

Histomorphological Analysis of Thyroglossal Duct Cyst with a Rare Case of Primary Papillary Carcinoma: A Case Series of 17 Cases

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Abstract

Background: Thyroglossal duct cyst (TGDC) is the most common congenital midline neck mass in children and young adults, arising from remnants of the thyroglossal tract. Primary malignancy arising within a thyroglossal duct cyst, most commonly papillary thyroid carcinoma, is an exceedingly rare occurrence with an estimated incidence of less than 1% of all TGDCs. The histomorphological spectrum of TGDCs remains undercharacterised in larger case series from the Indian subcontinent.

Aim: To describe the clinicopathological and immunohistochemical features of thyroglossal duct cysts in a case series of 17 consecutive surgically excised specimens, with particular emphasis on the single case harbouring primary papillary carcinoma.

Materials and Methods: All thyroglossal duct cyst specimens received at our department were retrospectively reviewed. Clinical data, gross and microscopic findings, and immunohistochemical results were analysed. Immunohistochemistry for Galectin-3, CK19, HBME-1, and TTF-1 was performed in cases with suspicious microscopic features.

Results: The series comprised 17 cases (11 females, 6 males) with ages ranging from 19 to 63 years. The infrahyoid midline was the most common site (11/17). One case (5.9%) was found to harbour papillary carcinoma within the cyst wall. The malignant case demonstrated Galectin-3 and CK19 positivity, with focal HBME-1 and TTF-1 positivity. The remaining 16 cases showed benign histomorphology including squamous-lined cysts, ciliated columnar-lined cysts, thyroid follicles within the cyst wall, and varying degrees of chronic inflammation.

Conclusion: Thorough sampling and careful histopathological evaluation of all thyroglossal duct cyst specimens is essential to detect incidental papillary carcinoma. Immunohistochemistry with Galectin-3, CK19, and HBME-1 serves as a valuable adjunct in confirming malignancy.

Keywords: Thyroglossal duct cyst; papillary carcinoma; histopathology; immunohistochemistry; Sistrunk's procedure; case series.

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Introduction

Thyroglossal duct cysts (TGDCs) are the most commonly seen congenital anomalies of the midline neck, constituting about 70% of congenital neck lumps.

They develop due to the persistence of the thyroglossal tract, which is an anomaly that occurs as a result of the migration of the thyroid gland from the foramen caecum at the base of the tongue to the anterior neck region [1]. Even though the

thyroid normally migrates in the fourth and seventh weeks of fetal life, the remnants of the tract can persist in 7% of the adults [2].

The presence of a soft and non-tender midline mass that moves on deglutition and tongue protrusion is the clinical presentation seen in thyroglossal duct cysts (TGDCs), with this being a feature pathognomonic of the attachment of the lesion to the hyoid bone [3]. It reaches its maximum

prevalence in the first decade of life although presentation in all other ages is not uncommon. The infrahyoid region is the most common anatomic location of the cyst (about 65%) [4].

The standard management includes Sistrunk's technique, consisting of en bloc resection of the cyst, the middle segment of hyoid bone, and core of tissue till the foramen caecum, which provides recurrence rates less than 5% [5].

Primary malignancy in thyroglossal duct cyst is a rare entity, first reported by Brentano in 1911 [6]. The overwhelming majority (85-95%) of cases are represented by Papillary Thyroid Carcinoma (PTC), while Squamous cell carcinoma, follicular carcinoma and Hurthle cell carcinoma constitute the remaining [7,8]. The frequency of occurrence ranges between 0.7% and 1.5% of all TGDC [9]. The exact mechanism is still under discussion; the ectopic thyroid tissue, existing in the cyst wall, is considered to be a substrate for the development of primary tumour, stimulated by TSH action and molecular changes similar to those in papillary thyroid carcinoma [10]. Markers like Galectin-3, CK19, HBME-1, and TTF-1 have been used extensively as adjuvants in diagnosing papillary carcinoma and differentiating it from nuclear atypia in ectopic thyroid glands [11,12]. Despite the clinical relevance of this entity, there are no large case series with morphological details available, especially from tertiary centres in South Asia. The current study is focused on describing the clinical and pathological features of 17 consecutive Thyroglossal Duct Cysts, paying special attention to the single case of incidental primary papillary carcinoma.

