REVIEW ARTICLE

Occult Papillary Thyroid Carcinoma Arising in a Branchial Cleft Cyst: A Review of Cases

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ABSTRACT

An asymptomatic lateral neck mass initially thought of as branchial cleft cyst (BrCC) may be an apparent manifestation of head and neck cancer. In this article, we report such unexpected findings in a patient, followed by literature review of similar reported cases. A 69-year-old man presented with longstanding, painless left lateral neck swelling which gradually increased in size. A bedside ultrasound revealed a cystic mass with presence of mural nodules, of which cytology revealed atypical cells suspicious of papillary thyroid carcinoma (PTC). A 50mm neck mass extending from level II to V was subsequently excised. Histopathological examination confirmed PTC arising from a branchial cleft cyst. Despite no clinical or radiological suspicion of thyroid malignancy, a follow up total thyroidectomy was performed, revealing a benign thyroid gland. He received radioactive ablation therapy for remnant disease. He remained well 6 years post diagnosis. Literature review shows most similar patients undergo total thyroidectomy to allow better prognosis.

Malaysian Journal of Medicine and Health Sciences (2025) 21(SUPP12):79-82. doi:10.47836/mjmhs.21.s12.12

Keywords: Branchial cleft, Thyroidectomy, Neck cyst, Metastasis, Papillary thyroid carcinoma

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INTRODUCTION

Branchial cleft cysts are benign lateral congenital neck mass that can enlarge and become painful in the setting of infection. However, a lateral neck mass initially thought as branchial cleft cyst in an adult may be an early or clinically apparent manifestation of head and neck tumours, such as squamous cell carcinoma (SCC), lymphoma, thyroid carcinoma, salivary gland carcinoma or metastasis [1]. Occult or metastatic papillary thyroid carcinoma (PTC) to branchial cyst (BrCC) have been reported, albeit rare. Here, we report such a case, with a literature review on similar cases and their management.

CASE REPORT

A 69-year-old man presented with a painless left lateral neck swelling for 10 years. The swelling gradually increased in size, but he denied other symptoms. Bedside ultrasound noted a cystic neck mass with presence of two mural nodules. Clinical impression at the time was an infected BrCC. He underwent an ultrasound-guided fine needle aspiration of the neck cyst, revealing atypical cells that were suspicious of PTC. Subsequent excision of a 50 x 40mm oval, brownish cystic mass extending from level II, III, IV and V was performed. Histopathological examination revealed PTC arising from the branchial cleft cyst (Figure 1). A decision was made for him to have a total thyroidectomy despite no clinical or radiological suspicion of thyroid malignancy. Histological examination revealed an unremarkable thyroid gland with no evidence of malignancy. He

received radioactive ablation therapy for remnant disease. Postoperative thyroid scintigraphy and whole-body F18-fluorodeoxyglucose–positron emission tomography/computed tomography (FDG–PET/CT) follow-up found no residual disease or distant metastasis. He remained well 6 years post diagnosis.

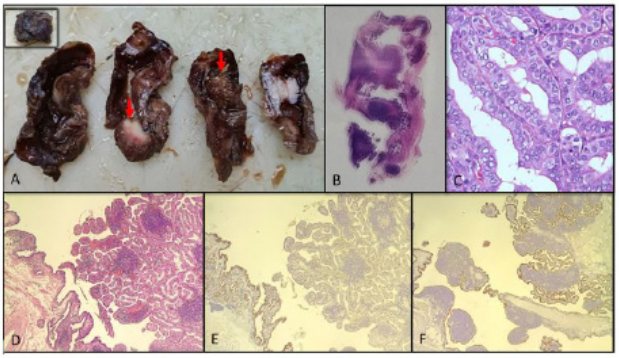

Figure 1: A) A cystic tissue measuring 50 x 40mm was excised (inset). Serial sectioning showed the presence of 2 papillary excrescences within the cyst (red arrows). B) Full-mount Hematoxylinand Eosin section (H&E) of the cyst C) Microscopic examination confirmed papillary thyroid carcinoma (PTC) exhibiting papillary and follicular architecture with classic PTC nuclear features of oval, enlarged, optically clear nuclei, nuclear pseudo-inclusions and occasional nuclear grooves (H&E, 400x). D) PTC with adjacent cyst lining (H&E, 40x). E) Cyst epithelial lining was positive for p63 immunohistochemistry. F) Both PTC and cyst epithelial lining were positive for TTF-1 immunohistochemistry. "

