Case Report

Dyshormonogenetic goiter with papillary hyperplasia mimicking papillary carcinoma: A rare entity

Nasheeda Sobah[1], Shalini Kuruvilla[2]

From [1]DNB Resident, [2]Senior Consultant, Department of Pathology, Aster Malabar Institute of Medical Sciences, Kozhikode, Kerala, India

ABSTRACT

Dyshormonogenetic goiter is a rare genetically determined thyroid hyperplasia that causes congenital hypothyroidism. It occurs due to a lack of enzymes necessary for the synthesis of thyroid hormones. It is morphologically characterized by architectural and cellular pleomorphism that may mimic thyroid malignancy and cause difficulties in differential diagnosis. It occurs due to mutations in genes encoding enzymes, which participate in thyroid hormone synthesis. This is a case report of a 34-year-old male who presented with slow-growing right neck swelling for the past 5 years. Ultrasonography of the neck showed TIRAD 4 nodules, and the lesion was diagnosed as dyshormonogenetic goiter microscopically. The focal area showed papillary hyperplasia mimicking papillary carcinoma of the thyroid (PCT). Immunohistochemistry was done, and the possibility of PCT was ruled out.

Key words: Congenital hypothyroidism, Dyshormonogenetic goiter, Genes, Mutation, Papillary hyperplasia, Thyroid

Dyshormonogenetic goiter is a rare genetically determined cause of thyroid enlargement due to defects in thyroid hormone synthesis [1]. It can present with architectural and cytological atypia mimicking thyroid malignancy. The coexistence of papillary hyperplasia in dyshormonogenetic goiter can simulate papillary carcinoma of the thyroid both clinically and histologically, posing a diagnostic challenge.

Reporting this case highlights the importance of recognizing this benign mimic to avoid overdiagnosis and unnecessary aggressive treatment. This is a case report of a 34-year-old male who presented with left-sided neck swelling, which was clinically diagnosed as multinodular goiter and histologically confirmed as dyshormonogenetic goiter with papillary hyperplasia mimicking papillary carcinoma. The possibility of papillary carcinoma was ruled out using immunohistochemistry (IHC).

CASE REPORT

A 34-year-old male presented with slow-growing right-sided neck swelling for the past 5 years. There was no associated pain, breathing difficulty, dysphagia, or hoarseness of voice. He had a history of hypothyroidism since the age of 14. Since then, he has been on L-thyroxine. He underwent left hemithyroidectomy at the age of 21 for an enlarged left lobe, which was microscopically diagnosed as thyroid follicular nodular disease.

On examination, the swelling was moving with deglutition, and the skin over the swelling appeared normal. No pulsation or venous engorgement was noted.

Laboratory investigation showed an elevated thyroid-stimulating hormone (TSH) level of 34.8 ul/mL. Free T3 and free T4 levels were low, and the values were 2 pg/mL and 0.6 pg/mL, respectively. Ultrasonography of the neck showed multiple hypoechoic TI-RAD 4 nodules involving the right lobe of the thyroid gland.

Right hemithyroidectomy was done under general anaesthesia, and the specimen was sent to the pathology department. Macroscopic examination showed an enlarged right thyroid lobe weighing 150 g and measuring 6.5 cm × 6 cm × 3.6 cm. Cut section showed multiple gey-tan nodules with areas of fibrosis (Fig. 1).

Microscopy showed no normal thyroid tissue. Predominant pattern of nodules, separated by fibrous septae, was a microfollicular pattern. No colloid was noted in the follicles (empty follicles). Areas mimicking capsular invasion due to extensive fibrosis were seen. Myxoid change was noted. The focal area showed papillary hyperplasia with cells showing nuclear grooving, crowding, and overlapping (Fig. 2). Papillary carcinoma was ruled out after performing IHC CK19 and CD56. CK 19 was negative, and CD 56 was retained in the suspicious area (Fig. 3).

Access this article online	
Received - 30 September 2025 Initial Review - 24 October 2025 Accepted - 17 November 2025	Quick Response code
DOI: 10.32677/ijcr.v11i12.7892	

Correspondence to: Nasheeda Sobah, Department of Pathology, Aster Malabar Institute of Medical Sciences, Kozhikode, Kerala, India. E-mail: nasheedasobah@gmail.com