Materials and Methods

Study Design and Case Selection: The current study is an analysis of cases carried out retrospectively at the Department of Pathology (from 2023 to 2025). All surgical specimens of thyroglossal duct cysts collected in that period were selected for the study. Clinical details such as age, gender, chief complaint, period of complaints, and clinical diagnosis were obtained from the patient's history.

Gross Examination: All the surgical specimens were fixed in 10% neutral buffered formalin. The gross examination was carried out noting all dimensions, shape, consistency, and characteristics of the cut surface. The presence of any solid, papillary, or nodular areas was carefully noted.

Histopathological processing: Histological sections of 4-5 μ m thickness were taken from the tissue blocks embedded in paraffin and stained by Hematoxylin and Eosin (H&E). The parameters examined were: nature of cystic lining epithelium, nature of cyst wall, presence or absence of thyroid follicles, presence of inflammation and malignant changes if any.

Immunohistochemistry: In those cases where microscopic features suspicious for malignancy were present (nuclear enlargement, vacuolation, grooves and/or papillary architecture), immunohistochemistry was done using the standard Streptavidin-Biotin Peroxidase technique. The antibodies used were: Galectin-3 (clone 9C4; 1:200); CK19 (clone RCK108; 1:100); HBME-1 (clone HBME-1; 1:50); TTF-1 (clone 8G7G3/1; 1:200). Positive and negative controls were done.

Ethical Issues: The study has been conducted in compliance with the Helsinki declaration. Institutional ethical clearance was obtained. Patient data were anonymised prior to analysis.

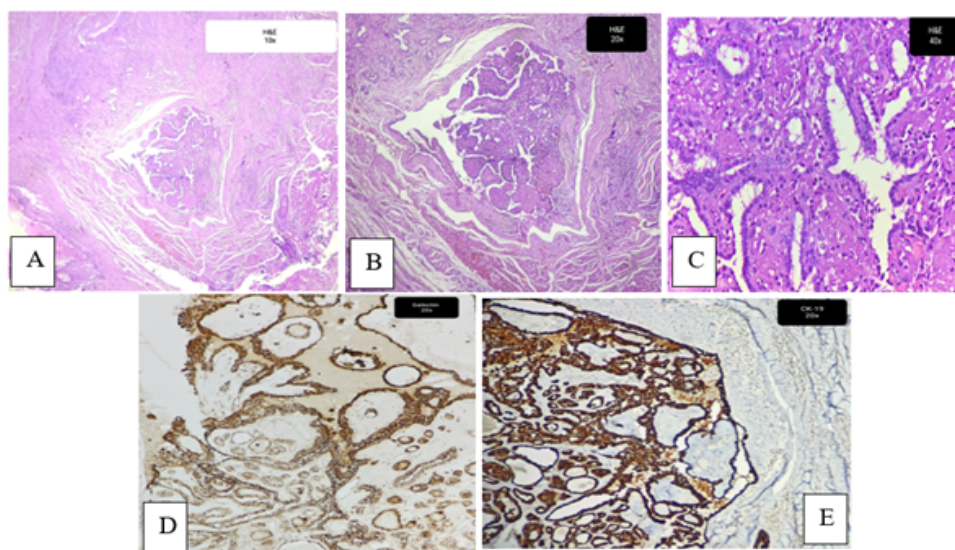


Figure 1: Histopathological and immunohistochemical features of primary papillary thyroid carcinoma arising in a thyroglossal duct cyst

(A) H&E stain (10×) showing a cystic lesion with an intracystic papillary epithelial proliferation arising within the wall of a thyroglossal duct cyst.; (B) H&E stain (20×) demonstrating complex branching papillary fronds with fibrovascular cores projecting into the cyst lumen.; (C) H&E stain (40×) revealing characteristic cytological features of papillary thyroid carcinoma, including enlarged overlapping nuclei, nuclear clearing (Orphan Annie eye nuclei), nuclear grooves, and occasional intranuclear cytoplasmic inclusions; (D) Immunohistochemical staining for Galectin-3 (20×) showing diffuse strong membranous and cytoplasmic positivity in the neoplastic epithelial cells, supporting the diagnosis of papillary thyroid carcinoma.

