Acta clin Croat 2000; 39:83-87 Professional paper

PRIMARY MUCOEPIDERMOID CARCINOMA OF THE THYROID WITH AGGRESSIVE BEHAVIOR – CASE REPORT

Božo Krušlin[1], Hrvoje Čupić[1], Vladimir Bedeković[2], Vlado Petric[2], Mirko Ivkić[2] and Mladen Belicza[1]

[1]Ljudevit Jurak Clinical Department of Pathology, and [2]Department of Otorhinolaryngology Sestre milosrdnice University Hospital, Zagreb, Croatia

SUMMARY - This report describes a primary high-grade mucoepidermoid carcinoma of the thyroid in a 33-year-old male. The patient presented with a rapidly enlarging mass in the left thyroid lobe. Cytologic analysis suggested a poorly differentiated thyroid carcinoma. Total thyroidectomy was performed. On gross examination, a poorly circumscribed, gray-white tumor measuring up to 5.5 cm in the largest diameter was found. Light microscopy showed atypical, large epithelial cells forming solid islands and nests with variable, focal production of mucin and up to 5 mitotic figures per 10 high-power fields. Squamous cell foci without keratinization were also observed. Tumor cells were immunohistochemically negative for thyroglobulin and calcitonin, and positive for cytokeratin. Electron microscopy showed squamous cells with intracytoplasmic aggregates of tonofilaments, well-developed desmosomal attachments and mucous cells characterized by numerous mucin granules. Six months after the initial treatment, ipsilateral radical neck dissection revealed 25 positive out of 44 lymph nodes. Computed tomography performed a month later revealed a large tumor located behind the larynx, compressing the trachea, with retrosternal spread into the mediastinum. The patient underwent radiotherapy for a widespread metastatic disease. We think that primary thyroid mucoepidermoid carcinoma may show an aggressive clinical course.

Key words: *Carcinoma – mucoepidermoid; Thyroid neoplasms; Thyroid neoplasms – pathology; Thyroidectomy*

Introduction

Mucoepidermoid carcinoma most commonly arises in the salivary gland but has also been reported at other locations including respiratory and gastrointestinal tract and breast[1-3]. Mucoepidermoid carcinoma of the thyroid is an extremely rare condition. In 1977, Rhatigan et al. were the first to report on a case of mucoepidermoid carcinoma of the thyroid[4]. To our knowledge, about 30 cases have been reported in the English language literature to date[1-3]. The etiology of this tumor is unknown, but its morphology closely resembles the features of ultimobranchial body vestiges or so-called solid cell nests of the thyroid[1,5-7]. Some authors have suggested a common origin with papillary carcinoma[8,9], or that mucoepidermoid carcinoma may be a simple metaplastic transformation of papillary carcinoma[9]. Many authors believe that these tumors are of a low-grade malignant potential[3-10].

Case Report

A 33-year-old male presented with a rapidly enlarging mass in the left thyroid lobe. The patient was clinically euthyroid; serum thyroxine (T4), serum triiodothyronine (T3), resin uptake and serum thyroid-stimulating hormone (TSH) were within the normal limits. The thyroglobulin antibody test and microsomal antibody test were negative.

Correspondence to: *Božo Krušlin, M.D., Ph.D., Ljudevit Jurak* Department of Pathology, Sestre milosrdnice University Hospital, Vinogradska c. 29, HR-10000 Zagreb, Croatia

e-mail: kruslin@mef.hr

Received February 14, 2000, accepted March 18, 2000

Routine blood counts and biochemical tests including serum calcium and phosphorus levels were normal. There was no history of neck irradiation, familial disease of the thyroid, or other endocrine disorders.

Aspiration cytology suggested a poorly differentiated carcinoma. Total thyroidectomy was performed. Tumor tissue was fixed in 10% formalin and embedded in paraffin. Five μm sections were cut and stained with hematoxylin and eosin, alcian blue and periodic acid Schiff stain. Immunohistochemical study was performed using the peroxidase/antiperoxidase method. Primary antibodies were purchased from DAKO, Glostrup, Denmark. Pathologic examination including histochemical, immunohistochemical and ultrastructural analysis indicated a mucoepidermoid carcinoma. After histologic diagnosis, an extensive clinical examination was performed to exclude occult primary cancer of the head, neck and lungs. There was no history of mucoepidermoid carcinoma developing previously at some other, more typical locations, and no other primary tumor was found.

