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Medullary Carcinoma of Thyroid Gland with Co-existing Papillary Carcinoma

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— **Abstract** —

We report a medullary carcinoma of the thyroid gland with a coexisting occult sclerosing papillary carcinoma. This rare case, in that the two types of carcinoma are completely separated and not intermixed together, is different from the previously reported mixed follicular and parafollicular cell carcinomas of the thyroid gland, so-called "differentiated thyroid carcinoma, intermediate type". The two separate tumors of the present case are undoubtedly of coincidental double primaries, and it can be assumed that at least some of the mixed follicular and parafollicular cell carcinomas are results of collision of carcinomas derived from two embryogenetically different cell types.

Key Words: Thyroid gland, Thyroid carcinoma, Medullary carcinoma, Papillary carcinoma

INTRODUCTION

The majority of the thyroid carcinomas can be classified into papillary, follicular, medullary and anaplastic types. Medullary carcinoma was first described as an unusual neoplasm in 1951, but it was Hazard et al in 1959, who recognized that medullary carcinoma represented an unique variant of throid carcinoma. It is characterized by solid and/or cribrifrom arrangements of round or spindle-shape cells that are separated by amyloid containing stroma. In contrast to follicular, papillary and anaplastic carcinomas of the follicular cell origin, medullary carcinoma is known to arise from the parafollicular C-cell, which is believed to produce such neuropeptides as calcitonin, somatostatin and neurotensin. These findings emphasize the validity of its separation from the other types of thyroid carcinoma.

However, subsequent reports described atypical variants of medullary carcinoma intermixed with follicular, papillary and pseudopapillary growth patterns with or without amyloid stroma. In view of the current concept that follicular cells and parafollicular C-cells have distinct embryogenesis, being derived from entoderm and neuroectoderm, respectively, the histogenesis of this atypical medullary carcinoma would be in conflict. In this context, it is worth reporting a rare case we have experienced, in which medullary and papillary carcinomas occurred independently.

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CASE RECORD

The patient, a 59 year-old female, visited the Department of Surgery of this hospital because of a palpable mass with pain on the anterior neck for 7 years. She has a history of anorexia, weight loss,