Results

Clinicopathological Overview: A total of seventeen specimens with TGDC were obtained within the study period. The series included eleven (64.7%) females and six (35.3%) males. Age of patients varied from 19 to 63 years with an average age of 38.7 ± 12.4 years. Symptom duration varied from 1 month to 18 months.

The most common site of origin was the infrahyoid midline (11/17; 64.7%), while others were suprahyoid region (3/17; 17.6%) and submental region (3/17; 17.6%). Size of specimens varied from 1.5×1.2 cm to 4.0×3.2 cm. All cases were managed surgically by Sistrunk's procedure.

Table 1: Clinicopathological summary of all 17 cases

Case	Age (yrs)	Sex	Location	Duration	Size	Diagnosis
1	42	Female	Submental	3 months	2.5×2 cm	Thyroglossal duct cyst
2	28	Female	Midline neck	6 months	3.0×2.5 cm	Thyroglossal duct cyst
3	35	Male	Infrahyoid midline	8 months	2.8×2.2 cm	Thyroglossal duct cyst
4	19	Female	Suprahyoid midline	2 months	1.8×1.5 cm	Thyroglossal duct cyst
5	55	Male	Midline neck	12 months	3.5×3.0 cm	Thyroglossal duct cyst with chronic inflammation
6	47	Female	Submental	5 months	2.2×1.8 cm	Thyroglossal duct cyst with Hurthle cell change
7	31	Male	Infrahyoid midline	4 months	2.0×1.6 cm	Thyroglossal duct cyst
8	63	Female	Midline neck	18 months	4.0×3.2 cm	Papillary carcinoma in thyroglossal duct cyst
9	22	Female	Suprahyoid	1 month	1.5×1.2 cm	Thyroglossal duct cyst
10	38	Male	Infrahyoid midline	7 months	2.6×2.0 cm	Thyroglossal duct cyst with cholesterol granuloma
11	50	Female	Midline neck	10 months	3.2×2.7 cm	Thyroglossal duct cyst
12	44	Male	Subhyoid midline	9 months	2.4×2.0 cm	Thyroglossal duct cyst with lymphocytic thyroiditis-like change
13	29	Female	Midline neck	3 months	2.0×1.8 cm	Thyroglossal duct cyst
14	57	Female	Infrahyoid midline	15 months	3.8×3.0 cm	Thyroglossal duct cyst
15	33	Male	Midline neck	4 months	2.2×1.7 cm	Thyroglossal duct cyst
16	26	Female	Suprahyoid	2 months	1.6×1.3 cm	Thyroglossal duct cyst
17	49	Male	Infrahyoid midline	11 months	3.1×2.5 cm	Thyroglossal duct cyst with reactive atypia

*Red shading denotes the case with primary papillary carcinoma.

Gross Findings: Most of the specimens consisted of unilocular cystic structures with smooth inner surfaces. The cystic contents were heterogeneous and included serous fluid (seven specimens), mucoid substance (five specimens), yellow-turbid fluid (three specimens), and blood-containing or brown fluid (two specimens). Focal mural thickening or a nodular firm structure was noted in one specimen (Case 8). No specimen exceeded 4.0 cm in diameter.

Microscopic Findings: The histopathological spectrum of the benign group (16 cases) was as follows: pseudostratified ciliated columnar (respiratory type) epithelial lining (8), squamous epithelial lining (3), and squamous and ciliated columnar epithelium (3), and cuboidal to columnar epithelium (2). Follicular structures resembling normal thyroid follicles in the cyst wall were seen in 12 out of 16 benign cases. Other observations included: lymphocytic infiltration (5), cholesterol

granuloma (1), Hurthle cell change in ectopic thyroid follicles (1), mucous glands (2), lymphoid tissue (2), and reactive nuclear atypia in ectopic follicles (1).

