Association of a medullary carcinoma, papillary carcinoma of the thyroid and lung adenocarcinoma : case report

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INTRODUCTION

The simultaneous occurrence of several malignancies of different origin is rare, however, reported in the literature.Its etiology remains obscure. The purpose of this observation is to report a case involving 3 neoplasia: medullary thyroid carcinoma, papillary thyroid carcinoma and lung adenocarcinoma with bone metastases.

OBSERVATION

A 39-year-old man without personal history of radiation exposure or family history of thyroid neoplasia ,pheochromocytoma, or other pathology, was referred for intense back pain. Thoracolumbar CT performed revealed multiple bony secondary locations primarily lytic (thoracic spinal stepped (T3-T5) ,left clavicle) and anterior superior mediastinal lymphadenopathy. Through research of primary cancer, cervical ultrasound found a homogeneous goiter.The histological examination of right cervical lymphadenopathy after excisional biopsy conclud initially papillary carcinoma, then medullary carcinoma with positive thyrocalcitonine immunoreactivity.The thyroglobulin (Tg) was not elevated (3.6 ng/ml) in the absence of anti-thyroglobulin antibodies, and thyrocalcitonin at basal measurement (6.1 pg / ml) and after calcium stimulation were normal as well as chromogranin A (37.5 ng / ml); the rate of ACE (39.4 U / ml) was high.

The patient underwent total thyroidectomy without lymphadenectomy. Histologic evaluation with immunostaining of multiple sections from both lobes of the thyroid shows an association of micro papillary carcinoma and medullary carcinoma with oncocytic variant(figure 1)

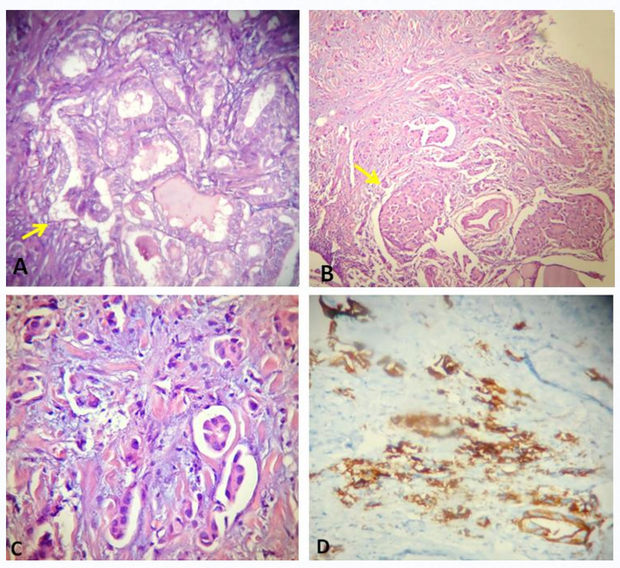

Figure 1 (A) micro papillary carcinoma, (B,C) medullary carcinoma, (D) Positive CEA immunostaining for medullary thyroid carcinoma

The spread assessment of tumors found bone secondary locations (rib, left clavicle, vertebral T3 to T5 and L1, L2, left humeral head, left acetabulum) and a solitary lung nodule 18 mm in the right upper lobe (Figure 2) which histological examination after biopsy conclud lung adenocarcinoma (Figure 2).

