism (1). Dysembryogenesis includes agenesis, i.e., the complete absence of the thyroid gland, and also an ectopically positioned thyroid gland (2). In CH patients, early diagnosis is critical for appropriate therapy planning to avoid future growth and development disorders. The determination of the etiology of CH is crucial for predicting its severity and outcome, as well as the impact of the dose of L-thyroxine during substitution. Imaging with high resolution ultrasound (HRUS) and thyroid scintigraphy and their successful interpretations are a big aid for patients with thyroid developmental anomalies of different ages and clinical presentations. Though the sensitivity and specificity of thyroid scintigraphy are high for detecting thyroid gland abnormalities, some conditions may mimic thyroid agenesis(3). Because of its simplicity, thyroid ultrasound examination is now an essential part of routine thyroid gland evaluation, but it requires a solid theoretical foundation and an experienced hand.

CASE REPORT

A 13-year-old, hypothyroid teenage girl visited the Institute of Nuclear Medicine and Allied Sciences (INMAS), Dinajpur, for routine thyroid hormone tests. She was a known case of CH since she was 10 days old, with a history of normal delivery from non-consanguinous parents who never had any thyroidal illness. Initially, her mother noticed constipation, and then medical investigations confirmed her diagnosis as a case of CH. She has been taking thyroxine (LT4) supplements in different doses from local doctors but has failed to achieve biochemically euthyroid status.

The young girl looked short statured for her age, slightly overweight rough skin, scanty and rough hair with mild mental retardation and delayed puberty (recent onset of menarche at 13 years). She was born at home to a family of low socio-economic conditions and her mother was never screened for hypothyroidism. The girl appeared

hypoactive and not interested in the surroundings with poor class performance at school.

Physical examination revealed that the patient was overweight (59 kg) with a height of 5 feet only. Mentionable physical features included short neck, slightly coarse facial features and dry skin. Vital signs were normal with no evidence of pot belly or umbilical hernia. Abdominal ultrasound revealed normal findings as well. Neurological examination showed minimal hyporeflexia of deep tendon reflexes. Pulmonary and cardiac examinations were within normal limits but her pulse rate was 90 beats /min.

Surprisingly, serum TSH measured at INMAS, Dinajpur was found lower than normal (0.08 µIU/ml). Previous serum TSH levels and irregular follow-ups since her birth (Table 1) revealed that, while the diagnosis of primary hypothyroidism was established immediately after her birth and replacement therapy with LT4 was initiated to normalize TSH levels, the doses were insufficient, with a recent overdose causing iatrogenic hyperthyroidism.

Table I: Thyroid function status of a congenitally hypothyroid girl at different time intervals of her life.

Age of the patient	Serum triiodothyronine (T3)	Serum Thyroxine (T4)	Serum TSH	Normal Reference levels	Comments
Day-10	37ng/ml	4.2 µg/dl	75.8 µIU/ml	T_3-52-185 ng/ml T_4-4.4-12 µg/dl TSH-0.50-5µIU/ml	Hypothyroidism
5 months	0.69ng/ml	11.6 µg/dl	13.9 µIU/ml	T_3-0.80-1.90 ng/ml T_4-5-13 µg/dl TSH-0.40-5.5µIU/ml	Hypothyroidism
2 years	2.73 nmol/L	148.20nmol/L	1.11 µIU/ml	T_3-1.30-3.40 nmol/L T_4-54-1.74 nmol/L TSH-0.4-4.80µIU/ml	Euthyroid Status
10 years		2.10 ng/dl	32.09µIU/ml	T_4-0.93-1.7 80 µg/dl??? TSH-0.3-4.2 µIU/ml	Sub Clinical Hypothyroidism
13 Years			32.09µIU/ml	TSH-0.7-6 µIU/ml	Hypothyroidism
13 years 3 months			0.08 µIU/ml	0.37-6 µIU/ml	Hyperthyroidism

An HRUS of neck was done with a Philips L12-5 linear probe of Philips Affiniti 70G ultrasound machine and no thyroid tissue was found in thyroid bed or other ectopic locations. Neck vessels were normal in calibre and vascularity was unremarkable in the thyroid area (Figure 1).