One patient (Case 8; 5.9%) showed features diagnostic of papillary carcinoma arising from the cyst wall. Criteria used to confirm the diagnosis were as per the World Health Organisation classification of thyroid tumours and included: papillary architecture, nuclear enlargement with ground glass chromatin, nuclear grooves, pseudoinclusions, and lack of nuclear crowding.

Immunohistochemical Findings: Immunohistochemistry was carried out on Case 8, which showed suspicious morphological features. Galectin-3, CK19, and TTF-1 were positive. HBME-1 was focally positive. No positivity for Galectin-3, CK19, or HBME-1 was identified in the adjacent benign thyroid follicular tissue.

Table 2: Immunohistochemical profile of the malignant case

Case	Galectin-3	CK19	HBME-1	TTF-1
8	Positive	Positive	Focally positive	Positive

Individual Case Descriptions

Case	Clinical Presentation	Gross Findings	Microscopic Findings	Immunohistochemistry	Final Diagnosis
Case 1	42-year-old female presented with a midline neck swelling in the submental region for 3 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Soft tissue 2.5 × 2 cm; cystic with serous fluid; no solid areas.	Squamous-lined cyst wall with focal pseudostratified ciliated columnar epithelium. Thyroid follicles within the wall. No malignant features.	—	Thyroglossal duct cyst.
Case 2	28-year-old female presented with a midline neck swelling in the midline neck region	Soft tissue 3.0 × 2.5 cm; cystic with yellowish turbid fluid; no solid areas.	Squamous-lined cyst wall with focal pseudostratified ciliated columnar epithelium. Thyroid follicles within the wall. No	—	Thyroglossal duct cyst.

	for 6 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.		malignant features.		
Case 3	35-year-old male presented with a midline neck swelling in the infrahyoid midline region for 8 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Soft tissue 2.8 × 2.2 cm; unilocular cyst with clear serous fluid; wall smooth.	Cyst lined by ciliated columnar epithelium with areas of squamous metaplasia. Lymphoid tissue within cyst wall. No atypia.	—	Thyroglossal duct cyst.
Case 4	19-year-old female presented with a midline neck swelling in the suprahyoid midline region for 2 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was	Small cystic structure 1.8 × 1.5 cm; mucoid content; wall thin and translucent.	Cyst wall lined by pseudostratified ciliated columnar epithelium. Mucous glands within the wall. Mild chronic inflammatory infiltrate.	—	Thyroglossal duct cyst.

	made and the patient underwent Sistrunk's procedure.				
Case 5	55-year-old male presented with a midline neck swelling in the midline neck region for 12 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Cystic mass 3.5 × 3.0 cm; brownish fluid; wall thickened; no grossly solid nodule.	Fibrocollagenous cyst wall with chronic inflammation. Focal squamous lining. Thyroid follicles identified. No malignancy.	—	Thyroglossal duct cyst with chronic inflammation.
Case 6	47-year-old female presented with a midline neck swelling in the submental region for 5 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Soft tissue 2.2 × 1.8 cm; cystic; gelatinous content; wall intact.	Squamous epithelial-lined cyst. Dense fibrocollagenous wall with a focus of thyroid follicles showing Hurthle cell change. No atypia.	—	Thyroglossal duct cyst with Hurthle cell change.
Case 7	31-year-old male presented with a midline neck swelling in the infrahyoid midline	Cystic mass 2.0 × 1.6 cm; clear serous fluid; no mural nodule.	Ciliated columnar epithelium-lined cyst. Subepithelial chronic inflammation. Thyroid follicles in cyst wall. No malignancy.	—	Thyroglossal duct cyst.

	region for 4 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.				
Case 8 (Malignant)	63-year-old female presented with a midline neck swelling in the midline neck region for 18 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Cystic mass 4.0 × 3.2 cm; haemorrhagic content; small firm mural nodule (0.6 cm) on posterior wall.	Fibrocollagenous cyst wall with papillary projections lined by cells showing ground-glass nuclei, nuclear grooves, and pseudoinclusions. Consistent with papillary carcinoma.	Galectin-3 positive; CK19 positive; HBME-1 focally positive; TTF-1 positive.	Papillary carcinoma in thyroglossal duct cyst.
Case 9	22-year-old female presented with a midline neck swelling in the suprahyoid region for 1 month. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the	Small cystic tissue 1.5 × 1.2 cm; clear fluid; wall smooth and thin.	Cyst lined by stratified squamous epithelium. No thyroid follicles identified. No inflammation or atypia.	—	Thyroglossal duct cyst.

