Rare disease

De-differentiation of papillary thyroid carcinoma into squamous cell carcinoma. A case of coexistence within an excised neck lesion

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Summary

An 80-year-old man with papillary thyroid carcinoma of the neck underwent surgery and radioiodide therapy. He presented 11 years later with a lesion adjudged from fine needle aspiration to be a squamous cell carcinoma (SCC). Histological analysis of the excised mass revealed a lymph node overwhelmed with papillary thyroid carcinoma and moderately differentiated SCC thought to have transformed from papillary cells. A very small number of similar transformations specifically involving the 'tall cell variant' of papillary carcinoma transforming to spindle cell carcinoma have been reported previously. This case report demonstrates clear images of this rare occurrence and briefly considers factors leading to de-differentiation. The clinician should consider possible transformation from papillary thyroid cancer in cases of SCC of the head and neck as this variation may be more aggressive.

BACKGROUND

The 'tall cell variant' (TCV), a more aggressive form of papillary thyroid carcinoma (PTC) was discovered by Hawk and Hazard in 1976.¹ Since then only a handful of studies have recorded the transformation of PTC into squamous cell carcinoma (SCC) or spindle cell squamous carcinoma.^{2–7} This case provides further evidence and images of this de-differentiation.

Very little is known about this disease and no authoritative prognostic data exist. Of the three individual case studies, one case was seen to make a good recovery² whereas the other two patients died within 6 months of diagnosis.^{3–4} The remaining three studies do not offer formal follow-up data, most likely because of small case numbers. However, two of these studies^{5–7} found the transformed SCC to be particularly aggressive with high invasive potential. Much further work is needed both in terms of understanding the mechanism of transformation and the role of suspicious genes as well as prognosis.

CASE PRESENTATION

An 80-year-old man, a non-smoker, was diagnosed with having a right-sided PTC. The tumour was a stage 2 carcinoma without lymph node metastasis. Shortly afterwards, he underwent a lobectomy then complete thyroidectomy. Histology showed no residual malignancy. Four years later a biopsy of the patient's right cervical lymph node showed PTC and he was treated with two courses of radio iodine ablation therapy (figure 1). Despite slightly elevated thyroglobulin levels 1 year on (1.45 mcg/l), bone scan and abdominal CT scan, followed by neck MRI and thoracic CT were also negative.

The patient presented again, 2 years and 3 months, later with a clinically enlarged right cervical lymph node in the level III region. Neck dissection and lymph node

clearance of levels II–IV found papillary carcinoma in 9 of the 41 lymph nodes obtained from levels II, III and IV with some soft tissue invasion in level III. External beam radiotherapy was withheld in favour of observation and follow-up as thyroglobulin levels were normal and an ultrasound examination of the neck was negative.

At routine follow-up 2 years and 4 months later, the patient complained of lower superficial neck discomfort, ultrasound confirmed the presence of recurrent disease. Blood samples showed serum thyroid-stimulating hormone at 0.05 µIU/ml, free T4 at 24.5 pmol/l and thyroglobulin <5 mcg/l. Repeat ultrasound, 3 months on, showed a mass 2×2×2 cm in size adjacent to the trachea. Fine needle aspiration yielded 'keratinised atypical squamous cells individually and in clusters, consistent with squamous cell carcinoma' (figure 2). An 18FDG PETCT scan with FDG acquisition from skull base to thigh with

Figure 1 Histology images from the largest of the three masses. High-power image of the papillary thyroid carcinoma cells.

Figure 2 Histology images from the largest of the three masses. High-power image of the squamous carcinoma cells.

Figure 3 Histology images from the largest of the three masses. Low-power image of squamous and papillary carcinoma cells together.

low-dose CT for attenuation correction was performed showing intense FDG uptake in the residual right hemithyroid and cutaneous FDG activity in the caudal left axilla. Interestingly, prior to the CT scan, the patient complained of an inflamed lesion in the same axilla.

The following month, the patient underwent direct pharyngoscopy, laryngoscopy and oesophagoscopy. Tonsillectomy was performed and a biopsy taken from the right tongue base. The pharynx, larynx and oesophagus were otherwise noted to be clear to 40 cm. Right-sided levels IV and VI neck dissection with division of veins, strap muscles and lateral displacement of the recurrent laryngeal nerve found a mass invading the trachea.

DIFFERENTIAL DIAGNOSIS

If a patient with a trachea invasive lesion was to present in the first instance, follicular, hürtle cell, medullary and anaplastic carcinoma would have to be considered as differential diagnoses.

Given the history, it would appear here as though this may be a straightforward recurrence of PTC. However, the moderately differentiated SCC yielded from the invasive lesion suggests a possible secondary malignancy. For instance, a laryngeal carcinoma given the invasive nature.

OUTCOME AND FOLLOW-UP

Histopathology of the tongue base and tonsil biopsies showed no signs of malignancy. The excised neck mass was found to be composed of three pieces of tissue. The first piece consisted of an aggregate of three lymph nodes with each node containing PTC cells. The second mass consisted of a single node also containing the same papillary carcinoma cells. The third mass and the largest of the three consisted of a lymph node containing and overwhelmed by a mix of PTC and moderately differentiated squamous carcinoma (figure 3).

Both the papillary and squamous cells stained moderately well for thyroid transcription factor (TTF)-1 stain (figures 4 and 5). Cytokeratin 19 stain was also used on both tissue types and stained the papillary cells strongly but the squamous cells were weakly stained. The patient was followed up in clinic 2 weeks postoperatively and from here referred for external beam radiotherapy. Despite

this, the disease metastasised to the patient's lungs and he deteriorated, passing away 1 year later.

DISCUSSION

Given the close histological association of the two cell types and the apparent absence of a primary SCC along with negative biopsies, the SCC was believed to have transformed from papillary carcinoma cells. This is a rare and sparsely documented occurrence. In the case studies²⁻⁴ the authors concluded that SCC had also transformed from a pre-existing PTC. The corroborative studies noted a close histological association between papillary and squamous cells, and islands of SCC were observed to merge 'imperceptibly' or in close 'apposition' with TCV cells.

Three papers²⁻⁵ noted some common pathological similarities in the form of seemingly high concentrations of Ki-67 mutations in the TCV specimens and evidence of p53 mutations in the SCC specimens. One case study also noted that the papillary carcinoma and squamous carcinoma were both positive for some of the same types of keratin proteins.² Gopal *et al*⁶ also noticed strong staining of both cell lines in the same specimen with TTF-1.

Figure 4 Histology images from the largest of the three masses. High-power image of papillary carcinoma cells stained with TTF-1.

Figure 5 Histology images from the largest of the three masses. High-power image of squamous carcinoma cells stained with TTF-1.

Kleer *et al*⁵ suggested that the detection of p53 and Ki-67 mutations may have a future role in predicting prognosis for this disease.

Learning points

- ▶ This case provides further evidence to suggest that papillary cell carcinoma can transform into differentiated squamous cell carcinoma (SCC). It is important to consider this possibility in any new case of SCC of the head and neck following previous papillary thyroid carcinoma.
- ▶ On the basis of pathological results elsewhere, this malignancy appears highly aggressive and may be as aggressive as the anaplastic type. It is important to consider whether transformation has occurred from papillary tall cell variant when histological biopsy from the head and neck yields SCC.
- ▶ The case is a reminder that disease does not always adhere to strict pathological classification.
- ▶ Much further work is needed both in terms of understanding the mechanism of transformation and the role of suspicious genes.

Competing interests None.

Patient consent Obtained.

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