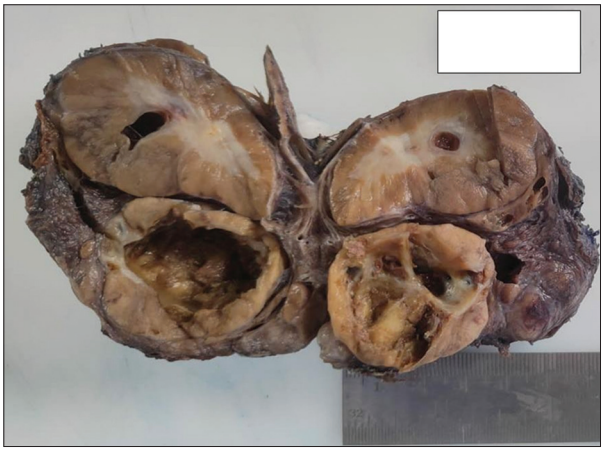

Figure 1: Gross photograph of the right hemithyroidectomy specimen showing multiple grey-tan nodules

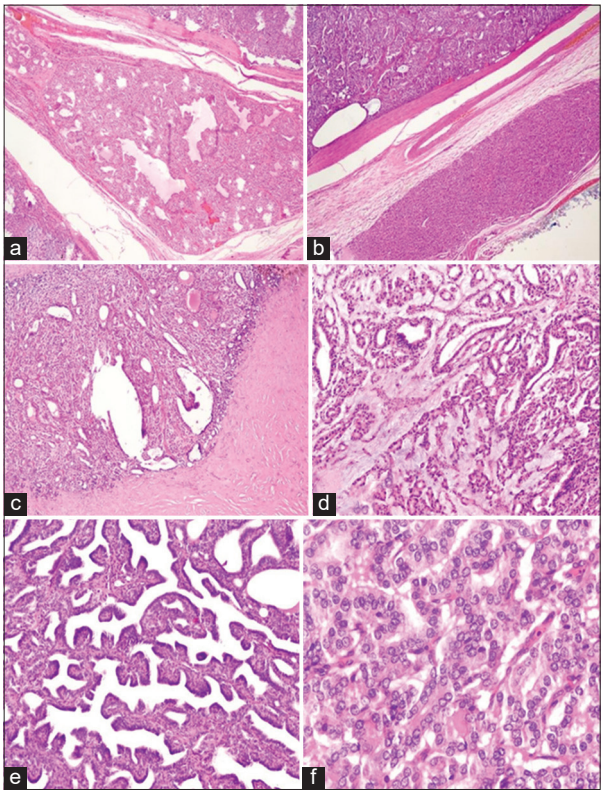

Figure 2: (a) Nodules of microfollicles separated by fibrous septae; (b) Entapped nodule mimicking capsular invasion; (c) Empty follicles surrounded by fibrosis; (d) thyroid tissue showing myxoid change; and (e) Papillary hyperplasia mimicking papillary carcinoma; (f) Nuclear features of papillary carcinoma, such as nuclear grooving, crowding, and overlapping

DISCUSSION

Dyshormonogenetic goiter is a rare entity that affects 1 in 30,000–50,000 live births, and it is the second most common cause of permanent congenital hypothyroidism [2]. It is morphologically characterized by architectural and cellular pleomorphism that may mimic thyroid malignancy and cause difficulties in differential diagnosis [3]. Thyroid dyshormonogenesis continues to be a significant cause of congenital hypothyroidism after thyroid dysgenesis [4].

There are several studies on biochemical defects involved in the pathophysiology of dyshormonogenetic goiter. They include lack of responsiveness to TSH and defects in iodide transport, organification, coupling, thyroglobulin synthesis and secretion, deiodinisation, and thyroid hormone transport. The defect in iodide organification is frequently the result of mutations in the thyroid peroxidase (TPO) gene [5]. Dual oxidase 2 and dual oxidase maturation factor 2 are the principal elements generating the hydrogen peroxide needed for TPO function. Various studies have concluded that TPO is the most common enzyme deficiency involved. Iodide transport defect includes defects in iodide trapping (NIS:Na[+]/I[−] symporter), in the facilitated iodide efflux across the apical membrane [6,7]. The impaired synthesis of thyroid hormone leads to a loss of the negative feedback to the pituitary gland, which leads to overproduction of TSH. The overproduction of TSH results in constant stimulation of the thyroid follicular cells. The clinical presentation depends on the severity of the inborn error. A severe defect will lead to neonatal or congenital hypothyroidism, goiter, mental retardation, and growth abnormalities (cretinism). Milder defects will present later in life (adolescence or young adulthood) as goiter and minimal thyroid dysfunction [8].