	patient underwent Sistrunk's procedure.				
Case 10	38-year-old male presented with a midline neck swelling in the infrahyoid midline region for 7 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Cystic mass 2.6×2.0 cm; yellowish fluid; wall shows focal thickening.	Mixed ciliated columnar and squamous epithelium lining. Cholesterol clefts and foreign body giant cell reaction in wall. Thyroid follicles present. No atypia.	—	Thyroglossal duct cyst with cholesterol granuloma.
Case 11	50-year-old female presented with a midline neck swelling in the midline neck region for 10 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Cystic mass 3.2×2.7 cm; pale yellow fluid; wall intact with no gross nodule.	Fibrocollagenous cyst wall. Mixed squamous and pseudostratified ciliated epithelium. Multiple thyroid follicles with colloid. No malignancy.	—	Thyroglossal duct cyst.
Case 12	44-year-old male presented with a midline neck swelling in the subhyoid midline	Cystic mass 2.4×2.0 cm; mucoid fluid; wall slightly thickened; no solid component.	Cyst wall with pseudostratified ciliated epithelium. Dense lymphocytic infiltrate in wall. Follicular thyroid tissue with reactive changes. No	—	Thyroglossal duct cyst with lymphocytic thyroiditis-like change.

	region for 9 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.		atypia.		
Case 13	29-year-old female presented with a midline neck swelling in the midline neck region for 3 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Soft cystic tissue 2.0 × 1.8 cm; clear serous content; wall smooth.	Squamous epithelial lining with foci of ciliated columnar cells. Thyroid follicles in cyst wall. No atypia or malignancy.	—	Thyroglossal duct cyst.
Case 14	57-year-old female presented with a midline neck swelling in the infrahyoid midline region for 15 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the	Cystic mass 3.8 × 3.0 cm; turbid fluid; wall fibrotic; no grossly suspicious nodule.	Cyst wall with ciliated columnar and squamous epithelial lining. Thyroid follicles in wall with reactive nuclear changes. No features of papillary carcinoma. Dense lymphoplasmacytic infiltrate.	—	Thyroglossal duct cyst.

	patient underwent Sistrunk's procedure.				
Case 15	33-year-old male presented with a midline neck swelling in the midline neck region for 4 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Cystic mass 2.2×1.7 cm; serous fluid; smooth internal surface; no nodule.	Cyst wall lined by cuboidal to columnar epithelium. Subepithelial fibrosis. Thyroid follicles with normal colloid. No features of malignancy.	—	Thyroglossal duct cyst.
Case 16	26-year-old female presented with a midline neck swelling in the suprahyoid region for 2 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	Cystic structure 1.6×1.3 cm; mucoid; wall thin; no solid area.	Pseudostratified ciliated columnar epithelium. Goblet cells identified. Submucosal mucous glands. No thyroid follicles. No atypia.	—	Thyroglossal duct cyst.
Case 17	49-year-old male presented with a midline neck swelling in the infrahyoid midline	Cystic mass 3.1×2.5 cm; yellowish fluid with flecks; wall thickened; no obvious mural	Fibrocollagenous wall with mixed squamous and ciliated epithelial lining. Thyroid follicles with reactive atypia. Dense	—	Thyroglossal duct cyst with reactive atypia.

	region for 11 months. The swelling was mobile with deglutition and tongue protrusion. A clinical diagnosis of thyroglossal duct cyst was made and the patient underwent Sistrunk's procedure.	nodule.	lymphoplasmacytic infiltrate. No malignancy.		
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Discussion

TGDCs are by far the commonest congenital lesions of the neck found in surgical pathology departments; however, the identification of a primary tumour arising from the cyst wall is rare. In this case series of 17 consecutive TGDCs, we have described the histomorphology of this lesion, with one (5.9%) of 17 TGDCs harbouring a coexisting primary papillary carcinoma – an incidence consistent with the 0.7–1.5% range reported in the literature [7,9].

