

Fine Needle Aspiration Cytology of Poorly Differentiated “Insular Carcinoma” of the Thyroid

- A Case Report -

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= Abstract =

A case of poorly differentiated “insular” carcinoma of the thyroid is presented and discussed with references to the literature. In fine needle aspiration cytology of our case, the aspirates were highly cellular with tumor cells appearing as dispersed isolated cells as well as in dense clusters and syncytial formations. Occasional microfollicles containing colloid were evident. Most of nuclei were fairly uniform with considerable variability and a few showed definite atypical features. Nuclear grooving was additional features. Necrotic debris was not seen. Our cytologic findings were correlated well with histology, confirming typical insular pattern of tumor cells with the presence of occasional pleomorphic cells and papillary carcinoma-like features. With much attention to cytological features of insular carcinoma, it would be possible to diagnose a preoperative suggestive diagnosis, even though not definitive.

Key words: Insular carcinoma, Thyroid, Fine needle aspiration cytology

Introduction

The curious tumor termed “insular carcinoma” by Carcangiu et al¹⁾ consists of a small cell tumor of follicular histogenesis (thyroglobulin positive) which is composed of well defined solid nests, microfollicles and occasional papillae. It is a distinc-

tive, rare, aggressive and often lethal type of thyroid cancer. Recognition of this tumor type is essential for planning the kind of surgery and patient management^{1,2)}, however, the cytologic features of insular carcinoma are not widely recognized³⁾. Although much attention has been paid to the criteria used to diagnose papillary, follicular,

medullary and anaplastic carcinoma, few cytologic descriptions of poorly differentiated, or "insular" carcinoma are found in the literature.

We describe the cytologic features of the uncommon insular carcinoma of thyroid and discuss with references to the literature. This case will be the first Korean case report for the cytologic features of insular carcinoma of thyroid revealed by fine needle aspiration cytology (FNAC).

Case Report

A 38-year-old woman presented with a large mass in the right anterior neck. The mass had progressively increased in size since the patient first noticed it, one year earlier. She had had the previous history of a neck mass with spontaneous regression in the same site, fourteen years before. There was no history of prior radiation exposure. Physical examination revealed a painless movable lobular mass with poor circumscription, measuring about 6x4 cm, in the right anterior neck. The functional states of thyroid were normal, however, the serum level of thyroglobulin was high up to 1949. 60 ng/ml. It was a cold nodular lesion on thyroid scan. An FNAC was performed. The aspirated material was expressed onto glass slides, smeared, alcohol-fixed and stained with the Papanicolaou method.

The aspirates were highly cellular with tumor cells appearing as dispersed isolated cells as well as in clusters and syncytial formations (Fig. 1). Occasional microfollicles containing colloid were evident (Fig. 2). The nuclei were larger than those of normal cells, varying considerably in size and shape. Most of the cells were fairly uniform with scanty cytoplasm and showed definite atypical features, including nuclear enlargement and hyper-

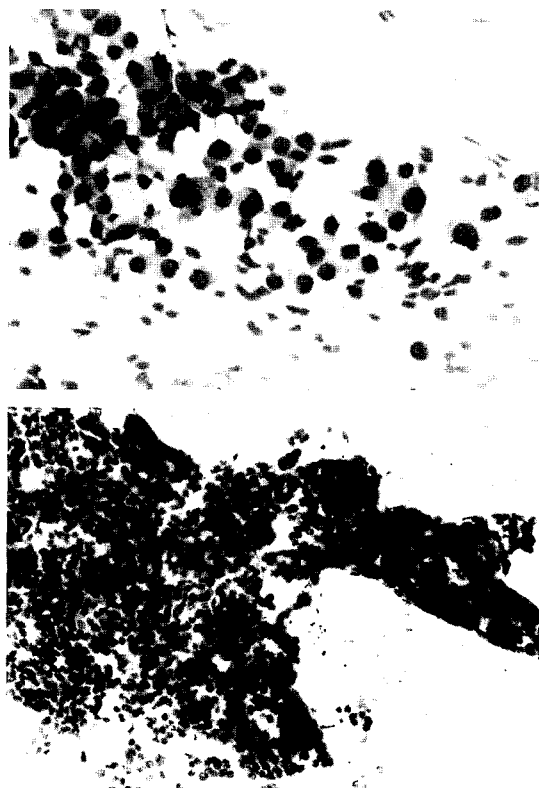


Fig. 1. a) The neoplastic cells are single and dispersed or arranged in small clusters with some nuclear overlapping. The cells are fairly uniform and some show mild variability of size (Papanicolaou, $\times 100$). b) The cells are arranged in solid aggregates, in part mimicking trabeculae (Papanicolaou, $\times 50$).