Six months after the initial presentation, the patient underwent ipsilateral cervical lymph node dissection. Pathologic analysis showed a metastatic tumor histologically consistent with primary tumor in 25 out of 44 lymph nodes. Computed tomography performed a month later revealed a large tumor located behind the larynx, compressing the trachea, with retrosternal spread into the mediastinum. The patient underwent radiotherapy for disseminated metastatic disease. Sixteen months after the diagnosis the patient was lost from the follow-up.

Pathohistologic findings

On gross examination, the left thyroid lobe measured 6.0x5.0x3.0 cm with a smooth capsule. On cut section, a poorly circumscribed, gray-white tumor measuring up to 5.5 cm was observed. The right lobe was macroscopically normal. Light microscopic examination revealed atypical large squamoid epithelial cells forming solid islands and nests (Fig. 1). Some tumor cells showed mucin production. The amount of mucin in cells varied. Foci of squamous cells without keratinization were observed throughout the tumor. Up to 5 mitotic figures *per* 10 high-power fields were detected. Alcian blue-positive reaction was observed in the majority of mucin producing cells (Fig. 2). The tumor was not encapsulated, and it invaded the surrounding thyroid parenchyma and adjacent soft tissues. The non-neoplastic thyroid tissue showed focal collections of lymphocytes. The

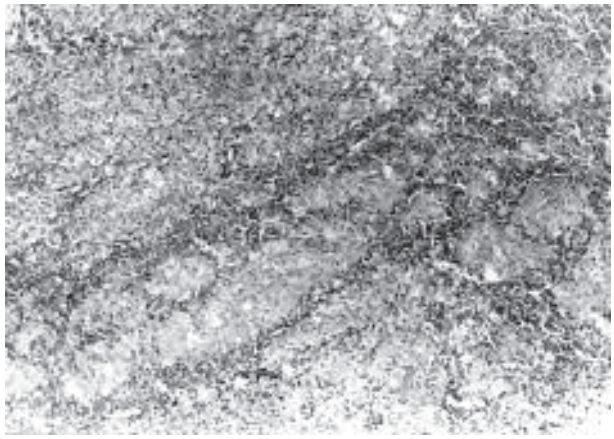

Fig. 1. Primary high-grade mucoepidermoid carcinoma of the thyroid gland (HE x100).

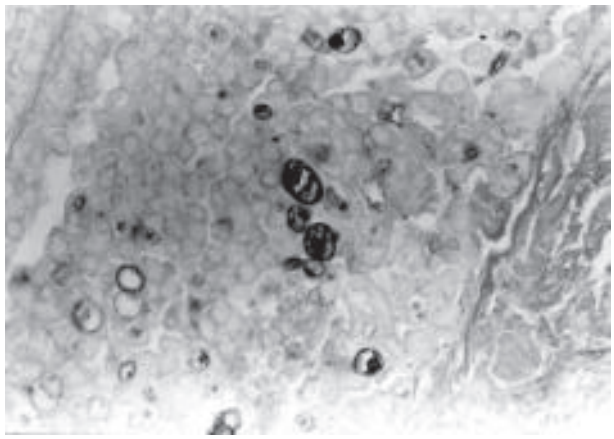

Fig. 2. Thyroid mucoepidermoid carcinoma showing alcian blue-positive reaction in the majority of mucin-producing cells (alcian blue x400).

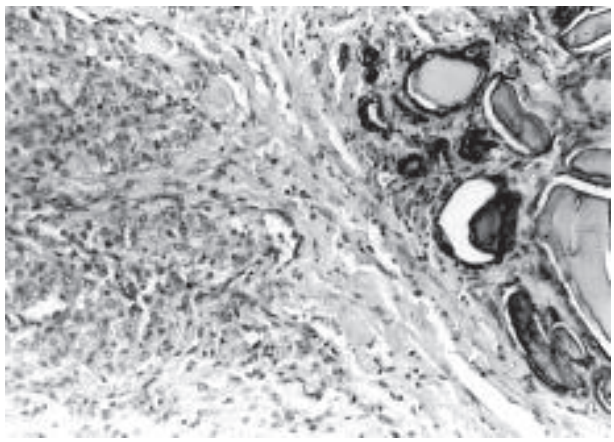

Fig. 3. Negative immunostaining for thyroglobulin in mucoepidermoid carcinoma (PAP x100).

