Simultaneous medullary-papillary thyroid carcinoma

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Differentiated thyroid carcinoma is the commonest malignancy affecting the thyroid gland. Medullary thyroid carcinoma accounts for 5% to 10% of all thyroid neoplasms. In recent years, a combination of medullary-follicular and medullary-papillary carcinomas has been reported, with immunoreactivity for calcitonin and thyroglobulin.[1] This is a rare association with an unclear histogenesis. We describe a case of medullary-papillary carcinoma in a female patient who presented with respiratory distress due to a huge goiter and was treated by lobectomy and isthmectomy.

Case

A 40-year-old patient presented to the emergency department with progressive upper airway obstruction of 10 days duration. She gave a history of long-standing goiter, which was neglected. She was also a bronchial asthma patient. There was no family history of goiter, neoplasms or previous neck irradiation. Systemic review revealed decreased weight and appetite. She was not currently receiving any medications. On examination, she was in severe respiratory distress. Her pulse was 110 beats/minute, blood pressure 80/40 mm Hg and the respiratory rate was 43 breaths/minute. Immediate intubation was done and the patient was transferred to I.C.U. Complete blood count, urea and electrolytes, blood glucose, clotting profile, thyroid function tests, serum calcium and albumin were within normal limits. Thyroid antibodies were negative. Blood gas analysis showed a picture compatible with respiratory acidosis. Chest x-ray revealed pulmonary oedema with a normal heart size and a straight left bronchus. An echocardiogram showed an ejection fraction of 80% (>50%) with other parameters normal and no pericardial effusion. Neck ultrasound demonstrated a huge cystic lesion occupying the whole left thyroid lobe and displacing the trachea to the right side. The lesion contained some solid elements. The patient was closely observed in the ICU.

Emergency left thyroid lobectomy and isthmectomy were performed. The histopathology result was a 9x7.5x0.2-cm encapsulated cyst containing a 1.0-cm firm nodule. Histopathologically, this nodule showed crowded, colloid-filled thyroid follicles lined by columnar-cuboidal cells with an eosinophilic cytoplasm and crowded, pleomorphic, large, pale nuclei with focal areas of nuclear grooving and prominence of nucleoli (Figure 1). These cells stained positively with a thyroglobulin tumour marker (Figure 2). In another area of the nodule, abundant, Congo red-positive amyloid deposits were seen among which irregular islands of plump cells, showing a microglandular formation with the presence of cellular discohesion, were observed. These cells had round nuclei and a pale-eosinophilic cytoplasm (Figure 3). Tumor cells stained strongly positive with calcitonin (Figure 4). The rest of the thyroid showed hyperplastic changes with the presence of cystic degeneration. The tumour was diagnosed as a collision tumour of mixed papillary and medullary carcinoma.

Discussion

Papillary thyroid carcinoma is the most common tumour affecting the thyroid gland, while medullary thyroid carcinoma accounts for about 5% to 10% of cases. The first descriptions of mixed medullary-follicular carcinoma were those of Hales et al (1982) and Pfaltz et al (1983).[1] Recently, a combination of these two tumours in the same gland has been described.[1] The demonstration by in situ hybridization and Northern blot methods of mRNAs for calcitonin and thyroglobulin in the neoplastic cells of some of these tumours conclusively proved the existence of mixed carcinomas.[2] Thyroid tumours with differentiation of both parafollicular and papillary epithelial cells are extremely rare.[3,4,5,6] Because of the presence of two discrete intermingled cell populations, Aple proposed to call these tumours composite thyroid carcinomas, as opposed to mixed thyroid tumours, which describes tumours with a single cell population that exhibits features of two cell types.[5]

The medullary thyroid carcinoma arises from the parafollicular (C cells), which are concentrated in the

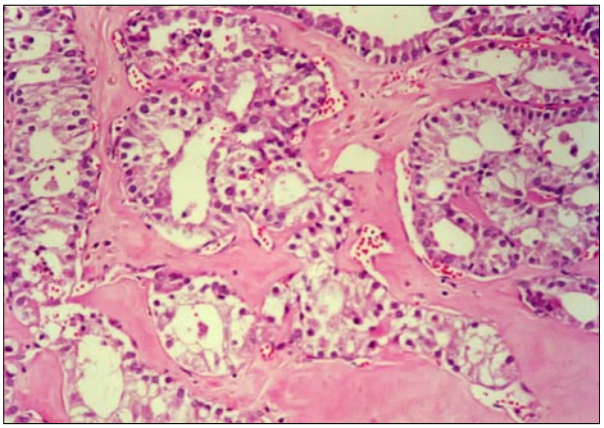

Figure 1. Part of thyroid follicle lined by columnar cells with pleomorphic grooved nuclei (H & E x 400).