chromasia. A few large pleomorphic cells were also noted (Fig. 3). Nucleoli were not prominent. Rare mitotic figures were observed. Cytoplasm was faintly eosinophilic or almost amphophilic on Papanicolaou stain and was fine and fibrillar. Hürthle cell change was not observed. Neither papillae nor psammoma bodies were seen, but nuclear grooving was occasionally seen. The aspirates contained neither necrotic material nor appreciable inflammatory component. The presence of colloid indicated a primary thyroid tumor, and

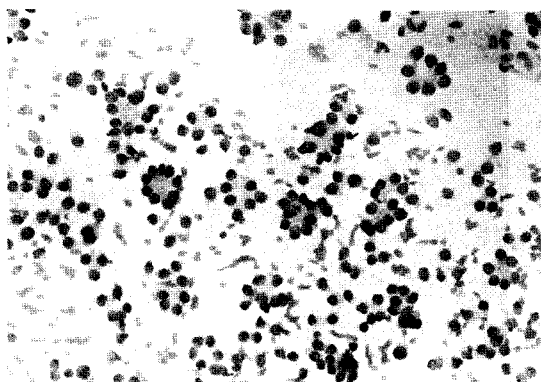


Fig. 2. Microfollicles containing colloid are found in the dispersed cell population (Papanicolaou, $\times 100$)

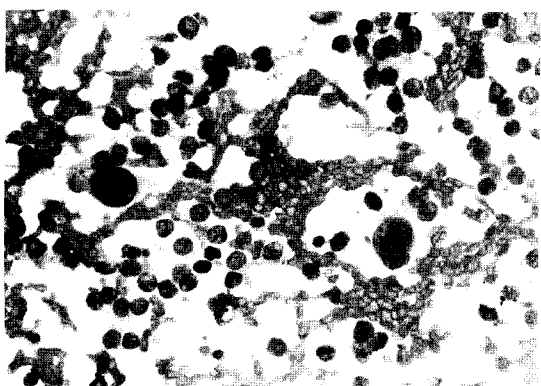


Fig. 3. A few neoplastic cells show definite atypical features, including nuclear enlargement and hyperchromasia (Papanicolaou, $\times 200$).

it was limited in the microfollicles.

Total thyroidectomy was done. The right lobe was completely replaced by a large multilobated tumor mass with homogeneously gray-white cut surface, measuring $7 \times 4 \times 5$ cm. The left lobe was grossly unremarkable. Microscopic examination showed a neoplasm composed of cells arranged in a "pseudotheliomatous" pattern (Fig. 4). Most were composed of round to oval islands of cells

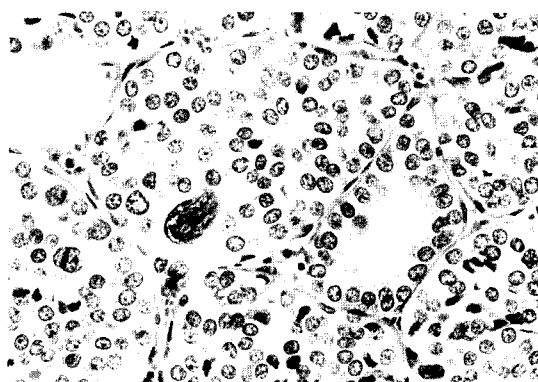


Fig. 4. Histologic section showed "pseudotheliomatous" pattern composed of nests of cells separated by fine fibrovascular septae (H-E, $\times 100$).

separated by fine fibrovascular septae. Within the islands, microfollicular pattern was evident in some areas. Solid pattern without nests and a small area of pseudopapillary feature were also present. The nuclei were moderately pleomorphic with occasional large bizarre nuclei. A small portion of the tumor consisted of less pleomorphic cells with optically clear nuclei and nuclear grooves. Intranuclear cytoplasmic pseudoinclusions and psammoma bodies were not identified. Occasional mitotic figures were noted (less than 1 per 10 high-power fields) with cellular pleomorphism and hyperchromasia were evident. Immunoreactivity for thyroglobulin was demonstrated in the neoplastic cells, within cytoplasmic paranuclear vacuoles. Immunoreactivity for calcitonin was absent and Congo-red staining for amyloid were also negative. The left lobe showed goitrous change without tumor.