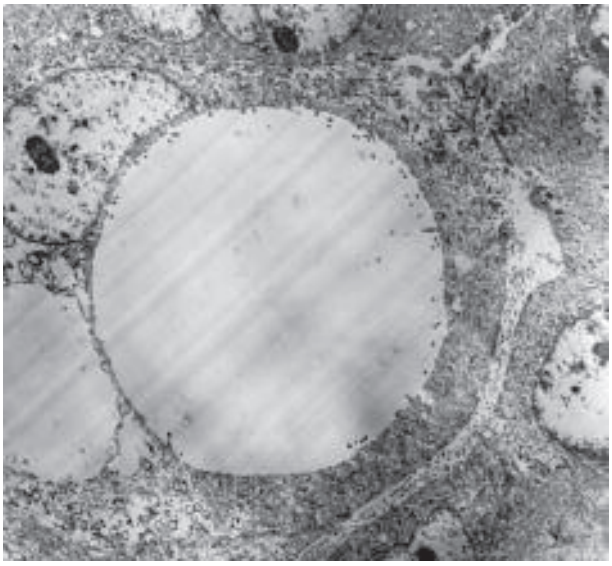

Fig. 4. Ultrastructural analysis of thyroid mucoepidermoid carcinoma showed squamous cells with intracytoplasmic aggregates of tonofilaments, well-developed desmosomal attachments, and mucous cells characterized by numerous mucin granules and intracellular lumina.

tumor cells were negative for thyroglobulin (Fig. 3) and calcitonin, and positive for cytokeratin. Electron microscopic study revealed squamous cells containing intracytoplasmic aggregates of tonofilaments with well-developed desmosomal attachments and mucous cells characterized by numerous mucin granules and intracellular lumina (Fig. 4). The histologic features of the lymph node metastases were identical to those found in the primary tumor.

Discussion

To date, 36 cases of thyroid mucoepidermoid carcinoma have been reported in the literature, including 12 cases of sclerosing mucoepidermoid carcinoma with eosinophilia[8,10-14]. Concurrence of papillary and mucoepidermoid thyroid carcinoma was found in three of these patients[7,11,15]. In ten of all reported cases, histologic characteristics of thyroid papillary carcinoma including nuclear features and psammoma bodies were observed[10,15,16]. One of the cases reported by Fransilla et al.[10] probably represented a high-grade neoplasm with foci of undifferentiated carcinoma. A unique thyroid tumor showing features of papillary and mucoepidermoid carcinoma with anaplastic transformation in a 62-year-old woman has been reported by Cameselle-Teijeiro et al.[12]. Thyroid mucoepidermoid carcinoma is more common in females with an age range from 29 to 70 (median 50) years[3]. Five reported cases occurred in patients in the first or second decade of life[3]. Primary mucoepidermoid carcinoma of the thyroid usually is of a low-grade malignant potential, resembling papillary carcinoma in its natural history. However, one patient reported by Fransilla et al. died 13 months after the diagnosis[10]. Another patient with primary thyroid mucoepidermoid carcinoma arising from a papillary epithelial neoplasm died 11 months after the diagnosis[15]. Our patient also had an aggressive course of the disease. Among all patients reviewed by Wenig et al.[3], nodal metastases were found in 13 cases. Nodal metastases were also observed in patients with sclerosing mucoepidermoid carcinoma recently reported in the literature[8,14]. Extrathyroidal extension occurred in seven of the cases reported in the literature[3,10,13]. Distant metastases were recorded in four patients[8,10,13]. It is well known that salivary gland mucoepidermoid carcinomas display a continuum from low- to high-grade neoplasms. Some authors suggest that histologic features of thyroid mucoepidermoid carcinoma parallel to some degree the salivary gland low-grade mucoepidermoid carcinomas[3]. They think that the overall histologic differences call for distinctly separate entities with no specific parallels in biological behavior[3]. However, our case as well as other reported cases indicates the potentially aggressive behavior of mucoepidermoid carcinoma[15,16]. Therefore, we think that not all mucoepidermoid carcinoma might be indolent tumors with low-grade potential.

