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ScienceDirect
Pathology – Research and Practice 206 (2010) 263–269
PATHOLOGY RESEARCH AND PRACTICE
www.elsevier.de/prp

TEACHING CASES

Thyroid carcinoma with papillary and squamous features: Report of a case with histogenetic considerations ☆

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Received 12 November 2008; received in revised form 27 March 2009; accepted 12 May 2009

Abstract

We present a case of an 82-year-old female with a painless left latero-cervical swelling, which increased in size over the course of 6 months, compressing adjacent organs. The histopathological examination, following dissection of the left thyroid lobe and ipsilateral cervical lymph nodes, yielded two intermingled morphologically distinct histotypes that included conventional papillary thyroid carcinoma (PTC) and poorly differentiated squamous cell carcinoma (SCC) with cystic features. The clinical presentation, the immunophenotype, and the genotype, especially of the malignant squamous component with partial expression of TTF1, marked expression of p63 and mutation of BRAF, were consistent with the diagnosis of a papillary thyroid carcinoma with squamous component. The possibility of a squamous cell carcinoma of unknown origin metastasizing to a primary papillary thyroid carcinoma cannot be completely ruled out. This particular presentation of thyroid carcinoma carries a poor prognosis in 20% of cases, with high recurrence rates and distant metastasis.

Keywords: Thyroid; Papillary carcinoma; Squamous cell carcinoma

Introduction

Papillary thyroid carcinoma (PTC) associated with poorly differentiated squamous cell carcinoma (SCC) denotes a rare tumor of the thyroid displaying morphological and immunophenotypical features of both components within the same lesion. The frequency of this so-called rare malignant tumor represents less than 2% of all the thyroid cancers. Primary squamous cell carcinoma of the thyroid is very rare, with a reported incidence of 0.7–3.4% [4,5]. According to some authors, SCC occasionally presents with papillary formation and could be considered a variant of PTC [7]. Transformation from a well-differentiated thyroid carcinoma into a poorly differentiated carcinoma is infrequent and is usually associated with a dismal prognosis [18]. Such transformation often mimics the clinical course of anaplastic carcinoma and is generally treated with aggressive surgery followed by postoperative radiotherapy [22]. It is well known that squamous metaplasia can occur in association with either PTC [16] or an inflammatory process [11], and can also be found in embryologic remnants.

We describe a case in which preoperative fine needle aspiration (FNA) suggested a squamous cell carcinoma,

☆ This work was presented during the 3rd Intercontinental Congress of Pathology, Barcelona, Spain, May 17–22, 2008.

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doi:10.1016/j.prp.2009.05.003

while post-operative histology of the same specimen revealed a biphasic tumor comprising areas of PTC merged with poorly differentiated SCC. The patient had lymph node metastases and succumbed to the disease within 2 months after the histologic diagnosis.

Material and methods

Clinical case

An 82-year-old woman presented with a 6-month history of a painless swelling on the left side of her neck, which had rapidly increased in size over the course of a few weeks, resulting in the compression of the trachea. Clinical examination revealed a tense and fluctuant mass ($8 \times 6\,cm^2$) at the anterior border of the sternocleidomastoid muscle, extending to the left lobe of the thyroid. Several ipsilateral lymph nodes measuring up to 2 cm were observed. An ultrasonography of the neck revealed a poorly demarcated hypoechogenic lesion with a cystic space measuring 4 cm (Fig. 1a). The tumor was not fixed to the skin, but had affected the surrounding soft tissues by direct infiltration of the trachea, larynx, and hypopharynx. Fine needle aspiration showed atypical squamous cells and macrophages. Exhaustive clinical, endoscopic, and radiological examinations did not reveal any primary site of SCC or any contiguous spread from neighboring structures. There was no personal or family history of thyroid cancer or endocrine disorders. The proposed clinical diagnosis was a branchial cleft cyst with malignant transformation. Lymph node metastasis with cystic degeneration of an unknown primary tumor was considered as an alternative diagnosis. A surgical resection involving the left lobe of the thyroid and a radical ipsilateral cervical dissection in monobloc were performed. The patient succumbed to the disease within 2 months after the histological diagnosis, and, to our knowledge, no autopsy was performed.

Conventional histology

The surgical specimen was fixed in 10%-buffered formalin. The whole lesion, including cystic and solid components, was sampled. Sections (5 μm thick) were stained with hematoxylin and eosin and analyzed by conventional microscopy.

Immunohistochemistry

Representative tissue sections, including squamous and PTC components (Fig. 2a), were used for immunohistochemical analysis with commercially available antisera to thyroglobulin (Novocastra), thyroid transcription factor (TTF)-1 (Zymed) Pancytokeratines C11 (C-11, Novocastra, dilution 1/100), and Cytokeratin 5/6 (D5/16B4, Dako, dilution 1/50). In addition, the expression of Vimentin (Progen, dilution 1/3200-automatic), p63 (4A4, Dako, dilution 1/100), and p53 (Dako, dilution 1/50) was analyzed, as well as the proliferation labeling index for ki-67 (Mib-1, Dako, dilution 1/50).

Molecular analysis

DNA analysis

After deparaffinization and staining in 0.1% toluidine blue, histologically selected areas of tissue sections were microdissected [2]. Genomic DNA was then extracted using the DNeasy Tissue Kit (Qiagen, Germany).

Mutation screening of BRAF

The most common T1799A transverse mutation (*BRAF* V600E) was studied by direct sequencing after PCR amplification of exon 15 of the *BRAF* gene. DNA was amplified using the following primers: forward 5′-TCTTCATAATGCTTGCTCTGATAG-3′, and reverse 5′-TGGAAAAATAGCCTCAATTCTTAC-3′. Sequencing was performed with the internal primer 5′-TCTACTGTTTTCCTTTACTTACT-3′.

Mutation of p53

Exons 5–9 of the p53 gene were amplified and sequenced, as previously described [14].

Microsatellite instability (MSI) analysis

Extracted DNA was amplified by PCR using the markers BAT25, BAT26, D2S123, D5S346, and D17S250. MSI was defined as the presence of novel fragment sizes in tumor DNA, which was absent in corresponding normal DNA.

Results

The surgical specimen weighed 75 g and measured $9 \times 6 \times 3\,cm^3$. The left thyroid lobe was enlarged and measured $8 \times 6 \times 3\,cm^3$. It was almost completely replaced by a gray-beige tumor with solid and cystic components, which extended to the surgical margins (Fig. 1b). The cut surface revealed a central cystic area that measured 4 cm at the greatest diameter and contained a dark serous liquid. Its wall was firm and thickened. There were only a few scattered foci of recognizable thyroid tissue in the upper part of the lobe. The excised fatty tissue from the neck dissection was carefully examined, and 18 lymph nodes were identified and submitted for histologic examination.