DISCUSSION

Traditionally the most common cause of lateral neck mass has been thought to be a branchial cleft anomaly [2]. However, a single cervical lymph node metastasis can mimic a BrCC clinically, radiologically and histologically if not examined thoroughly [3]. The incidence of cancer in neck cystic mass in the general population ranges from 4 to 24% but increases to 80% in adults of more than 40 years old [1]. Reports of primary PTC metastasizing as BrCC are rare in the literature [4].

Lymph node metastasis may form cystic structures, therefore mimicking BrCC, hence a comprehensive immunohistochemistry workup using p63, TTF-1, thyroglobulin is essential. While TTF-1 is typically negative in BrCC epithelium, positivity towards TTF-1 such as this case suggests ectopic thyroid tissue arising within the BrCC [5]. This is further supported by the absence of primary thyroid tumour despite extensive sampling.

Most ectopic thyroid tissue occurs at midline, following the path of its embryogenic descend. Ectopic thyroid tissue in the lateral neck is uncommon. There are two theories for this abnormal location – a congenital anomaly and an acquired condition. In the first theory, branchial cleft cyst occurs due to failure of involution of branchial cleft structure during embryogenesis. Failure of fusion of the fourth branchial pouch - which supplies cells to the lateral thyroid glands- result in the presence of ectopic thyroid cells within the branchial cleft cyst. The second theory suggests that branchial cleft cysts are due to epithelial cell inclusion within lateral cervical lymph nodes which undergoes cystic degeneration. Thyroid follicular cells may be part of these included epithelial cells [6].

We performed a literature review looking at 17 reported cases of PTC within branchial cysts (including current case) and their subsequent management [6-20]. We found that most cases (94.1%, 16 out of 17 cases) underwent total thyroidectomy regardless of subsequent workup findings (Table 1). One patient declined surgery following a negative radiological investigation and opted for vigilant follow-up [15]. Five patients had primary PTC in the thyroid gland, while the rest were diagnosed as occult PTC arising in BrCC (Table I).

Table I: Literature review looking at 17 cases, including current case, of papillary thyroid carcinoma arising in a branchial cleft cyst with subsequent management of the thyroid gland. n/a = not analysed.

Papillary thyroid carcinoma in branchial cleft cyst in the literature						
Case No	Author (Year)	Age / Gender	Surgical excision	Thyroidectomy result	Post-operative management	Follow-up duration and outcome
1	Matusumoto et al[6] (1999)	46/F	Branchial cyst and hemithyroidectomy	No evidence of carcinoma within the thyroid gland	-	n/a
2	Sidhu et al[7] (2000)	42/F	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	Hormone replacement therapy	5 years with no recurrence
3	Fumarola et al[8] (2006)	36/F	Surgical excision of branchial cyst and total thyroidectomy	Multifocal papillary carcinoma	Radioactive iodine	n/a
4	Mehmood at al[9] (2006)	31/M	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	Hormone replacement therapy and radioactive iodine	2 years with no recurrence
5	Lanzafame et al[10] (2006)	29/F	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	-	n/a

continue

Table I: Literature review looking at 17 cases, including current case, of papillary thyroid carcinoma arising in a branchial cleft cyst with subsequent management of the thyroid gland. n/a = not analysed. (cont.)