Discussion

The first descriptions and illustrations of poorly differentiated insular thyroid carcinoma (PDITC)

were published in 1907 by Langhans, who described 16 cases of thyroid carcinoma using the term "wuchernde struma" (proliferating stroma)⁴⁾. This lesion was characterized by a distinct nesting pattern, uniform cells and a "peritheliomatous" arrangement of the nests¹⁾. This neoplasm was later classified as a subtype, or variant of follicular carcinoma. In the past, PDITC may also have been classified as a poorly differentiated type of papillary carcinoma or as the compact subtype of small cell undifferentiated carcinoma⁵⁾. Carcangiu et al, in 1984, published a series of 25 cases of poorly differentiated carcinoma of the thyroid, reinterpreting Langhans' original tumor type¹⁾. They first used the term insular thyroid carcinoma to emphasize the most characteristic histologic feature of this neoplasm. This review described a tumor composed of large, round to oval nests of tumor cells that were sharply separated from the surrounding stroma. Small follicles containing colloid focally also were present. Psammoma bodies were not found, but papillae common in papillary carcinoma were present in two of the cases. The behavior of this tumor was intermediate between well differentiated and undifferentiated carcinoma in the high rate of metastases and local recurrence^{2,4)}. Killeen et al.⁴⁾ emphasized the tumor should be termed solely "insular thyroid carcinoma" and the additional term "poorly differentiated" might be avoided to prevent confusion of this neoplasm with the poorly differentiated carcinoma of Sakamoto et al.⁶⁾ or the undifferentiated thyroid carcinoma.

Little attention has been paid to the cytologic appearance of this tumor. The cytologic features of this tumor type have been mentioned briefly in three earlier reports^{2,3,7)}. Flynn and associates²⁾ described four cases of insular carcinoma; in one

of these FNAC had been done and showed "cytologically bland follicular cells". Pietribasi and associates³⁾ described the cytologic features of six cases of insular carcinoma. A cytologic detail that they regarded as highly indicative for insular carcinoma was the presence of loose sheets of follicular cells with small intracytoplasmic vacuoles. In FNAC the presence of microfollicular structures is rather common and can be found in different kinds of lesions: follicular adenoma, well differentiated follicular carcinoma and the follicular variant of papillary carcinoma, however, the presence of small loose clusters of cells with poor overlapping can be considered a useful criterion for differentiating this condition from follicular carcinoma³⁾. And they concluded that the main cytologic features by FNAC allowed a suggestive but not a definitive diagnosis of insular carcinoma, with emphasizing high cellularity, low grade atypia, presence of cell clusters, nests and trabeculae of cells with poorly outlined cytoplasm, nuclear inclusions and grooving, and cytoplasmic vacuoles containing thyroglobulin. Zakowski and associates⁷⁾ described in their case a population of follicular cells showing nuclear pleomorphism. They described cytologic findings correlated with histology, confirming the presence of occasional markedly pleomorphic cells and papillary carcinoma-like features.