The predominance of females in this case series (64.7%) is in accordance with the established sexual predilection of thyroid diseases, which include papillary carcinoma [13]. The broad range of ages (19–63 years) highlights the fact that TGDCs can occur as a *de novo* lesion or become symptomatic at any time during adult life.

The site-wise distribution (the infrahyoid area in 64.7% of cases) correlates very well with published literature [4]. Anatomically speaking, the hyoid bone represents the terminal structure penetrated by the descending thyroid anlage, and the portions of the tract with direct relationship to the hyoid are the most predisposed to dilatation in case of incomplete obliteration [14]. In terms of histopathology, the benign cases revealed typical TGDC features: the presence of ciliated columnar epithelium because of embryonic development from the foregut endoderm, squamous metaplasia due to chronic inflammation, ectopic thyroid follicles in connection with totipotent stem cells not eliminated during the process of organogenesis, and the infiltration of various levels of chronic inflammation. Noteworthy is Case 12, which revealed the stromal reaction similar to that observed in lymphocytic thyroiditis surrounding ectopic follicles – such a correlation has been proposed as a sign of local autoimmune response [15].

The single malignant case (Case 8) demonstrated the classic gross and microscopic manifestations of

papillary carcinoma in TGDC. Grossly, a firm mural nodule was appreciated on the posterior wall. Microscopically, the case met the stringent criteria for the diagnosis of papillary carcinoma with typical nuclei of papillary thyroid carcinoma (PTC): ground glass nuclei, nuclear grooves, and pseudoinclusions. These features seen in the wall of the fibrous cyst derived from thyroid follicles indicate the diagnosis of carcinoma of TGDC differentiating it from metastasis from occult orthotopic thyroid carcinoma [16].

The differentiation of TGDC carcinoma from metastatic thyroid carcinoma to TGDC is of utmost importance and depends on criteria described by Widström and Bauer: (1) a histologically normal thyroid gland on preoperative images or postoperative examination; (2) absence of lymph node metastasis; and (3) the carcinoma restricted within the cyst wall [17]. Case 8 fulfilled all the mentioned criteria according to clinical and imaging studies. The optimal management of TGDC carcinoma after diagnosis remains debated; while some advocate total thyroidectomy, others support observation alone after Sistrunk's procedure given the generally excellent prognosis [18]. Histological identification of papillary carcinoma in TGDC is especially important because of the possibility of atypia of thyroid follicles mimicking malignant tumour. In our malignant case, positive immunostaining for Galectin-3 and CK19 – two markers of high specificity and sensitivity for PTC – confirmed the diagnosis [11]. Focal HBME-1 and TTF-1 positivity provided additional support. The uniform negativity of adjacent benign follicles for these markers validates their utility in distinguishing carcinoma from reactive change and supports their routine inclusion in the diagnostic workup of any TGDC with suspicious morphology [12].

In clinical practice, several key points emerge from this study. All specimens of TGDC require adequate sampling with a minimum of one section

per cm of maximum dimension, while any suspicious macroscopic finding (mural thickening, nodule, or papillary projection) warrants additional sampling. Immunohistochemistry should be applied judiciously in cases of nuclear atypia and architectural complexity. Preoperative ultrasound and fine-needle aspiration cytology in suspicious TGDCs can also be of help, but the sensitivity of cytological examination is relatively low for TGDC carcinoma [19].

Conclusion

This series of 17 thyroglossal duct cysts illustrates the wide range of histomorphological features of this lesion and emphasises the diagnostic dilemma created by the rare occurrence of primary papillary carcinoma within the cyst wall. One patient (5.9%) was diagnosed with papillary carcinoma, confirmed by immunohistochemistry using Galectin-3, CK19, HBME-1, and TTF-1. Meticulous gross examination, comprehensive histopathological sampling, and liberal use of immunohistochemistry are crucial to avoid overlooking this rare but clinically significant pathology.

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