Papillary thyroid carcinoma in branchial cleft cyst in the literature						
Case No	Author (Year)	Age / Gender	Surgical excision	Thyroidectomy result	Post-operative management	Follow-up duration and outcome
6	Lanzafame et al[10] (2006)	21/F	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	-	n/a
7	Park et al[11] (2006)	49/M	Surgical excision of branchial cyst, selective right neck dissection and total thyroidectomy	No evidence of carcinoma within thyroid gland	-	n/a
8	Cho et al[12] (2011)	41/F	Right lateral neck dissection and total thyroidectomy	No evidence of carcinoma within thyroid gland	Hormone replacement therapy	28 months with no recurrence
9	Kushwaha et al[13] (2012)	34/F	Surgical excision of branchial cyst, modified radical neck dissection, and total thyroidectomy	No evidence of carcinoma within thyroid gland	-	1 year with no recurrence
10	Karras et al[14] (2013)	35/F	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	Hormone replacement therapy followed by radioactive iodine after recurrence	Recurrence at lateral neck after 2 months, treated with radioactive iodine; no recurrence after 2 years
11	Sagit et al[15] (2013)	41/F	Surgical excision of branchial cyst; patient refused thyroidectomy	Not available (Declined thyroidectomy)	Conservative surveillance	5 years with no recurrence
12	Papadakis et al[16] (2017)	40/M	Surgical excision of branchial cyst and total thyroidectomy	Papillary thyroid carcinoma	Radioactive iodine	36 months with no recurrence
13	Agosto-Vargas et al[17] (2017)	33/M	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	Hormone replacement therapy followed by radioactive iodine after recurrence	Recurrence at lateral neck after 1 month, treated with radioactive iodine; disease at lateral neck disappear afterwards (duration not mentioned)
14	Yehuda et al[18] (2017)	35/F	Surgical excision of branchial cyst and total thyroidectomy	Papillary thyroid carcinoma	-	n/a
15	Tazegul et al[19] (2018)	22/F	Surgical excision of branchial cyst and total thyroidectomy	Multifocal papillary thyroid carcinoma	Hormone replacement therapy followed by radioactive iodine	n/a
16	Marotta et al[20] (2021)	28/M	Surgical excision of branchial cyst and total thyroidectomy	Multifocal papillary thyroid carcinoma	Hormone replacement therapy and radioactive iodine	6 weeks with no recurrence
17	Current case, 2019	69/M	Surgical excision of branchial cyst and total thyroidectomy	No evidence of carcinoma within thyroid gland	Radioactive iodine	6 years with no recurrence

Although PTC may well arise from ectopic thyroid tissue in branchial cleft cyst, potential primary thyroid gland harboring a primary PTC is hard to ignore. The challenge lies in whether to undergo complete total thyroidectomy despite no primary thyroid neoplasm detected clinically or radiologically. A review by Yehuda et al suggests an algorithm whereby features such as cysts with mural nodules on imaging should be evaluated with fine needle aspiration; in addition to investigation of thyroid gland and thyroglobulin level to exclude thyroid malignancy [18].

Postoperative adjuvant RAI was administered due to the lesion's atypical location and uncertain origin. Despite thorough thyroidectomy examination, an occult primary thyroid could not be definitively excluded. Thus, RAI remnant ablation was performed to eliminate any potential microscopic tumour deposits. This approach aligns with international guidelines [21].

CONCLUSION

Lateral cystic neck mass with malignant transformation of ectopic thyroid tissue should be kept in mind, albeit rare. The discovery of papillary carcinoma on ectopic thyroid tissue raises the possibility of a primary in the thyroid gland and should prompt an exploration of the gland, primarily through imaging techniques. Despite the absence of clear guidelines for managing occult PTC in a branchial cyst, total thyroidectomy continues to be the primary option in these cases. However, the optimal approach, whether operative intervention or vigilant follow-up should be adopted, warrants further exploration.

ACKNOWLEDGEMENT

This case report was presented as a poster at the 48th Annual Scientific Meeting of the Australasian Division of the International Academy of Pathology (IAP), held in Brisbane from May 31 to June 2, 2024.

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