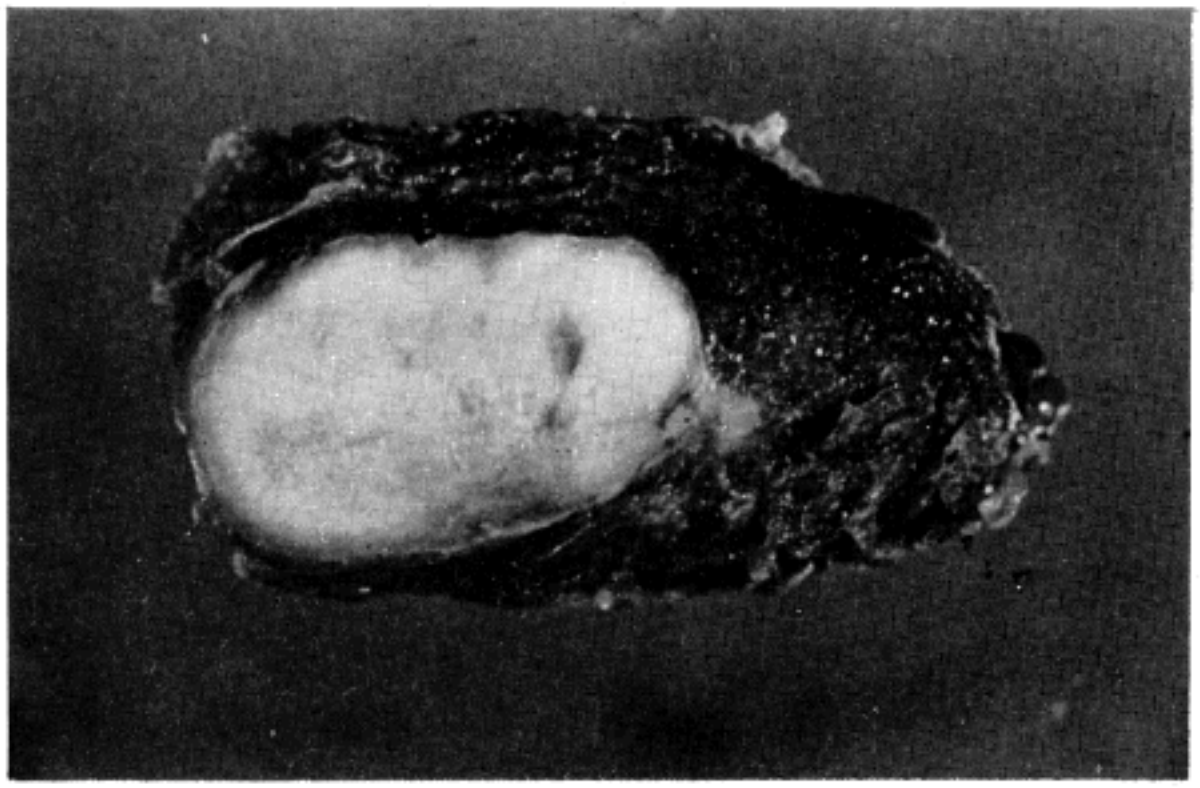

Fig. 1. The cut surface showing a well demarcated gray-white solid mass and an ill-defined minute scar adjacent to the mass.

