

## Thyroid papillary carcinoma in lateral neck cyst: missed primary tumour or ectopic thyroid carcinoma within a branchial cyst?

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### Abstract

We report a case of thyroid papillary carcinoma lying within a lateral cervical cyst for which no occult primary tumour of the thyroid was identified. We explore the possible diagnoses and include a discussion of how ectopic thyroid tissue may come to lie within a branchial cyst.

**Key words:** Thyroid Neoplasms; Carcinoma, Papillary; Branchioma

### Case report

A 42-year-old man presented with a four-week history of a painless right-sided neck swelling. Clinical examination demonstrated an 8 × 5 cm smooth, non-tender, oval, cystic swelling at the junction of the upper and middle one third of the anterior border of the right sternocleidomastoid muscle. There was no associated cervical lymphadenopathy and cytological examination of a fine needle aspiration biopsy revealed the presence of cholesterol crystals and foamy macrophages suggestive of a branchial cyst. Ultrasonography confirmed the presence of a well-defined cystic lesion distinct from the right lobe of the thyroid gland. At resection no tract was discovered connecting the cyst to the pharynx or hyoid bone and it was removed intact. Macroscopic examination of the excised specimen revealed a thick wall with a haemorrhagic component and a 0.75 cm white nodule within the wall. Histological examination demonstrated a cyst lined

by a single layer of columnar epithelium with dense subepithelial lymphoid aggregates. Nestled within the cyst wall were groups of thyroid follicles and at one point a focus of papillary carcinoma was identified (Figure 1). At high magnification, occasional psammoma bodies and overlapping optically clear nuclei typical of papillary thyroid carcinoma were seen. The cyst columnar epithelium as well as the thyroid follicular epithelium and colloid stained positive for thyroglobulin (Figure 2).

Clinical examination of the thyroid gland was unremarkable and ultrasonography, isotope and computed tomography (CT) scans demonstrated no overt pathology within the thyroid gland. Despite these negative investigations, it was impossible to exclude a small primary malignancy within the thyroid gland and total thyroidectomy was performed. No macroscopic abnormality of the thyroid was detected at operation. The thyroid specimen was embedded and extensively examined using 1 mm cuts

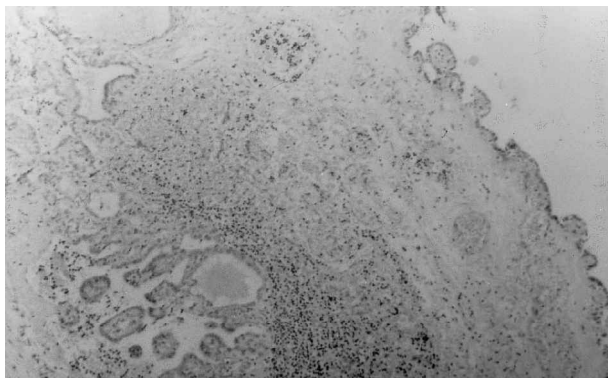


FIG. 1

Low power view of the papillary carcinoma lying within the cyst wall (H & E; ×4).

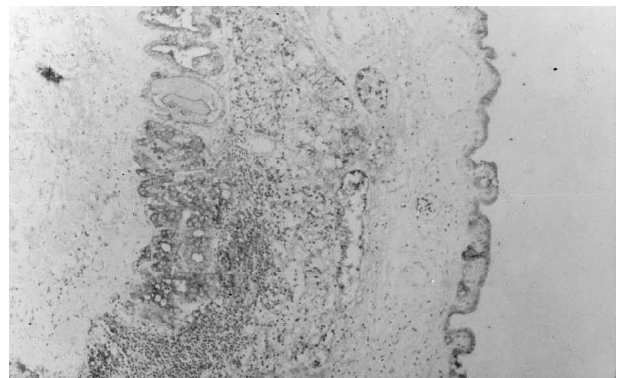


FIG. 2

Low power view (×4) of the papillary carcinoma within the cyst wall staining positive for thyroglobulin.

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however no evidence of an occult focus of papillary carcinoma was identified. The patient is on thyroid replacement and remains well after five years.

