Letter to the Editor

Mucinous carcinoma of the thyroid: A case report and review of the literature

Carcinome mucineux de la thyroïde : à propos d’un cas et revue de la littérature

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Abstract

We report the case of a primary mucinous carcinoma of the thyroid in a man of 74 who had a 4-cm nodule in the right lobe of the thyroid, with a solido-cystic appearance on ultrasound associated with lymph node metastases. On scintigraphy, the nodule was hot and not extinctive. The patient underwent total thyroidectomy with a ipsilateral right lymph node dissection. The immunohistochemical study showed the negativity of CK 7 and CK 20 and the positivity of thyroglobulin and TTF 1. Postoperatively the rate of blood thyroglobulin 3 months after surgery had collapsed to 0.17 ng/ml. The evolution was marked by the appearance of pulmonary metastasis and the patient died 4 months after surgery. Histological study showed the presence of almas of neoplastic cells surrounded by large deposits of extracellular mucin. Primitive mucinous carcinoma of the thyroid is a rare tumor which differential diagnosis is established on the positive immunohistochemistry of thyroglobulin and TTF1 but negative for other markers.

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Keywords: Mucinous carcinoma; Thyroid cancer; Mucin; TTF1

Résumé

Nous rapportons le cas d’un carcinome mucineux primitif de la thyroïde chez un homme de 74 ans qui présentait un nodule de 4 cm au niveau du lobe droit de la thyroïde, avec un aspect solido-kystique à l’échographie associé à des métastases ganglionnaires. À la scintigraphie, le nodule était chaud et non extinctif. Le patient a bénéficié d’une thyroïdectomie totale avec un curage ganglionnaire homolatéral droit. L’étude immuno-histochemique montrait la négativité de la CK 7 et CK 20 et la positivité de la thyroglobuline et du TTF 1. En postopératoire, le taux de thyroglobuline sanguin 3 mois après la chirurgie était effondré à 0,17 ng/ml. L’évolution a été marquée par l’apparition de métastases pulmonaires et le décès du patient 4 mois après la chirurgie. L’étude anatomopathologique a montré la présence d’almas de cellules néoplasiques entourées par des dépôts larges de mucine en extracellulaire. Le carcinome mucineux primitif de la thyroïde est un tumeur rare dont le diagnostic différentiel est établi sur l’immunohistochimie positive de la thyroglobuline et de la TTF1 mais négative pour les autres marqueurs.

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Mots clés : Carcinome mucineux ; Cancer thyroïde ; Mucine ; TTF1

1. Introduction

The mucinous carcinoma of the thyroid was first described in 1976 by Diaz-Perez [1].

It is an extremely rare non-epithelial primary malignant tumor of the thyroid. Only seven cases have been reported in the literature [2], thus, the clinical and histological features have not been widely documented. Our patient was a 74-year-old man who was a chronic smoker (60 pack years). He had no history of neck radiation or familial thyroid disease. A year before admission, he perceived a mass growing on his neck with dysphonia.

The clinical examination revealed a hard and painless nodule of 4 centimeters in the right lobe of the thyroid, with ipsilateral
cervical lymph nodes, without dyspnea or deterioration of general condition. By naso-endoscopy it was identified that the right vocal cord was atrophied and immobile in its anterior half. Biochemical tests, routine blood counts, and biochemical tests were normal and TSHus concentration was within the normal range at 2.12 μU/ml (0.25–4 μU/ml). The blood rate of the Prostate Specific Antigen (PSA) was normal (0.36 ng/l). Ultrasonography identified an increased size of the right lobe of the thyroid (measuring 25.8 × 50 × 38.7 mm), within it, a solid and cystic heterogeneous nodule, in contact with the sidewall of the trachea, measuring 35 × 25 mm. The vascularization was essentially peripheral. The nodule was rated TI-RADS 4a. The presence of bilateral infra-centimetric cervical lymph nodes, which preserved architecture, were noted. Thyroid scintigraphy showed high uptake of the radioiodine by the thyroid nodule, with a fairly significant hypertrophy of the thyroid (Fig. 1). The patient underwent a total thyroidectomy with right cervical lymph nodes resection with no postoperative complications. Macroscopically, the tumor was a white and solid mass. Microscopically, the parenchyma was massively occupied by a moderately differentiated carcinomatous proliferation, made of solid glandular and cellular cords with a pool of extracellular mucin (Fig. 2). The cells were large with eosinophilic cytoplasm. This proliferation invaded the pericapsular tissue and there were vascular invasions. The cervical lymph nodes were massively invaded by the

Fig. 1. Thyroid scintigraphy showing a high uptake of the radioiodine by the thyroid nodule.

Fig. 2. a: thyroid parenchyma invaded by a carcinomatous proliferation with extracellular mucin. (Hematoxylin Eosin Staining); b: carcinomatous mass in a mucinous stroma; c: lymph node metastasis of a mucinous carcinoma of the thyroid; d: immuno-histochemistry: focal positivity to thyroglobulin.
Table 1
Reported cases of primitive mucinous carcinomas of the thyroid.

