CASE REPORT

Thyroid papillary carcinoma arising in ectopic thyroid tissue within a branchial cleft cyst

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SUMMARY

Ectopic thyroid tissue comprises a rare clinical entity which can clinically manifest with the whole spectrum of thyroid disorders, including thyroid malignancy. Thyroid carcinoma arising in ectopic thyroid tissue is extremely rare, with only a few cases described in the literature so far. We present a very unusual case of a primary papillary thyroid carcinoma arising in a left lateral branchial cyst, describing our diagnostic and therapeutic approach for this uncommon clinical entity. This is the first case where recombinant thyrotropin was used along with radioiodine treatment in primary ectopic thyroid cancer.

BACKGROUND

Ontogenesis of the human thyroid gland comprises the primary basis for the identification of several anomalies, which can be manifested as diagnostic dilemmas in daily clinical practice. Ectopic thyroid tissue is a rare entity characterised by anatomical abnormalities involving the thyroid gland's migration route from the floor of the primitive pharynx to its final position in front of the trachea. These defects take place at early stages of embryogenesis.^{1 2} Ectopic thyroid tissue can be clinically manifested within all spectra of thyroid nosology, ranging from asymptomatic neck masses to hyperfunctioning ectopic thyroid tissue and thyroid malignancy.^{1 2} The most common location of ectopic tissue is at the base of the tongue (lingual thyroid),¹ although various cervical³ or remote sites have been reported.⁴ Based on this concept, an ectopic thyroid tissue can be identified on a pre-existing benign branchial neck developmental cleft cyst.

We present a very unusual case of a primary papillary thyroid carcinoma (PTC) arising in a left lateral branchial cyst, describing our diagnostic and therapeutic approach, regarding this uncommon clinical entity.

CASE PRESENTATION

A 35-year-old woman was referred to our outpatient department, for evaluation of a palpable, painless, left-sided neck mass. On clinical examination, no other masses were palpable and no signs of local compression were evident.

INVESTIGATIONS

Neck ultrasonography (US) showed a well-circumscribed, heterogeneous cystic structure (1.2×2.5×3.1 cm), located in the left lateral cervical region. No lymph node involvement was

evident. The imaging evaluation of the thyroid gland (US) was normal. A neck CT scan was performed to further identify the topography of the existing cervical mass, which demonstrated a round-shaped cystic mass (3.5 cm), with low-density features. A US-guided fine needle aspiration biopsy (FNAB) was performed. The FNA showed papillary tissue fragments and monolayered sheets of cuboidal tumour cells. Nuclei were elongated, enlarged, with thick membrane capsule. Psammoma bodies were evident.

TREATMENT

The patient underwent surgical resection of the neck mass. Histopathology demonstrated the presence of a partially encapsulated tumour with extensive cystic degeneration, with a predominantly complex papillary appearance, consisting of fibrovascular cores, some with oedematous stroma, lined by a neoplastic epithelium (figure 1A). The tumour cells nuclei were large, of oval shape, with irregular borders. Nuclear grooves, pseudoinclusions and nuclear overlapping were detected (figure 1B). The cellular atypia was moderate. Rare mitoses were counted. The non-neoplastic epithelium of the cyst was predominantly cuboidal. Abundant lymphoid tissue, often with germinal

Figure 1 Histological findings. (A) Representative area of the cyst showing a neoplasm with a complex papillary appearance, consisting of fibrovascular cores, some with oedematous stroma, lined by a neoplastic epithelium. At the cyst wall, abundant lymphoid tissue was also observed. (B) At higher magnification, the tumour cells exhibited cytological and nuclear features of papillary carcinoma.

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Figure 2 Immunohistochemistry. The neoplastic cells expressed cytokeratin 7 (A) and thyroid transcription factor-1 (B).

centres, was observed at the wall of the cyst, beneath the epithelium. The carcinoma cells were reactive for cytokeratin 7 (figure 2A), thyroid transcription factor-1 (TTF-1) (figure 2B) and thyroglobulin (Tg). The above histopathological and immunocytochemistry findings were suggestive of an ectopic PTC arising on a branchial neck cyst.

Consequently, a primary orthotopic PTC was suspected, and accordingly, the patient was submitted to total thyroidectomy. Histological examination demonstrated no evidence of a primary thyroid tumour.

OUTCOME AND FOLLOW-UP

Replacement therapy with levothyroxine 0.15 mg daily was initiated and 2 months later a whole body I^{131} scan (4.8 mCi) after administration of recombinant thyroid stimulating hormone (rh-TSH) was conducted. The TSH levels rose up to 120.9 mU/l and thyroxine and triiodothyronine were 159.8 nmol/l (58–154) and 1.7 nmol/l (1.2–3.1), respectively, while Tg levels after rh-TSH were 1.3 ng/ml with low titres of Tg antibodies. A whole body scan demonstrated two residual masses in the left lateral neck region. Subsequently, 150 mCi I^{131} were given after stimulation with rh-TSH. Nine months later, the whole body scan showed no residual tumour and the Tg levels after rh-TSH were 1.1 ng/ml. Two years after initial evaluation, the patient is on remission and her physical status is excellent.