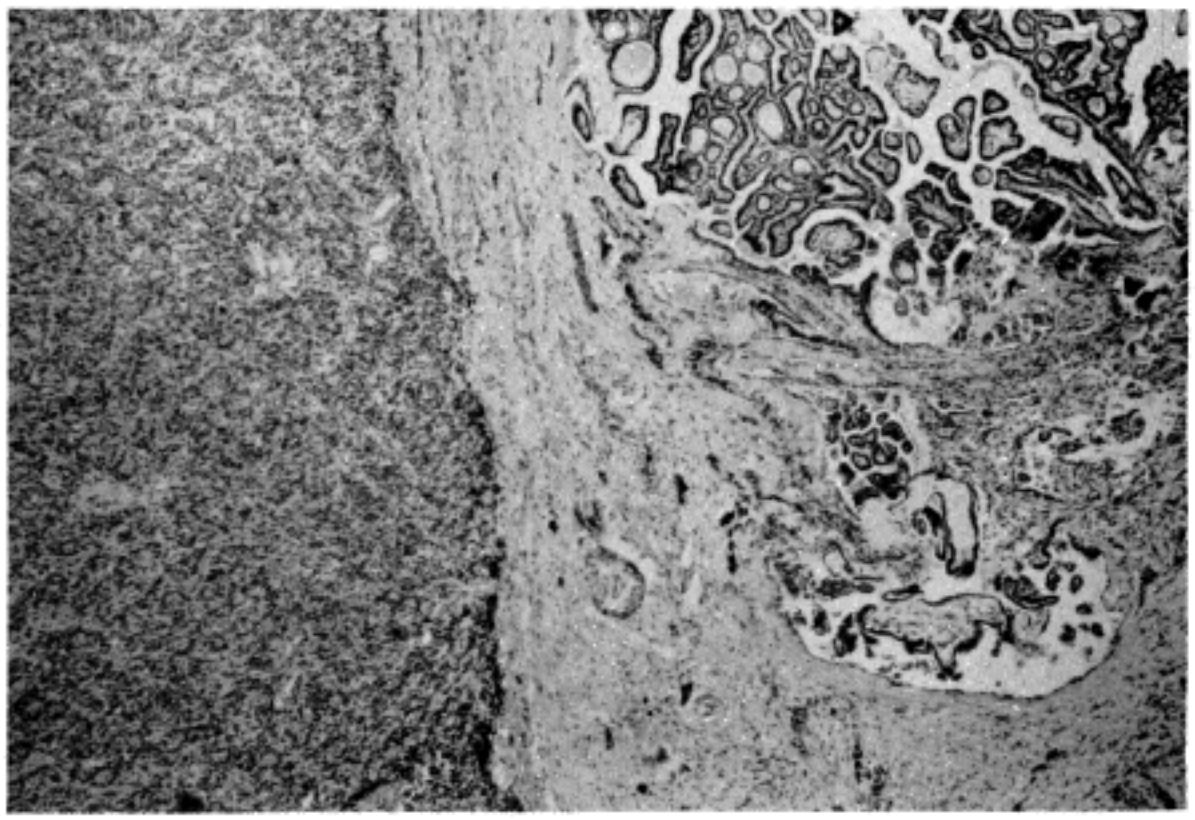

Fig. 2. Low power micrograph showing a medullary carcinoma (left) and a papillary carcinoma (right). (H & E, x40).

palpitation and cold intolerance for the last 3 years. On physical examination, a tender, ill-defined round to oval mass was palpated on the right side of the anterior neck. The laboratory tests including the thyroid hormonal assay (T_3, T_4, TSH) were all within normal ranges. The thyroid scan revealed a space occupying lesion on the lateral portion of right lobe of the thyroid gland. The right lobe including the tumor was excised.

The thyroid gland weighed 5 gm and the cut surface showed a well demarcated but not encapsulated gray-white solid mass, measuring 2×1.3 cm. There was an ill-defined minute scar located adjacent to the mass. Microscopically, the mass was composed of irregular solid groups of round or oval tumor cells separated by an amyloid stroma with a characteristic apple-green birefringence under polarization. The tumor cells demonstrated a positive immunoperoxidase staining for calcitonin. The minute scar was composed microscopically of papil-