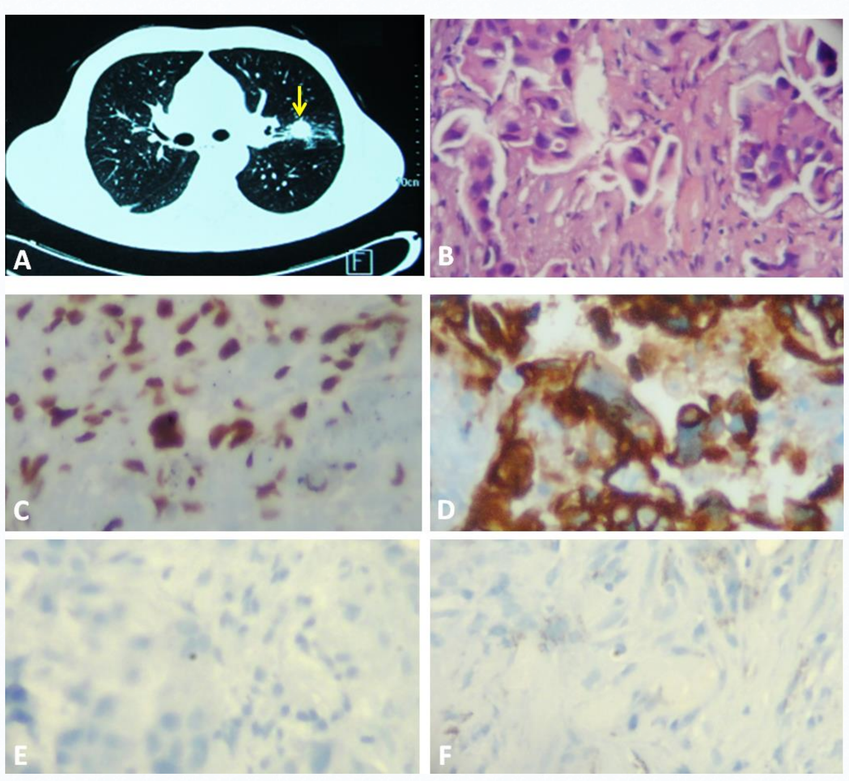

Figure 2 (A) CT scan:lung nodule(B) lung adenocarcinoma (C) Positive TTF1 immunostaining for lung adenocarcinoma (D)) Positive CK7 immunostaining for lung adenocarcinoma (E) and (F) negative thyroglobuline and calcitonin immunostaining for lung adenocarcinoma respectively.

The patient underwent a Radioactive Iodine (RAI) Ablation ,after what, bone metastases have not fixed iodine.Moreover, the thyroglobulin and thyrocalcitonin rates were still normal and scintigraphic aspect of bone metastasis rather evokes lung origin.

During 11 months of evolution, other bone metastases (sternal, right mandible and pelvic bones) and a right pulmonary parenchymal infiltration appeared. Vertebral locations were complicated by spinal cord compression for which the patient received radiotherapy. Chemotherapy for pulmonary neoplasia was initiated.

DISCUSSION

Papillary carcinoma is the most common thyroid neoplasms (80%), with good prognosis in general(1). It occurs from follicular cells of endodermal origin and secrete thyroglobulin. Least commonly medullary carcinoma accounts for only 5-10% of thyroid carcinoma (2).It originates from parafollicular C cells derived from the fourth pharyngeal pouch, and secrete the calcitonin its most specific and sensitive marker (3) and the carcinoembryologic antigen .

Account held the different origin of these two neoplasia , their coexistence, increasingly described in the literature, raises several etiopathogenic hypotheses not confirmed untilnow.It is a rare entity to distinguish from mixed thyroid carcinoma introduced in the 1988 WHO classification, and defined as the existence on the same tumor of both morphological features of papillary carcinoma with positive immunoreactivity to thyroglobulin, and morphological features of medullary carcinoma with positive immunoreactivity to calcitonin .

In the literature, the prevalence of this association is variable and has been estimated at 13.8 to 19% (4,5), greater than the combination of a papillary carcinoma with multinodular goiter (3-7%)or Graves' disease (3-5%) (6) which has not been demonstrated in other series.

Some authors explain that as a coincidence (4,7) especially whether it is an association with papillary microcarcinoma in the majority of cases described, as was the case in our patient. This form is the most common and represents 77% of papillary carcinoma (4,7) . In fact it could be considered as "incidentalomas" most often diagnosed through a careful histopathological examination of thin slices of thyroidectomies for medullary carcinoma .

Other etiopathogenic theories regarding mixed thyroid carcinoma, as the theory of stem cells that converts into two cell types, follicular and parafollicular (8); the theory of "hostage"suggesting a trapping medullary carcinoma normal follicular cells which proliferate in response to the trophic factor and microenvironement promoted by medullary carcinoma (4),the effects of oncogenic stimulus on both cell populations (9) involvement of a mutation in the RET proto-oncogene was also mentioned (2).

As already stated, the medullary carcinoma is characterized by the secretion of calcitonin which the assessment is done by measuring the basal rate or after pentagastrin or calcium stimulation. This is the most important diagnostic criterion and follow up. Nevertheless, rare cases of medullary carcinoma with normal calcitonin levels were described (10).This feature was found in our patient, in whom calcitonin basal levels and after calcium stimulation measured several times, came back normal. the rate of Chromogranin A ,marker of neuroendocrine tumor was also normal, besides , high rate of CEA was found , a common tumor marker with pulmonary adenocarcinoma . Medullary carcinoma diagnosis was established based on histological features after biopsy of the lymph node metastatic, as well as thyroidectomy , especially the histological structure and immunoreactivity for calcitonin and ACE ,highlighting the significant contribution of immunohistochemistry in pathological diagnosis. In these particular forms, a mutation of calcitonin / CGRP associated with abnormalities of synthesis and / or secretion of this hormone may be involved (10).

Adenocarcinomas account for approximately 40% of lung cancers and it is non-small cell lung carcinoma . It is usually seen peripherally and in the upper lobes of the lung .It has an increased incidence in smokers, and is the most common type of lung cancer seen in non-smokers especially women. Generally, it grow more slowly and form smaller masses than the other subtypes.However, they tend to form metastases widely at an early stage(11).

To our knowledge the association of a papillary carcinoma of thyroid , medullary carcinoma and adenocarcinoma of the lung , has not been described earlier, a common etiologic research will be the subject of further study.

CONCLUSION

Coexistance of several neoplasms is rare, and we poses serious diagnostic and therapeutic problems. The pathogenesis is still poorly understood, impeding prognosis and management, which should be adapted and multidisciplinar.

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