Clinical case

Cribriform-morular variant of papillary thyroid carcinoma: Characteristic histologic feature of adenomatous polyposis. A case report

Carcinome papillaire de la thyroïde de forme morulaire et cribriforme : une forme histologique caractéristique de la polyadénomatose familiale : à propos d’un cas

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Abstract

We report the case of a 24-year-old woman with familial adenomatous polyposis and diagnosed with cribriform-morular variant of papillary thyroid carcinoma. Neck ultrasound and computed tomography identified multiple nodules in the thyroid gland and neck lymph nodes. The cytological analysis was compatible with the diagnosis of papillary cancer of the thyroid. Total thyroidectomy with lymph node dissection was performed. The histological analysis established the diagnosis of cribriform-morular variant of papillary thyroid carcinoma. Despite preoperative findings suggesting an aggressive form of thyroid cancer with lymph node involvement, the final diagnosis was a variant of papillary thyroid carcinoma often associated with familial adenomatous polyposis and known to have a good prognosis.

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Résumé

Nous rapportons l’observation d’une femme de 24 ans atteinte de polyadénomatose familiale (PAF) chez qui a été diagnostiqué un cancer papillaire de la thyroïde avec des caractéristiques histologiques de type morulaire et cribriforme. Un nodule thyroïdien a été découvert par autopalpation. L’échographie a mis en évidence des nodules multiples intrathyroïdiens associés à de nombreux ganglions cervicaux bilatéraux confirmés par le scanner. Une cytoponction thyroïdienne était en faveur du diagnostic de cancer papillaire de la thyroïde. Le traitement a consisté en une thyroïdectomie totale avec exérèse ganglionnaire. L’analyse histologique a confirmé l’existence d’un carcinome papillaire multifocal et bilatéral de la thyroïde de forme morulaire et cribriforme très évocateur de la PAF, de bon pronostic. Aucun ganglion n’était envahi. Un traitement complémentaire a consisté en l’administration d’iode radioactif et hormonothérapie frénatrice. En conclusion, malgré un aspect échographique inquiétant suggérant un envahissement ganglionnaire précoce, il s’agissait d’une présentation particulière de cancer papillaire de bon pronostic très fortement liée à la PAF.

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1. Introduction

Familial adenomatous polyposis (FAP) is an inherited condition transmitted in an autosomal dominant pattern related to germline mutation of the adenomatous polyposis coli (APC) gene predisposing to colorectal cancer. Various endocrine diseases described in association with FAP have been described: adrenals [1], pituitary [2], parathyroid [3], pancreas [4], MEN1 [5], 2b [6]. Cribriform-morular variant of papillary thyroid carcinoma (CMVPTC) is one of the most common endocrine tumors diagnosed in patients with FAP, observed in about 0.3 to 1% of cases [7,8].

The purpose of this work was to present the case of a female patient with FAP who developed CMVPTC and to recall the epidemiological, histological and prognostic features of this tumor as well as the therapeutic approach.

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2. Case report

A 24-year-old woman with familial colorectal polyposis was admitted for a multinodular goiter with a macronodule on the right measuring 3 cm. She was clinically and biologically euthyroid. Neck ultrasound confirmed the presence of a right isoechogenic parasthmic nodule measuring 3 cm in diameter with peripheral and central vascularization together with microcalcifications in a multinodular goiter. There were several lymph nodes measuring less than 1 cm and three enlarged nodes on the right. Two fine-needle aspiration cytology specimens obtained from the dominant nodule in the right lobe revealed the presence of potentially malignant cells without formally confirming papillary or medullary carcinoma. This latter diagnosis was ruled out by the normal serum calcitonin level. A computed tomography of the neck and mediastinum disclosed the presence of multiple nodal formations along the two jugulocarotid and spinal chains and several hypodense nodular formations in the right thyroid lobe at the arterial time. There was no evidence of spread to the mediastinal nodes. The tentative diagnosis was papillary carcinoma of the thyroid with suspected bilateral lymph node metastases. Total thyroidectomy was performed with pretracheal and right recurrential dissection. The gross aspect was compatible with predominantly right-lobe multinodular goiter with no evidence of local or regional extension (muscles, recurrent, esophagus, trachea). The dissected nodes were inflammatory. The conclusion of the intraoperative pathology examination of bilateral jugulocarotid node specimens was absence of metastasis. At examination of the surgical specimen, the pathology diagnosis was multilocular bilateral papillary carcinoma with specific characteristics of the cribriform and morular variant (Figs. 1 and 2). All 21 lymph nodes examined were free of neoplasia. Immunohistochemistry was positive for anti-estrogen receptor antibodies and anti-progesterone receptor antibodies. The staging was pT2(m)N0 with complete resection. Complementary radioactive iodine therapy was given for 8 months after the cervicotomy, in combination with inhibitory hormone therapy continued until remission criteria were met.