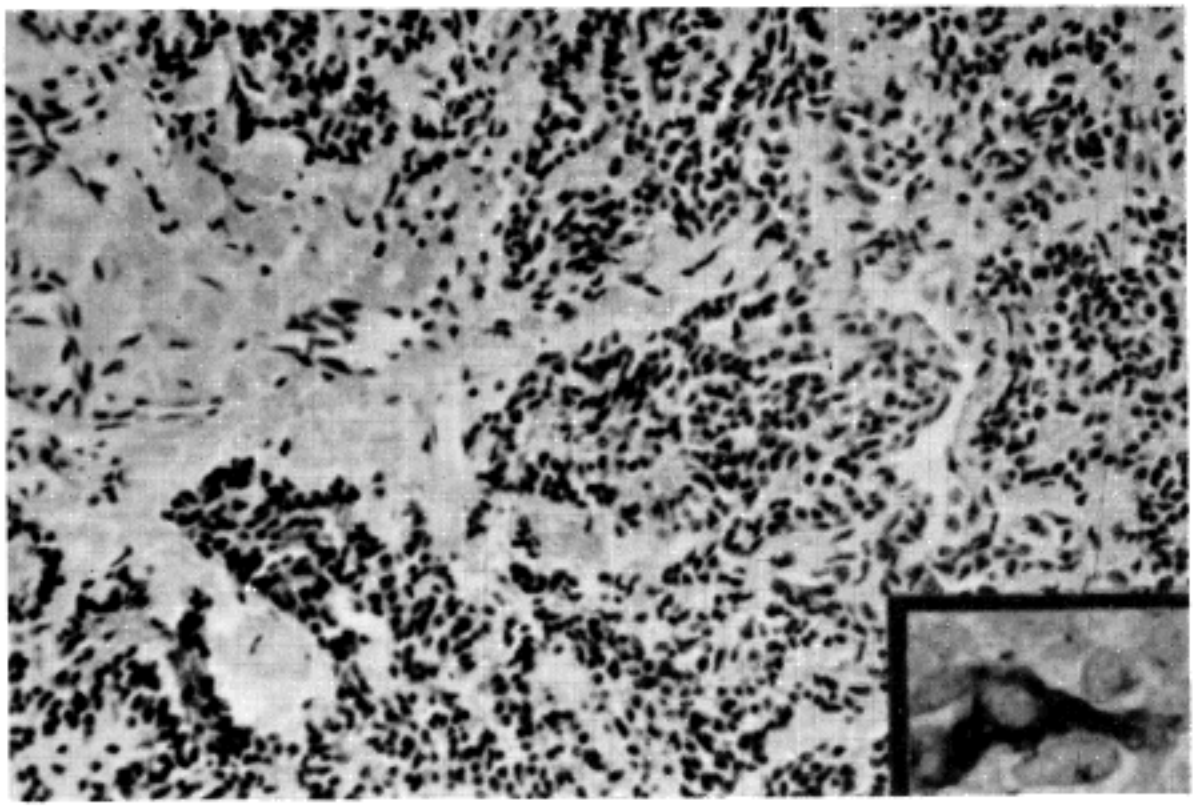

Fig. 3. Highe power micrograph showing a typical feature of medullary carcinoma with amyloid deposition. (H & E, x200)
Dark cytoplasmic staining for calcitonin in the tumor cells of medullary carcinoma. (Inlet) (H & E, x400).

lary fronds with a dense fibrous stroma, and was separated from the medullary tumor mass by fibrous connective tissues. A few psammoma bodies were found as well.

DISCUSSION

The orginal description on medullary carcinoma of thyroid gland stressed the lack of follicular and papillary differentiation and the presence of amyloid stroma, and in 1966, Williams[15] suggested that this tumor arises from parafollicular C-cell. However there have been several reports on atypical thyroid tumors, which showed a mixture of medullary type carcinoma and carcinoma of a follicular epithelial origin with or without amyloid stroma[7~10,13,14]. Furthermore the existence of medullary thyroid carcinoma showing some electron-microscopical features of follicular and/or papillary thyroid carcinomas is well documented[16~19]. The hybrid nature was also supported by the positive immunohistochemical stainings for thyroglobulin and neurohormonal peptides. Ljunberg et al[5] nominated differentiated thyroid carcinoma, intermediate type for these hybrid tumors.

With regard to the histogenesis of the mixed follicular and parafollicular cell carcinoma, it may be debatable whether the tumor cells are derived from a common progenitor of both follicular and parafollicular cells, or the tumor is a mixed collision tumor resulting from independent co-incidental malignant changes of both cell types. The first possibility seems more attractive, because, in almost all of the previously reported cases, both histologic types are intermingled and it has been demonstrated that both thyroglobulin and neuropeptides are present in the same tumor cells[11].

But assuming that neoplasia is a process of monoclonal derivation, this would be in conflict with the current belief that thyroid gland has two distinct primordia: the entodermal thyroglossal duct which gives rise to the follicular epithelium, and the branchial pouches which have neuroectoderm-derived progenitor of C-cells[20]. But the latter concept has been challenged recently. A study of dogs indicates that during embryonic life, undifferentiated stem cells in the ultimobranchial bodies are capable of differentiating not only into the follicular cells but also into parafollicular cells[21]. Then the two types of tumor cells may be derived from the common stem

cells[7,11]. Similarly there is a growing evidence that the entoderm is capable of developing neuroendocrine cells in the gut[22].

In the present case, the medullary carcinoma was clearly separated from the occult papillary carcinoma by a dense fibrous tissue and intervening nonneoplastic thyroid follicles. This is apparently not the same as the previously discussed mxed follicular and parafollicular cell carcinoma. Instead, it may represent a presyncytial stage of collision tumor, and the mixed follicular and parafollicular cell carcinoma might be a result of collision of carcinomas that are derived from two embryogenetically different cell types.

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＝국문초록＝

갑상선의 유두상선암과 동반된 후질성암종

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저자들은 59세 여자에서 갑상선의 수질성 암종과 잠재성 유두상 암종이 동반된 예를 경험하여 보고하는 바이다.

본 증례에서는 두 종류의 서로 다른 암종이 완전히 분리되어 있어서 소위 "분화된 갑상선암종의 중간형(differentiated thyroid carcinoma, intermediate type)으로 분류된 바 있는 혼합 여포세포암종-부여포세포암종과 상이하였다. 그러므로 혼합 여포세포암종-부여포세포암종의 적어도 일부는 발생학적 기원이 다른 2가지세포에서 발생한 별개의 암종들이 유합된 결과인 것으로 사료된다.