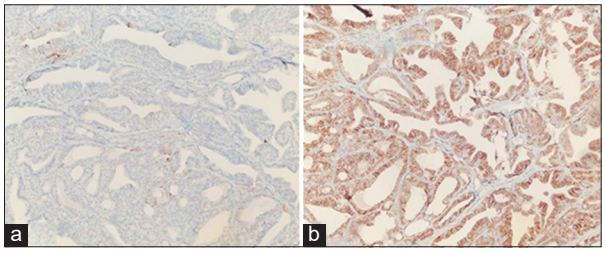

Figure 3: (a) Immunohistochemistry with CK 19 is negative in the papillary hyperplasia; (b) CD 56 is retained in the papillary hyperplasia (Hence ruled out papillary carcinoma)

Macroscopically, the thyroid gland would be multinodular and may show multiple grey-tan nodules separated by fibrous septae. Foci of thyroid cystic degeneration, thyroid hemorrhages, or myxoid changes may be seen. Histologically, the process is diffuse, without normal thyroid tissue. Features, such as papillary hyperplasia, hypercellularity, and microfollicular patterns, and decreased to absent colloid and myxoid change can be seen. The fibrosis entrapping abnormal follicles can simulate a malignancy. Irregularities at the edge of the nodules can simulate capsular invasion.

Clinically, the differential diagnosis for congenital hypothyroidism includes aplastic or hypoplastic thyroid and autoimmune thyroiditis. In this case, multinodular goiter was suspected. Dyshormonogenetic goiter can mimic follicular carcinoma or papillary carcinoma. In this case, histology showed dense fibrosis mimicking capsular invasion, and there was the presence of papillary hyperplasia mimicking papillary carcinoma of the thyroid and IHC was done for confirmation. Random nuclear atypia can occur in the form of enlarged pleomorphic nuclei with or without nuclear chromatin. These cellular changes can be mistaken for follicular, papillary, medullary, or undifferentiated thyroid

carcinoma in cytologic specimens [9]. The present case showed focal papillary infoldings and nuclear features in the area that resembled papillary carcinoma. IHC and mutational studies for BRAFV600E can help rule out the carcinoma.

Follicular carcinoma and papillary thyroid carcinoma or microcarcinoma are seldom reported in patients with dyshormonogenetic goiters. Despite the rare occurrence of thyroid carcinoma in dyshormonogenetic multinodular goiters, long-term follow-up and regular neck ultrasound imaging are recommended for early diagnosis of malignancy in dyshormonogenetic goiters.

Treatment can be medical in the form of thyroid hormone replacement or surgical if there is symptomatic enlargement. In our case, the patient was prescribed L-thyroxine 150 g after surgery. On follow-up, he is symptomatically better. Early treatment is important in severe cases to avoid mental retardation and growth Abnormalities. The prognosis is excellent with treatment.

CONCLUSION

Dyshormonogenetic goiter is a benign, rare condition that can present with a variety of architectural patterns. These patterns and cytological atypia may lead to overdiagnosis of malignancy if not well known. So this entity must be recognized in the lack of strict histological criteria of malignancy in a patient with a history of hypothyroidism since infancy. IHC can be used for confirmation. An exact molecular diagnosis allows genetic counseling and the identification of asymptomatic mutation carriers. Awareness of the clinical situation is, of course, extremely helpful, and strict histologic criteria would help to solve the dilemma.

REFERENCES

1. Rastogi MV, Lafranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis 2010;5:17.
2. Momin YA, Ansari SA. Dyshormonongenetic goiter: A rare and important entity. Arch Med Health Sci 2020;8:88-90.
3. Thompson LD. Dyshormonogenetic goiter of the thyroid gland. Ear Nose Throat J 2005;84:200.
4. Braham E, Ben Rejeb H, Marghli A, Kilani T, El Mezni F. A rare and particular form of goiter to recognize. Ann Transl Med 2013;1:21.
5. Sparling DP, Fabian K, Harik L, Jobanputra V, Anyane-Yeboa K, Oberfield SE, *et al*. Congenital hypothyroidism and thyroid dyshormonogenesis: A case report of siblings with a newly identified mutation in thyroperoxidase. J Pediatr Endocrinol Metab 2016;29:627-31.
6. Park SM, Chatterjee VK. Genetics of congenital hypothyroidism. J Med Genet 2005;42:379-89.
7. Lacka K, Maciejewski A. Rare thyroid non-neoplastic diseases. Thyroid Res 2015;8:5.
8. Bchir A, Mestiri S, Belakhdhar M, Abdelkefi M, Mokni M. Dyshormonogenetic goiter: A clinico-pathologic study of a rare disease with literature review. Int J Med Sci Clin Res 2022;4:24-8.
9. Dekhne A, Popat A, Chopwad A. Looking beyond thyroid malignancy: An unusual case of dyshormonogenetic goiter in rural India. Cureus 2024;8.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Sobah N, Kuruvilla S. Dyshormonogenetic goiter with papillary hyperplasia mimicking papillary carcinoma: A rare entity. Indian J Case Reports. 2025;11(12):650-652.