The origin of mucoepidermoid carcinoma is unclear. There have been different hypotheses on the histogenesis of this tumor, one of them suggesting the tumor to originate from ultimobranchial body vestiges or so-called 'solid cell nests' of the thyroid[1,5,6,17,18]. Ultimobranchial body nests were identified in 32.5% of fetal thyroids and showed anatomical, morphological and histochemical features similar to those of ultimobranchial postnatal thyroid solid cell nests[6]. Solid cell nests were found in 60% of thyroid glands in adults[5]. They were mainly composed of epidermoid cells arranged in solid structures or lining cystic, tubular or follicular structures[5]. Solid clusters usually showed lumina containing PAS-positive and mucin-positive cell debris[5]. However, solid cell nests were not observed in any of thyroid mucoepidermoid carcinoma cases reported by Wenig et al.[3]. Other authors advocate a common origin with papillary carcinoma[3,7]. They think that lymphocytic thyroiditis present in the non-neoplastic thyroid parenchyma may induce squamous metaplasia of thyroid follicular cells. These metaplastic cells may represent the foci for the sub-

sequent development of follicular epithelial cell tumors including mucoepidermoid carcinoma of the thyroid[3].

In our case, we did not find thyroglobulin positivity in tumor cells, while thyroglobulin reactivity was observed in five of six cases reported by Wenig et al.[3], in both squamous cells and mucocytes. In one of their patients, thyroglobulin reactivity was also detected within the ciliated epithelial cells.

Surgery is the treatment of choice; however, in cases of poorly differentiated tumors radiotherapy can be applied. There is still debate about adjuvant therapies, the results of which appear to be very poor at present. There is a need of such cases to be consistently reported to improve the treatment and prognosis, especially those with an aggressive clinical course.

Note added in proof:
The patient died two years after diagnosis due to widespread metastatic disease.

References

1. KATOH R, SUGAI T, ONO S, TAKAYAMA K, TOMICHI N, KURIHARA H, TAKAMATSU M. Mucoepidermoid carcinoma of the thyroid gland. Cancer 1990;65:2020-7.
2. MIRANDA RN, MYINT MA, GNEPP DR. Composite follicular variant of papillary carcinoma and mucoepidermoid carcinoma of the thyroid. Report of a case and a review of the literature. Am J Surg Pathol 1995;19:1209-15.
3. WENIG BM, ADAIR CF, HEFFESS CS. Primary mucoepidermoid carcinoma of the thyroid gland: a report of a case and a review of the literature of a follicular derived tumor. Hum Pathol 1995;26:1099-101.
4. RHATIGAN RM, ROGUE JL, BUCHER RL. Mucoepidermoid carcinoma of the thyroid gland. Cancer 1977;39:210-4.
5. HARACH HR. A study on the relationship between solid cell nests and mucoepidermoid carcinoma of the thyroid. Histopathology 1985;9:195-207.
6. HARACH HR, VUJANIC GM, JASANI B. Ultimobranchial body nests in human fetal thyroid: an autopsy, histological and immunohistochemical study in relation to solid cell nests of the thyroid gland. J Pathol 1993;169:465-9.
7. VICIANA MJ, GALERA-DAVIDSON H, MARTIN-LACAVE I, SEGURA DI, LOIZAGA JM. Papillary carcinoma of the thyroid with mucoepidermoid differentiation. Arch Pathol Lab Med 1996;120:397-8.
8. GEISINGER KR, STEFFEE CH, McGEE RS, WOODRUFF RD, BUSS DH. The cytomorphologic features of sclerosing mucoepidermoid carcinoma of the thyroid gland with eosinophilia. Am J Clin Pathol 1998;109:294-301.
9. LARSON RS, WICK MR. Primary mucoepidermoid carcinoma of the thyroid: diagnosis by fine-needle aspiration biopsy. Diagn Cytopathol 1993;9:438-43.
10. FRANSILLA KO, HARACH HR, WASENIUS V-M. Mucoepidermoid carcinoma of the thyroid. Histopathology 1984;8:847-60.
11. BONDESON L, BONDESON AG. Cytologic features in fine-needle aspirates from a sclerosing mucoepidermoid thyroid carcinoma with eosinophilia. Diagn Cytopathol 1996;15:301-15.
12. CAMESELLE-TEIJEIRO J, FEBLES-PEREZ C, SOBRINHO-SIMOES M. Papillary and mucoepidermoid carcinoma of the thyroid with anaplastic transformation: a case report with histologic and immunohistochemical findings that support a provocative histogenetic hypothesis. Pathol Res Pract 1995;191:1214-21.
13. CHAN JK, ALBORES-SAAVEDRA J, BATIFORA H, CARCANGIU ML, ROSAI J. Sclerosing mucoepidermoid carcinoma with eosinophilia: a distinctive low-grade malignancy arising from metaplastic follicles in Hashimoto's thyroiditis. Am J Surg Pathol 1991;15:438-48.
14. SIM SJ, RO JY, ORDONEZ NG, CLEARY KR, AYALA AG. Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: report of two patients, one with distant metastasis, and review of the literature. Hum Pathol 1997;28:1091-6.
15. AREZZO A, PATETTA R, CEPPA P, BORGONOVO G, TORRE G, MATTIOLI FP. Mucoepidermoid carcinoma of the thyroid gland arising from a papillary epithelial neoplasm. Am Surg 1998;64:307-11.
16. SAMBADE C, FRANSILLA K, BRASILIO-de-OLIVEIRA CA, SOBRINHO-SIMOES M. Mucoepidermoid carcinoma of the thyroid revisited. Surg Pathol 1990;3:271-80.
17. MIKUZAMI Y, MATSUHARA F, HASHIMOTO T, HARATAKE J, TERAHATA S, NOGUCHI M, HIROSE K. Primary mucoepidermoid carcinoma in the thyroid gland: a case report including an ultrastructural and histochemical study. Cancer 1984;53:1741-5.
18. OZAKI O, ITO K, SUGINO K, YASUDA K, YAMASHITA T, TOSHIMA K. Solid cell nests of the thyroid gland: precursor of thyroid carcinoma? World J Surg 1992;16:685-8.