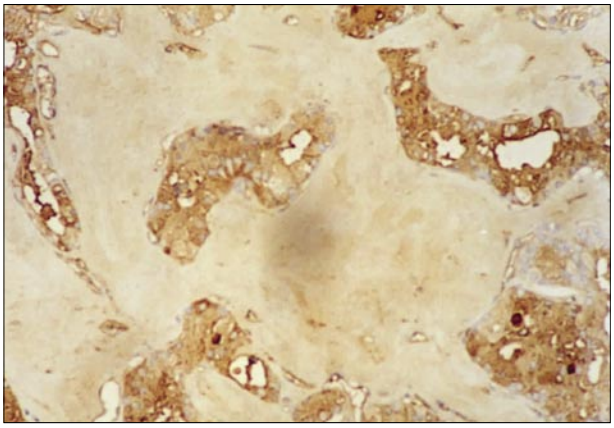

Figure 2. Thyroglobulin positive follicle cells in papillary carcinoma (Thyroglobulin x 200).

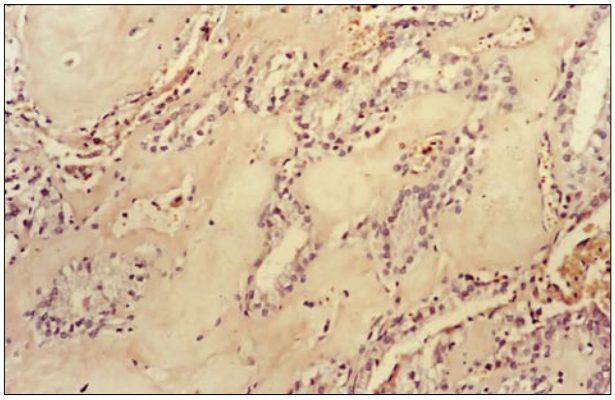

Figure 3. Congo red-positive staining of amyloid in the stroma (x 200).

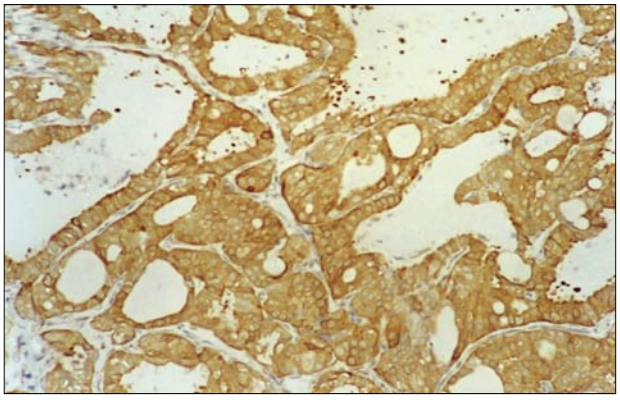

Figure 4. Calcitonin positive tumours cells in the medullary carcinoma (calcitonin x 400).

midportion or upper half of the gland.[7]. They secrete the hormone calcitonin, known to lower serum calcium and play an important role in calcium haemostasis. These C cells are derived from APUD cells (amine precursor uptake and decarboxylation), which are widely distributed in the body. Immunohistochemically, the tumour cells are reactive for epithelial markers such as keratin, pan-endocrine markers such as NSE, chromogranin A, B, and C, synaptophysin, opioid peptides, and most importantly, the specific product of C-cells, i.e. calcitonin. They are consistently positive for CEA and generally negative for thyroglobulin. Other products that have been detected in medullary carcinoma include somatostatin, adrenocorticotropic hormone (ACTH), calcitonin gene-related peptide, serotonin, melanocyte–stimulating hormone (MSH), prostaglandins, bombesin, gastrin-releasing peptide, substance P, L-dopa decarboxylase, histaminase, glucagon, insulin, human chorionic gonadotropin, and the polysialic acid of the neural cell adhesion molecule.[4]. For diagnosis, these rare tumours must show both the morphological features of medullary carcinoma together with immunoreactivity for calcitonin, and the morphological features of papillary carcinoma together with immunoreactivity for thyroglobulin.[1]. The metastatic lesions also display both the morphological and the immunohistochemical patterns of both cell lines.[5,8,9] The presence of immunoreactivity for the two hormones in metastases is an important diagnostic clue.[1] The tumours show immunoreactivity for calcitonin, usually in the solid foci, and for thyroglobulin in the glandular structures, but the two hormones can co-exist in the same area.[1]

The histogenesis of these tumours is debatable, but the following hypotheses have been put forward: origin from uncommitted stem cells, origin from differentiated cells with deregulation of gene expression allowing the production of both calcitonin and thyroglobulin, a dual origin of C cells, neuroectodermal and endodermal, and neoplastic transformation. The last hypothesis is unlikely because of the finding of calcitonin and thyroglobulin in the same neoplastic cells.[1]

The prognosis of these mixed tumours is not clearly defined because of the small number of reported cases.

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