DISCUSSION

The thyroid gland originates from the posterior migration of the thyroid anlagen, which arises from the embryonic endoderm in the floor of the primitive pharynx in the third week of gestation in humans.² Ectopic thyroid tissue can lie anywhere from the base of the tongue to its final position, as well as in more distant areas, such as the mediastinum and subdiaphragmatic regions.¹

Branchial cysts constitute a common aetiology of a neck mass in young adults. They are usually located anteriorly to the sternocleidomastoid, although other less common sites such as the parotid, the pharyngeal wall and the posterior triangle have

also been reported.⁵ Aberrant thyroid tissue located in the lateral submandibular regions (including the brachial cysts) is usually the result of a defective joint of the lateral anlage with the medial one.⁶ The presence of ectopic thyroid tissue in brachial cysts is generally rare.¹ The exact molecular mechanisms for thyroid ectopy are not known, but it has been hypothesised that some transcription factors, such as TTF-1, paired box 8 (PAX 8), haematopoietically expressed homeobox (HHEX) and forkhead box E1 (FOXE1), which are important for the early stages of thyroid development and migration, may be involved.¹ Mutations in the gene encoding FOXE1, which is essential for thyroid migration, have been reported in mice with sublingual thyroid.⁷

Primary thyroid carcinoma arising from an ectopic thyroid tissue is also a rare entity and has been mainly reported in lingual thyroids, thyroglossal duct cysts and struma ovarii.⁸ In the majority of cases, it involves PTC, although follicular and medullary carcinomas have also been described.⁹ The presence of a primary PTC in a branchial cleft cyst, however, is very rare. Eleven cases have been reported in the literature so far,^{10–16} two of which manifested as a metastatic lymph node disease at diagnosis.^{13 14} Branchial cysts may also be the initial site of detection of metastatic PTC.¹⁴

Scintigraphy imaging and CT or MRI are valuable diagnostic tools for detecting ectopic thyroid tissue, although the possibility of false-positive results is not negligible.¹ US-guided FNAB from the solid part of a cystic lesion and measurement of Tg protein and messenger RNA in needle washout are valuable tools that contribute to a more accurate diagnosis of ectopic thyroid tissue.¹⁷ In order to characterise a thyroid carcinoma in ectopic positions as primary, some criteria must be taken into account, such as the absence of an individual history of malignancy, a normal or absent orthotopic thyroid gland and separate blood supply from extracervical vessels.⁷ Immunohistochemical positive staining of Tg and TTF-1, as in our case, could help in the identification of a PTC located in the branchial cyst, although it cannot distinguish between primary and metastatic tumours.¹⁸ The differential diagnosis should also be made from a cystic lymph node metastasis of occult orthotopic PTC and is often difficult.¹⁹

On the basis of this hypothesis, some experts advocate that, except for excision of the cystic mass, complete thyroidectomy is recommended in order to eliminate the possibility of an occult thyroid carcinoma.²⁰

In our case, the histopathological and immunohistochemical findings were consistent with the presence of a PTC in a branchial neck cyst. According to these findings and the current literature, the exclusion of a metastatic PTC by performing complete thyroidectomy was necessary. Since no primary PTC was detected, we considered rh-TSH as an adjunctive tool in the radioiodine treatment of the two residual masses in the lateral neck region. To our knowledge, this is the first case of a PTC, arising in a branchial neck cyst where rh-TSH was used along with radioiodine treatment in primary ectopic thyroid cancer.

In conclusion, we have described a very unusual case of primary PTC located in a left lateral branchial cyst. Although rare, the clinician should always take into account the presence of thyroid tissue in these ectopic sites and the possibility of malignancy. In the latter case, the therapeutic approach should include surgical excision of the cyst, total thyroidectomy and rh-TSH-aided radioiodine ablation where indicated.

Learning points

- ▶ Branchial cysts should be considered in the differential diagnosis of a neck mass.
- ▶ The clinician should always take into account the presence of thyroid tissue in these ectopic sites and the possibility of malignancy.
- ▶ The therapeutic approach should include surgical excision of the cyst, total thyroidectomy and rh-TSH-aided radioiodine ablation where indicated.
- ▶ This rare entity requires a high index of clinical suspicion and a multidisciplinary approach by a group of specialists in order to provide an effective therapeutic outcome.

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