## Discussion

We report a case of papillary thyroid carcinoma arising in thyroid follicular epithelium lying within a lateral neck cyst in which no evidence of a primary thyroid carcinoma could be found. The diagnosis of thyroid carcinoma in the lateral neck cyst was secured by the presence of positive thyroglobulin staining within a focus of cells with the typical characteristics of thyroid papillary carcinoma. Consequently, we are left with the diagnostic dilemma – is this a case of metastatic thyroid carcinoma with missed primary tumour or does this case represent papillary thyroid carcinoma arising in ectopic thyroid tissue lying within a branchial cyst?

Papillary carcinoma accounts for 70 per cent of all thyroid tumours occurring predominantly in the third and fourth decades. Occult papillary carcinoma of the thyroid gland may be the initial presentation in up to 40 per cent of cases.<sup>1</sup> Occult metastases present commonly as a discrete, solid swelling, although they may rarely present as a larger cystic mass mimicking a branchial cyst,<sup>2,3</sup> and almost always a primary thyroid malignancy is discovered.<sup>4,5</sup> These tumours may be smaller than 1 mm.<sup>6</sup> There are descriptions, however, of patients in whom cervical lymph nodes containing papillary thyroid carcinoma have been excised without finding evidence of thyroid carcinoma in the subsequent thyroidectomy specimen.<sup>7</sup> These cases have been labelled as metastatic thyroid papillary carcinoma with failure to identify a tiny focus of papillary carcinoma within the thyroid gland. The prevailing wisdom is that the so-called lateral aberrant thyroid represents metastatic thyroid carcinoma.<sup>4</sup> Cystic degeneration within a lymph node replaced by metastatic thyroid carcinoma, with a missed primary thyroid tumour, could explain the findings in this case.

Recently, however, others have reported similar but not identical cases, in which an alternative diagnosis of thyroid papillary carcinoma arising in ectopic thyroid epithelium lying within a branchial cyst has been suggested.<sup>8–10</sup> The features of our case that would be consistent with this diagnosis were:

(1) The fine needle aspirate yielded cholesterol crystals and foamy macrophages typical of a branchial cyst. Fine needle aspiration of a lymph node replaced by papillary thyroid carcinoma characteristically yields a dark brown fluid.<sup>2</sup>

(2) The cyst lining consisted of an epithelial layer and a subepithelial collection of lymphoid tissue typical of a branchial cyst.<sup>11,12</sup> Most branchial cysts are lined by stratified squamous epithelium or respiratory-type epithelium with interspersed subepithelial lymphoid tissue. The columnar epithelium found in this case is unusual.<sup>12</sup>

(3) Normal thyroid tissue was found within the cyst wall adjacent to the focus of papillary carcinoma.

(4) There was no evidence of papillary carcinoma found within the thyroid gland when it was subsequently removed and subjected to meticulous histological examination.

(5) The other possible diagnosis of a laterally placed thyroglossal cyst<sup>13</sup> was excluded on the grounds that no tract was identified travelling from the cyst to the hyoid bone and beyond.

The reports presented by Balsubramaniam *et al.*<sup>8</sup> and Jadusingh *et al.*<sup>9</sup> give no evidence of the thyroglobulin-staining characteristics of the carcinomas identified within the branchial cysts, nor has the thyroid gland been excised

and submitted for histological examination. As Homan *et al.*<sup>7</sup> have demonstrated in three cases, a renal cell carcinoma metastasis to the thyroid may mimic papillary carcinoma of the thyroid. The one distinguishing test is thyroglobulin staining of the tumour epithelial cells. Furthermore, occult carcinoma of the thyroid in the cases of Balsubramaniam *et al.*<sup>8</sup> and Jadusingh *et al.*<sup>9</sup> cannot be reliably excluded without histology. The case presented by Matsumoto *et al.*<sup>10</sup> most closely resembles our situation in that a nodule of thyroid papillary carcinoma was found in the cyst wall, it stained positively for anti-thyroglobulin antibodies and no evidence of thyroid carcinoma was found in the thyroid specimen. No comment was made regarding the anti-thyroglobulin antibody staining characteristics of the cyst wall epithelium. Both the papillary thyroid carcinoma within our cyst and the cyst wall epithelium stained positive for thyroglobulin. This would tend to suggest our cyst arose as a consequence of cystic degeneration in a lymph node containing metastatic carcinoma. However branchial cysts with a cyst-lining epithelium staining positive for thyroglobulin have been described previously.<sup>14</sup> In that series, two of 20 branchial cysts were found to contain ectopic thyroid tissue. These cysts were then subjected to thyroglobulin staining and both the cuboidal epithelium lining the cysts and the thyroid follicles within the cyst walls stained positively for thyroglobulin. Parham concluded that these laterally situated neck cysts represented vestigial remnants of thyroid anlage developing from the branchial pouch walls. There have been three other reports, to our knowledge, of benign ectopic thyroid tissue found lying within a branchial cyst. However, in the five cases from these reports thyroglobulin staining of the cyst wall was not undertaken.<sup>15–17</sup>