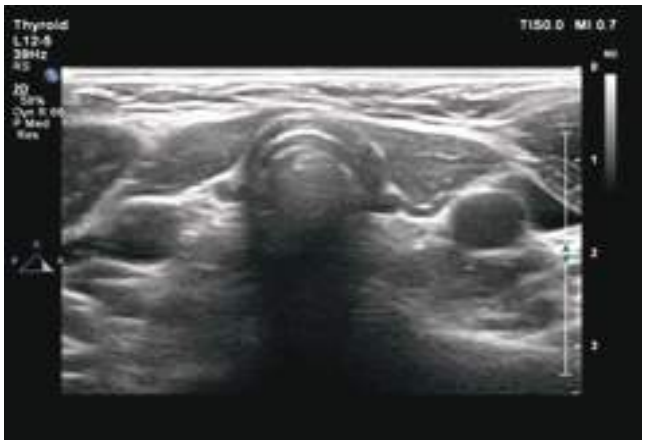

Figure 1: High resolution ultrasonography image of transverse section of neck showing a) empty thyroid bed.

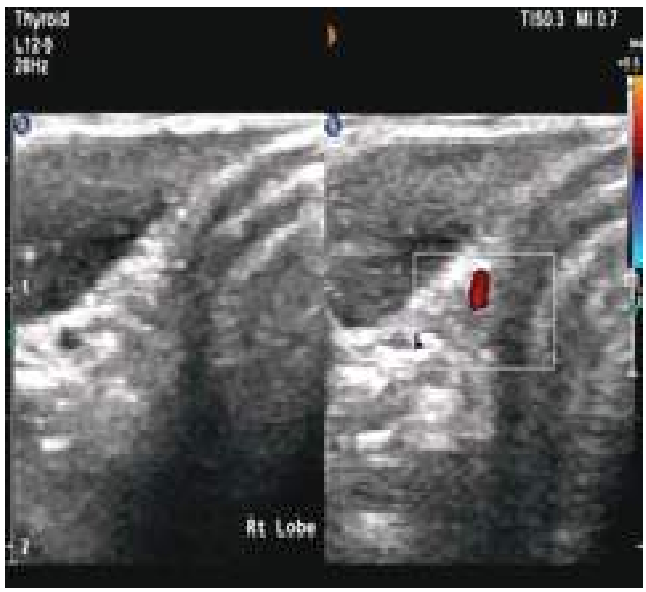

Figure 1: High resolution ultrasonography image of transverse section of neck showing b) Unremarkable vascularity in doppler mode, showing no thyroid like tissues in the areas of thyroid lobes.

After discontinuing oral LT4 for 2 weeks, a thyroid scan was done with I/V injection of 02 mCi 99mTc-pertehnetate and a waiting period of 30 minutes. Mediso Nucline TH 33 gamma camera was used for imaging and the scan images revealed no tracer concentration in the thyroid bed or in any other ectopic locations (Figure 2).

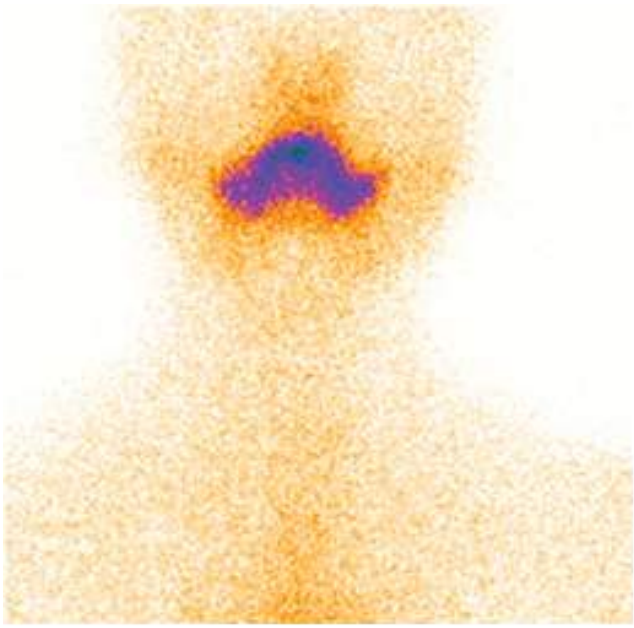

Figure 2: 99mTc- thyroid scan image showing nasal activity and bilateral salivary gland uptake of 9mTc with no radiotracer uptake in the thyroid bed or any other ectopic sites of neck, suggesting athyrosis.