3. Discussion

The preoperative work-up in this patient was highly suggestive of an aggressive papillary thyroid cancer (multifocal involvement, numerous bilateral nodes). The final diagnosis was in fact CMVPTC, a histological variant known to be associated with FAP and to have a good prognosis. More than 100 cases of CMVPTC associated with FAP have been published since the first case report by Crail in 1949 [9]. The estimated prevalence has varied from 0.3 to 1% of patients with FAP [7,8,10]. The risk of CMVPTC in women with FAP is 100 times higher than in women without FAP [11]. Compared with the general population, women aged less than 35 years with FAP have a 160-fold increased risk of papillary thyroid carcinoma [12].

A characteristic feature of thyroid cancers associated with FAP is that they are papillary carcinomas. The link between these two conditions is so strong that the diagnosis of CMVPTC should always lead to a search for FAP. Harach et al. [13] described the characteristic clinical, epidemiological and histological features of CMVPTC in 63 patients with FAP, noting that this variant is observed in only 1/1000 cases of sporadic papillary cancer.

Histologically, the CMVPTC exhibits a characteristic cribriform, morular, trabecular, follicular and papillary architecture [14]. The term “morular” designates cells in a spindled or whorled pattern forming nest-like structures or morula (from the Latin morula: mulberry) (Fig. 1). “Cribriform” designates a perforated appearance (Fig. 2) [15]. In the literature, immunohistochemistry studies of the tumor have described the characteristic cytoplasmic expression: thyroglobulin, neuron-specific enolase, epithelial membrane antigen, low-molecular-weight cytokeratin, vimentin, protein bcl2. Nuclear expression of progesterone and estrogen receptors is also described, as found in
our patient, as well as retinoblastoma protein and accumulation of beta-catenin in the nucleus and cytoplasm [14].

Mean age at diagnosis is 30 years, compared with 45 years in sporadic forms of the tumor [7]. The sex-ratio is 20F/1M [16]. CVMPTC is a multifocal bilateral tumor [17,18]. In one retrospective series of 1050 patients with FAP, 11 cases of CVMPTC were observed with no associated deaths [8]. Tomoda et al. [19] reported no cases of recurrence at 60 months follow-up in their seven patients with CVMPTC.

This explains why total thyroidectomy is required, yet extensive node dissection would not be necessary [20]. These conclusions have been based on series including a small number of patients.

Loss of APC gene function [21], gain in ret/PTC1 proto-oncogene function [22], and frequent mutations of the beta-catenin gene [14] have been incriminated as playing a role in the genetic basis of the disease. No consensus has been reached concerning the need for systematic screening for CVMPTC in patients with FAP because of the very low prevalence [7,8]. Nevertheless, a regular physical examination of the thyroid gland is recommended for these patients, with a thyroid ultrasound as needed. Prophylactic thyroidectomy is not recommended for patients with FAP [10].

Conversely, the diagnosis of CVMPTC in a patient without known FAP is highly suggestive of the familial disease, implying the need for a screening colonoscopy.

Disclosure of interest

The authors have not supplied their declaration of conflict of interest.

References