<table>
<thead>
<tr>
<th>Age/Gender</th>
<th>Tumor size (cm)</th>
<th>Treatment</th>
<th>Immuno-histo-chemistry</th>
<th>Metastases</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diaz-Perez et al. (1976) [1]</td>
<td>44/M</td>
<td>5.0 × 4.0 × 3.0</td>
<td>Partial thyroidectomy</td>
<td>NM</td>
<td>NM</td>
</tr>
<tr>
<td>Sobrinho-Simoes et al. (1985) [4]</td>
<td>40/M</td>
<td>2.8 × 2.5 × 1.5</td>
<td>Left lobectomy</td>
<td>Thy –</td>
<td>NM</td>
</tr>
<tr>
<td>Sobrinho-Simoes et al. (1986) [5]</td>
<td>56/M</td>
<td>8 × 6 × 2</td>
<td>Total thyroidectomy Chemotherapy Radiotherapy</td>
<td>Thy+</td>
<td>N+</td>
</tr>
<tr>
<td>Cruz et al. (1991) [6]</td>
<td>32/F</td>
<td>6 × 2.5 × 1.5</td>
<td>Total thyroidectomy Chemotherapy Radiotherapy</td>
<td>NM</td>
<td>N+</td>
</tr>
<tr>
<td>Tetsuo Kondo et al. (2005) [7]</td>
<td>82/F</td>
<td>3 × 2 × 2</td>
<td>Total thyroidectomy Radioisotope therapy</td>
<td>Thy+, TTF1+</td>
<td>N+</td>
</tr>
<tr>
<td>D’Antonio et al. (2007) [8]</td>
<td>59/F</td>
<td>NM</td>
<td>Total thyroidectomy</td>
<td>Thy+, TTF1+/+</td>
<td>N+</td>
</tr>
<tr>
<td>Mnif et al. (2013) [2]</td>
<td>56/M</td>
<td>4 × 3 × 2 (left) 3 × 3 × 2 (right)</td>
<td>Total thyroidectomy + Lymph node dissection</td>
<td>Thy+, TTF1+</td>
<td>N+</td>
</tr>
<tr>
<td>Present case (2014)</td>
<td>74/M</td>
<td>3.5 × 2.5</td>
<td>Total thyroidectomy + Lymph node dissection</td>
<td>Thy+, TTF1+</td>
<td>N+</td>
</tr>
</tbody>
</table>

F: Female; M: Male; Thy: Thyroglobuline; N+: Lymph Node; NEM: no evidence of disease; DOD: dead of disease; NM: not mentioned.

same proliferation with a capsular break (49N+/57). Immunohistochemical study showed a positive immune-reactivity for thyroglobulin and thyroid-specific transcription factor 1 (TTF-1) and a negative immune-reactivity for CK7 and CK20, which supports the diagnosis of primitive mucinous carcinoma of the thyroid.

Chest, abdomen and pelvis CT found metastatic pulmonary micro-nodules. A radioiodine therapy was discussed, but the postoperative thyroglobulin rate of 0.17 ng/ml was discouraging.

The follow-up tests showed lung and supraclavicular lymph node metastases.

The patient died within 4 months after surgery from respiratory distress. Autopsy was not permitted.

2. Discussion

Primitive mucinous carcinoma of the thyroid is an extremely rare tumor. Only seven cases have been reported in the literature [2]. According to the World Health Organization classification system [3], this type of thyroid carcinoma is characterized by the presence of clusters of neoplastic cells surrounded by extra-cellular mucin deposition, and by positive TTF1 and thyroglobulin, and negative calcitonin and CGRP.

The Table 1 summarizes the reported cases of primitive mucinous carcinomas of the thyroid. The time to diagnosis ranged from 2 months to 2 years. The most common clinical manifestation was a nodular goiter with cervical lymph nodes. One patient had dysphasia, and another patient had dysphagia. Only one patient received radioisotope therapy in which the tumor size was 3 cm. The thyroglobulin postoperative rate was not specified. In our case, the tumor expressed thyroglobulin and had some uptake at preoperative radio-iodine. However, although the patient was metastatic, the postoperative thyroglobulin level was very low. This might be explained by dedifferentiation of the lung metastases. Alternatively, this discrepancy can be explained by the presence of thyroglobulin antibodies. These can interfere with thyroglobulin assays, which, unfortunately was not tested [9]. Of the seven cases reported, five had nodal and lung metastases, with survival ranging from 1 month to 2 years. While the other two patients remained alive without significant recurrence during their follow-up [1,2,4–8]. In our case, the patient had supraclavicular lymph nodes and lung metastases and died 4 months after surgery.

Differential diagnosis must be discussed with other primary tumors of the thyroid expressing intracellular mucin, including papillary, medullary, mucoeidermoid carcinomas, and follicular adenomas [3,10]. In our patient, the diagnosis of medullary carcinoma of the thyroid was not retained because of the non-existence of criteria such as sheets, packets, or irregular islands traversed by delicate fibro vascular septa [11]. However, calcitonin was not initially measured.

Unusual follicular carcinoma is characterized by the presence of significant mucin [11]. However, histological study of the present tumor did not show any of the typical features of follicular tumors such as fibrous capsule or follicular architecture with variable amounts of colloid. Undifferentiated carcinomas sometimes have a mucin production [12]; however, the tumor cells in our case were not pleomorphic and mitotic activity was not high like conventional undifferentiated carcinomas.

Differential diagnosis should exclude metastatic carcinoma of the lung, breast, colon and other organs [3]. In our case, these diagnosis were ruled out at least for metastatic carcinoma by a normal PSA value, a digestive endoscopy and normal pelvic CT.

The histogenesis of mucinous carcinoma of the thyroid is still controversial.

The ultimobranchial body, the solid cell nests that are embryonic remnants and the minor intrathyroid salivary glands are proposed as the origins of mucinous carcinoma [3]. Despite the lack of follicular structure and colloidal substance, focal thyroglobulin and TTF-1 expression led to suggest that the primary mucinous carcinoma is a poorly differentiated carcinoma derived from thyroid follicular cells [7].
Disclosure of interest

The authors declare that they have no competing interest.

References