# Thyroid Dyshormonogenesis Presenting with Clinical Hypothyroidism Despite Biochemical Euthyroidism: A Case Report

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## ABSTRACT

Thyroid dyshormonogenesis is an uncommon cause of congenital hypothyroidism resulting from inherited defects in thyroid hormone synthesis. Although most patients present with biochemical hypothyroidism, atypical presentations may occur. This report describes a case of thyroid dyshormonogenesis presenting clinical features of hypothyroidism despite normal thyroid function tests, emphasizing the need for further investigations. A 15-year-old boy presented with neck swelling and clinical features suggestive of hypothyroidism, but biochemical euthyroidism. Ultrasonography showed an enlarged heterogeneous thyroid gland with cystic nodules in both lobes. A 99mTc-pertechnetate thyroid scan demonstrated nonhomogeneous tracer concentration with diffuse thyroid enlargement. Radioiodine uptake testing followed by a perchlorate discharge test confirmed a defect in iodide organification consistent with thyroid dyshormonogenesis. The patient was subsequently referred to levothyroxine therapy and follow up. This case highlights an unusual clinicobiochemical discordance in thyroid dyshormonogenesis, where clinical manifestations of hypothyroidism may occur despite biochemical euthyroidism.

***Keywords:*** Perchlorate discharge test, hypothyroidism, dyshormonogenesis, thyroid scintigraphy.

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## INTRODUCTION

Thyroid hormones carry out vital functions in metabolism and control metabolic processes necessary for normal growth and development (1). Normal function of the hypothalamic–pituitary–thyroid axis, as well as sufficient iodine intake, is essential for these processes. Primary congenital hypothyroidism affects roughly one in 3000–4000 neonates, rendering it the most prevalent congenital endocrine condition (2). Hypothyroidism (including congenital forms) results most commonly from iodine deficiency (3). Congenital forms are mostly caused by defects in thyroid development, leading to thyroid dysgenesis (85%), which includes thyroid agenesis (40% of all cases), failure of the gland to descend normally during embryological development (40%), and hypoplasia of the ectopic gland (4).

Inherited errors in the synthesis of hormones (dyshormonogenesis) are a sporadic cause of congenital hypothyroidism (CH) and constitute 10-15% of children with hypothyroidism (5). Thyroid dyshormonogenesis results from a deficiency or absence of one or more of the enzymes involved in thyroid hormone synthesis or secretion. The predominant enzyme problem is the absence or deficiency of thyroid peroxidase (TPO) activity, which is incapable of oxidizing iodide to iodine (6). This deficiency results in the entrapment of iodine without its organification.

Additional defects leading to dyshormonogenesis include mutations in iodide trapping, abnormalities in the coupling of iodotyrosines, and impairments in thyroglobulin production (5). Differentiating intrinsic anatomic defects from inherited disorders of thyroid metabolism is crucial not only from theoretical and epidemiological perspectives but also for the proper management of the affected children, their prognosis, and the genetic counseling of their parents. This case report describes a case of congenital hypothyroidism with features of dyshormonogenesis detected by a perchlorate discharge technique.

The perchlorate discharge test was performed to evaluate defects in thyroid hormone organification. After oral administration of 1 cc (10 μCi) of $^{131}I$, thyroid uptake was measured at 2 hours. On the following day, 1 gm of potassium perchlorate dissolved in water was administered to the patient. Thyroid uptake was reassessed 1 hour later, and the percentage discharge was calculated according to the standard perchlorate discharge test protocol (7, 8).

## CASE REPORT

The patient was a 15-year-old boy from a rural region of Bangladesh. He was referred to the National Institute of Nuclear Medicine and Allied Sciences (NINMAS) by an endocrinologist for thyroid function testing and thyroid scan to assess neck swelling. The boy was small in stature and had a calm, pale appearance, and his parents reported that he had struggled academically since he was a young child. No significant family history was observed. He was not on any medication.

On clinical examination, he had a large diffuse goitre (figure 1). The thyroid gland was soft to firm in consistency with an irregular surface with no cervical lymphadenopathy, bruit, or retrosternal extension. Other systemic findings were unremarkable.