DISCUSSION

Congenital hypothyroidism (CH) is a severe deficiency of thyroid hormone in newborns due to inborn errors of thyroid hormone biosynthesis (dyshormonogenesis) or improper development and/or abnormal position of the thyroid gland (dysgenesis) (4-6). It is the most common congenital endocrine disorder and a preventable cause of mental retardation. The overall incidence is about 1:4000, and among them, 85% of cases are sporadic, while 15% are hereditary (7). Thyroid agenesis is the complete absence of the thyroid gland, which is less common than ectopic glands or hypoplasia (8). Diagnosis of CH is done either by neonatal screening or estimation of hormones in a symptomatic patient showing high TSH and low levels of serum T4 and free T4 (9). Following a CH diagnosis, immediate administration of Levothyroxine is critical for newborn neuropsychological development (10). However, etiological diagnosis may be delayed until 3 years of age considering the priority to develop the central nervous system, growth, and cognitive functions first (11).

Some thyroidologists prefer the same management of CH regardless of etiology and do not search to establish a cause but in cases of an absent or ectopic thyroid gland, patients require lifelong therapy, whereas in cases of an ectopic thyroid gland, therapy can be discontinued later on. However, some parents and doctors are hesitant to stop treatment in children with CH if a scan reveals ectopic glands (12). Furthermore, patients with CH due to thyroid agenesis present with worse neuropsychological development than other causes of CH, thereby requiring higher doses of L-thyroxine (13). Thus, the determination of CH etiology is important for predicting severity, outcome, and the consequences of L-thyroxine titration and also for precise genetic counselling (14).

Thyroid ultrasonography is a cost effective, readily available, sensitive, non-invasive imaging modality which allows repeatable, safe and comfortable examination of thyroid gland without requiring patient preparation and radiation exposure (15). Despite its simplicity, ultrasonography requires sound theoretical background as well as experienced sonographer and quality equipment (16). Another weakness of this imaging tool is its limited value for the evaluation of thyroid gland function, whereas scintigraphy reflects the functional status of the gland. Takashima et al. have reported that ultrasonography showed 75% sensitivity for detecting thyroid ectopia. According to their recommendation, scintigraphy is necessary for patients with absent gland in normal location on ultrasonography to confirm ectopia and to differentiate between ectopia and true aplasia. According to their final report, careful ultrasonography of the neck in association with biochemical laboratory data is enough in more than 54% of CH patients and the indication of scintigraphy (16).

Thyroid scintigraphy is the gold standard to identify functioning thyroid tissue and provides proper functional information about thyroid gland as well as anatomical location, size, and absence (18).

Most of the guidelines recommend that scintigraphy be performed at the age of three to five years; during that period, LT4 supplementation should be discontinued for four weeks, which is also necessary for the differentiation of transient from permanent forms of CH (19-21) . Another guideline recommended that, despite administration of LT4 therapy, TSH levels may remain elevated for many days, during which time scintigraphy can be performed in the natal period when treatment has not yet been started if nuclear medicine services are available (22). Some clinicians hesitate to recommend neonatal scintigraphy for children with CH because of perturbation about delaying L-thyroxin therapy or concern about radiation exposure, or both (23).

To attain a secure diagnosis, HRUS of the neck should be performed as soon as possible and not much later, as it was in this reported case, after a long-term use of thyroid hormone supplementation. The limitation of ultrasonography is that when the thyroid is ectopic, its location is not always defined, in which case scintigraphy is superior, being effective in accurately locating the gland along the embryonic migration path (24). In the present study, we observed very good agreement between the two tests regarding thyroid location. As the thyroid gland was not visualized by HRUS of the neck, our facility could promptly allow us a scintigraphic correlation for this young girl. However, clinicians should keep in mind that scintigraphy results can be interrupted by prior exposure to iodine-containing agents or medical conditions that may mimic thyroid agenesis, e.g., autonomously functioning isthmus nodule, bilobar thyroiditis, bilateral cold nodules, or amyloidosis of the thyroid gland. In those situations, thyroid ultrasound provides higher diagnostic accuracy with higher sensitivity and specificity (25).

Thyroid agenesis patients need higher doses of medication and close monitoring, particularly early in life. The goals of treatment are to raise serum T4 as rapidly as possible into the normal range, adjust the L-thyroxine dose with growth to keep the serum T4 and free T4 in the upper limit of the normal range, and keep TSH normal, thereby maintaining normal growth and development while avoiding overtreatment (26).

CONCLUSION

Thyroid scintigraphy is more than a complementary test to ultrasonography. Following a CH diagnosis, an HRUS of the neck in the first years of life enables the diagnosis of hypoplasia or non-visualized thyroid glandbased on the clinical scenario, which may be confirmed with a thyroid scan, a simple imaging modality of Nuclear medicine.

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