In our case, the aspirates were highly cellular with tumor cells appearing as dispersed isolated cells as well as in dense clusters and syncytial formations. Occasional microfollicles containing colloid were evident. Most of nuclei were fairly uniform with considerable variability and a few showed definite atypical features. Nuclear grooving was occasionally seen. These cytologic findings of our case are quite similar to those of Za-

kowskiet al.⁷⁾ and Pietribasiet al.³⁾. Cytologic findings of our case was correlated well with histology, confirming typical insular pattern of tumor cells with the presence of occasional pleomorphic cells and papillary carcinoma-like features. In the cytologic smears, the lack of papillary structures excluded a diagnosis of papillary carcinoma, despite of the presence of intranuclear inclusions and grooved nuclei. Rupp et al.⁸⁾ evaluated the presence of the diagnostic value of nuclear grooving in the fine needle aspirates from a variety of thyroid lesions. They suggested that nuclear grooving, when seen in abundance (more than 25% of the HPFs), can be considered a reliable criterion for the diagnosis of papillary carcinoma in FNAC of the thyroid, however, the presence of nuclear grooving in an occasional cell should be regarded as a nonspecific finding⁸⁾. In our case, necrotic debris was not seen in cytologic smear. The abundant necrotic debris in the background of highly cellular smear and the presence of highly atypical nuclei are the main features that differentiate anaplastic carcinoma from insular carcinoma³⁾.

References

1. Carcangiu M, Zampi G, Rosai J: Poorly differentiated ("insular") thyroid carcinoma: A reinterpretation of Langhans' "wuchernde struma". *Am J Surg Pathol* 8:655-668, 1984
2. Flynn S, Forman B, Stewart A, Kinder BK: Poorly differentiated ("insular") carcinoma of the thyroid gland: An aggressive subset of differentiated thyroid neoplasm. *Surgery* 104:963-970, 1988
3. Pietribasi M, Sapino A, Papotti M, Bussolati G: Cytologic features of poorly differentiated "insular" carcinoma of the thyroid, as revealed by fine needle aspiration biopsy. *Am J Clin Pathol* 94:67-692, 1990
4. Killeen R, Barnes L, Watson C, Marsh W, Chase D, Schuller D: Poorly differentiated ("insular") thyroid carcinoma: Report of two cases and review of the literature. *Arch Otolaryngol Head Neck Surg* 116:1082-1086, 1990
5. Meissner WA, Warren S: Tumors of the Thyroid Gland. Atlas of Tumor Pathology, Armed Forces Institute of Pathology, Series 2, part 4, 1969, pp 85, 103
6. Sakamoto A, Kasai N, Sugano H: Poorly differentiated carcinoma of the thyroid: A clinicopathologic entity for a high risk group of papillary and follicular carcinoma. *Cancer* 52:1849-1855, 1983
7. Zakowski MF, Schlesinger K, Mizrahi HH: Cytologic features of poorly differentiated "insular" carcinoma of the thyroid: A case report. *Acta Cytol* 36:523-526, 1992
8. Rupp M, Ehya H: Nuclear grooves in the aspiration cytology of papillary carcinoma of the thyroid. *Acta Cytol* 33:21-26, 1989
1. Carcangiu M, Zampi G, Rosai J: Poorly differentiated

= 국문초록 =

갑상선의 저분화 “도암종”의 세침흡인 세포검사

- 1례 보고 -

원자력병원 해부병리과

이 승 숙 · 하 창 원 · 조 경 자 · 장 자 준

저자들은 접할 기회가 흔치 않은 갑상선의 저분화암종인 일명 “도암종”의 세침흡인 세포검사 1례를 경험하고 조직학적으로 확인하였기에 문헌검색과 함께 보고하는 바이다. 흡인 도말된 세포들은 비교적 깨끗한 도말배경에 중등도 이상의 높은 세포밀도를 보였으며, 세포들은 개개로 흩어지는 양상과 판상의 군집을 이루는 양상이 어우러져 관찰되었다. 때로 세포들이 소포배열을 이루는 곳도 관찰되었다. 대부분의 종양세포들은 비교적 비슷한 크기와 모양을 나타내었으나 일부의 세포들은 현저한 다형성을 보였다. 일부의 세포에서 핵에 주름을 보였으나 소수에 불과하여 이는 어떤 갑상선병변에서나 관찰할 수 있는 비특이적 변화로 간주되었다. 세포의 겹침이 별로 없이 높은 세포밀도를 보이는 점, 세포가 개개로 흩어지는 양상과 소수 다형성이 현저한 세포의 존재 등은 본 종양을 진단하는데 도움이 되는 소견으로 생각되며, 이러한 소견을 염두에 둬으로써 수술 전 진단에 도움을 줄 수 있으리라 생각된다.