The presence of ectopic thyroid tissue within a branchial cyst raises the question of the mechanism(s) whereby this situation arises. There are two major theories explaining the derivation of branchial cysts. Older theories describe branchial cysts as congenital abnormalities due to incomplete obliteration of pharyngeal pouches two to four. More recent theories allude to epithelial inclusions lying within cervical lymph nodes as triggering a phenomenon of cystic degeneration.<sup>12,18,19</sup> The presence of thyroid tissue within a branchial cyst may be explained by either theory.

The contribution of the fourth branchial pouch to the thyroid gland was suggested by Weller.<sup>20</sup> More recently, Hoyes and Kershaw<sup>21</sup> and Williams *et al.*<sup>22</sup> have described the fourth branchial pouch follicular cell contribution to the lateral thyroid lobes. The superior parathyroid glands arise from the dorsal expansion of the fourth branchial pouch remnants would therefore account for ectopic thyroid tissue within a ‘congenital’ branchial cyst.

Proponents of the ‘acquired’ theory for branchial cyst formation propose that epithelium from the upper aerodigestive tract enters a cervical lymph node via lymphatics and stimulates degeneration into a lateral cervical cyst.<sup>12,18,19</sup> Evidence sited in favour of this theory includes:

(1) the presence of cysts that lie outside the upper one third of the sternocleidomastoid muscle; (2) the presence of cysts within patients older than the third decade; (3) the rarity of finding a tract connecting a cyst to the pharynx; (4) the high lymphoid tissue content within a cyst wall; (5) the keratin content of the epithelium lining a branchial cyst. This strongly resembles the keratin content of squamous epithelium from the palatine tonsil<sup>19</sup> or respiratory-type epithelium from the upper aerodigestive tract. Regauer *et al.*<sup>11</sup> argue that the predominant epithelium in branchial cysts is respiratory, however, with the passage of

time, the epithelium undergoes squamous metaplasia to produce the characteristic stratified squamous epithelium reported in most series.

If benign thyroid epithelium was to come to lie within a lymph node and stimulate cystic degeneration then one could explain the presence of ectopic thyroid epithelium within an 'acquired' branchial cyst. The presence of benign thyroid metastases to cervical lymph nodes has been well described.<sup>23–25</sup> The estimated incidence is 0.03 per cent of internal jugular vein lymph nodes examined.<sup>25</sup> It is believed that thyroid tissue reaches cervical lymph nodes via lymphatics and that this phenomenon is equivalent to the benign metastases of endometrial tissue to pelvic lymph nodes.<sup>26</sup> Carcinoma occurring in ectopic thyroid tissue, other than in lingual and thyroglossal duct remnants, is extremely rare. It is predominantly of the papillary variety.<sup>27</sup>

In light of this evidence we suggest that ectopic thyroid epithelium may come to lie within a branchial cyst. Benign thyroid follicular epithelium in a branchial cyst may undergo malignant change and therefore this case could represent thyroid papillary carcinoma arising in ectopic thyroid epithelium lying within a branchial cyst.

### Conclusion

Thyroid papillary carcinoma in a lateral neck cyst is usually presumed to be a metastasis from a primary tumour in the thyroid gland and not the so-called 'lateral aberrant thyroid'.<sup>4</sup> When a primary tumour cannot be identified, it is presumed that it has been missed despite extensive histological examination.<sup>7</sup> We present a case where an alternative diagnosis may be considered – papillary thyroid carcinoma arising in ectopic thyroid tissue lying within a branchial cyst. Although this diagnosis has been suggested in three other reports, only the one case, presented by Matsumoto *et al.*<sup>10</sup> gives good evidence for such an entity. We describe mechanisms whereby ectopic tissue may come to lie within a branchial cyst and this evidence would therefore tend to support the possibility of thyroid carcinoma in a branchial cyst.

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