**Figure 1: Visible neck swelling of the patient.**

Thyroid function status of the patient revealed a normal levels of free thyroxine (FT4) at 12.37 pmol/l (normal range = 9.5–25.50 pmol/l), free triiodothyronine (FT3) at 8.65 pmol/l (normal range = 2.80–9.50 pmol/l) and thyroid-stimulating hormone (TSH) at 1.765 uIU/ml (normal range = 0.55–4.78 uIU/ml). Anti-TPO (thyroid peroxidase) antibody was performed and revealed a mildly increased level at 95.52 U/mL (normal range 60.00 U/mL).

An ultrasonogram of the thyroid gland revealed an enlarged heterogeneous thyroid gland with cystic nodules in both lobes. No calcifications were seen and involvement of any blood vessels was not observed. Furthermore, a 99mTc-pertechnetate thyroid scan was performed, which showed nonhomogeneous tracer concentration in both lobes of the thyroid gland with diffuse thyroid enlargement (figure 2).

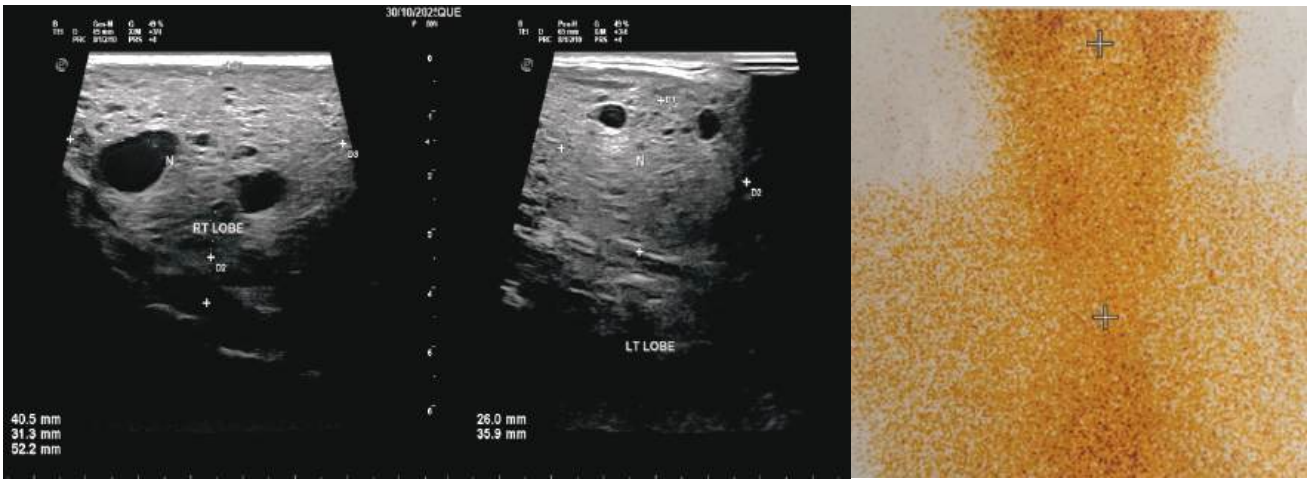


**Figure 2: High resolution neck ultrasound image showing an enlarged heterogeneous thyroid gland with cystic nodules in both lobes (A), and 99mTc-pertechnetate thyroid scan showing diffuse thyroid enlargement and nonhomogeneous tracer concentration in both lobes.**

Therefore, the patient was booked for radioactive iodine uptake (RAIU) and a perchlorate discharge test to check the thyroid uptake status. Two hours after oral administration of 1 cc (10 μCi) of Iodine-131, the radioactive iodine uptake (RAIU) was 17%. On the following day, one gram of potassium perchlorate dissolved in water was administered to the patient and radioactivity was subsequently measured. Radioactivity decreased significantly from 17% to 10%, corresponding to a 41% reduction. This decrease confirmed a defect in iodide organification into thyroglobulin. At this stage, the patient was referred for initiation of levothyroxine replacement therapy.