Sažetak

PRIMARNI MUKOEPIDERMOIDNI KARCINOM ŠTITNE ŽLIJEZDE S AGRESIVNIM PONAŠANJEM - PRIKAZ SLUČAJA

B. Krušlin, H. Čupić, V. Bedeković, V. Petric, M. Ivkić i Mladen Belicza

Prikazan je 33-godišnji bolesnik s primarnim mukoepidermoidnim karcinomom štitne žlijezde vrlo agresivnog ponašanja. Bolesnik se javlja liječniku poradi brzorastućeg tumora lijevog režnja štitne žlijezde. Citološka analiza je upućivala na slabo diferencirani karcinom štitnjače. Učinjena je totalna tiroidektomija. Makroskopski je nađen slabo ograničeni, sivobijeli tumor promjera do 5,5 cm. Histološki je tumor građen od atipičnih, krupnih epitelnih stanica koje tvore otočiće i gnijezda. Tumorske stanice mjestimice pokazuju stvaranje sluzi. Usto se nalaze žarišta pločastih stanica bez izraženog orožnjavanja. Imunohistokemijski tumorske stanice pokazuju pozitivnu reakciju na citokeratin i negativnu na tiroglobulin i kalcitonin. Elektronsko mikroskopska analiza pokazala je pločaste stanice s intracitoplazmatskim nakupinama tonofilamenata, dobro razvijenim dezmosomima i mucinozne stanice s brojnim mucinskim granulama. Šest mjeseci nakon prvog zahvata učinjena je istostrana disekcija vratnih limfnih čvorova, pri čemu je patohistološki većina čvorova bila zauzeta metastatskim tumorom. Kompjutoriziranom tomografijom učinjenom mjesec dana kasnije utvrđene su tumorske mase iza grkljana i traheje, koje se šire iza prsne kosti u medijastinum. Bolesnik je liječen zračenjem zbog raširenih metastaza. Ovakav tijek bolesti upućuje na to da primarni mukoepidermoidni karcinom štitnjače može pokazivati vrlo agresivan tijek.

Ključne riječi: *Karcinom - mukoepidermoidni; Neoplazme štitnjače; Neoplazme štitnjače - patologija; Tiroidektomija*