**Figure 3: Potassium perchlorate reagent used for perchlorate discharge test.**

## DISCUSSION

This case is notable because the patient presented with clinical features suggestive of hypothyroidism while thyroid function tests remained within the normal range, creating an important clinical and biochemical discordance. Such disagreement between clinical features and biochemical results is unusual but may occur in early or compensated stages of hormone synthesis defects. This type of presentation may occur in congenital hypothyroidism when long-standing tissue-level thyroid hormone insufficiency, delayed diagnosis, partial treatment effect, or adaptation in hormone metabolism produce symptoms and signs out of proportion to routine laboratory parameters (9). In congenital hypothyroidism, thyroid dyshormonogenesis is a well-recognized cause and results from an inborn error in one of the steps of thyroid hormone synthesis rather than abnormal gland development (10). Although thyroid dysgenesis remains the commonest cause overall, dyshormonogenesis accounts for a meaningful minority of congenital hypothyroidism cases and should be suspected, especially when the thyroid gland is present and there is supportive functional testing (11).

The occurrence of thyroid dyshormonogenesis in this patient is clinically noteworthy because it demonstrates that the presence of thyroid tissue does

not ensure effective or normal thyroid hormone production. One possible explanation is a partial defect in iodide organification, where thyroglobulin (Tg) traps iodide normally but cannot efficiently incorporate it into tyrosine residues of Tg. As a result, the gland compensates by increasing iodide trapping and hormone production, maintaining near-normal circulating levels of T4 and T3. Eventually hormone synthesis is inefficient and gland enlargement occurs (11). In the present case, the patient had clinically evident goiter despite biochemical euthyroidism, which may occur in partially compensated defects of thyroid hormone synthesis. Some patients may show severe permanent hypothyroidism, whereas others may demonstrate milder or fluctuating biochemical profiles, which can partly explain why clinical manifestations may at times appear more prominent than the laboratory abnormalities.

The perchlorate discharge test is a valuable diagnostic tool for detecting deficiencies in iodide organification. In standard thyroid physiology, iodide is actively carried into thyroid follicular cells and swiftly organified by thyroid peroxidase. When organification is impaired, iodide stays unbound within the thyroid gland. The administration of potassium perchlorate, which competitively obstructs iodide transport, results in the swift release of unbound radioiodine from the thyroid gland (12). A significant fall in thyroid radioiodine uptake after perchlorate administration indicates an organification defect, particularly involving thyroid peroxidase-related pathways (13). Therefore, in a patient with congenital hypothyroidism and preserved thyroid tissue, a positive perchlorate discharge test provides strong functional evidence for an underlying hormone synthesis defect rather than a developmental abnormality of the gland (14).

This case also emphasizes that isolated biochemical euthyroidism should not take precedence over clinical evaluation. Further etiologic assessment should be considered when symptoms and examination findings strongly suggest hypothyroidism, particularly in a patient with known congenital thyroid disease. Early recognition of dyshormonogenesis is important for appropriate management and long-term follow-up. Even in patients with biochemical euthyroidism, levothyroxine therapy may be considered to suppress TSH stimulation, reduce goiter size, and prevent progression to overt hypothyroidism (15). In addition, genetic counseling may be recommended because most forms of dyshormonogenesis follow an autosomal recessive inheritance pattern (5).

## CONCLUSION

The case presented clinical signs of hypothyroidism with goiter, despite biochemical euthyroidism, indicating a rare instance of thyroid dyshormonogenesis. A positive perchlorate discharge test suggested a partial iodide organification defect. Although this test, which requires only a small quantity of potassium perchlorate, is costly and infrequently utilized for congenital hypothyroidism assessment, continuous clinical and biochemical monitoring remains essential for evaluating thyroid function and early detection of overt hypothyroidism.

## ETHICAL APPROVAL

Written informed consent was obtained from the patient and his guardians for publication of this case report and accompanying images.

## CONFLICTS OF INTEREST

Authors have no conflicts of interest regarding this case report. The patient consented to the use of all images, which are not for further electronic distribution.

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