

# Aspiration Cytology of Insular Carcinoma of Thyroid

- A Case Report -

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## = Abstract =

Fine needle aspiration cytologic features of a case of insular carcinoma of the thyroid in a 23-year-old woman who presented a palpable neck mass is described. The aspirate showed cellular smear arranged in trabeculae, solid or loose clusters, and microfollicles in necrotic background. The tumor cells had uniform, small round, hyperchromatic nuclei. The chromatin was finely granular, and nuclear membrane was smooth. Nucleoli were not discernible. Nuclear pleomorphism was minimal. The cytoplasm was usually scanty, pale, poorly outlined, and almostly amphophilic. Sometimes paranuclear cytoplasmic vacuoles were noted. Final diagnosis was confirmed by total thyroidectomy as insular carcinoma.

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**Key words:** Thyroid, Aspiration cytology, Insular carcinoma, Poorly differentiated carcinoma.

## Introduction

Insular carcinoma (IC) is a morphologically distinctive form of the thyroid carcinoma composed of uniform cells in a characteristically insular architectural pattern. It, originally described by Carcangiu et al<sup>1)</sup>, in 1984, is biologically intermediate between well-differentiated (papillary and follicular) and anaplastic carcinoma. Fine needle aspiration (FNA) cytology of the thyroid is a well-docu-

mented and cost-effective method, however, only a few cytologic descriptions of poorly differentiated, or "insular" carcinoma are found in English literature<sup>2-4)</sup>. The FNA cytology of IC has been described less specific sharing some of features of papillary carcinoma<sup>3)</sup>. We describe the cytomorphologic characteristics of IC of the thyroid, compare it to the histology of the surgical specimen and try to characterize cytologic criteria that may facilitate preoperative diagnosis of this tumor.

## Case Presentation

### 1. Clinical Features

A 23-year-old woman presented a large mass in the anterior neck. The mass was found 10 years ago and had progressively increased in size since that time, becoming painful and tender recently. There was no history of prior radiation exposure. Physical examination revealed a 10X7 cm sized midline neck mass and another 3cm sized round mass in the right posterior triangle of the neck. Thyroid function tests, serum calcium and phosphate levels were all within normal limits. The FNA of the mass was performed, and the cytologic diagnosis was "malignant follicular neoplasam". We recommended thyroidectomy.

### 2. Cytologic Features

The aspirated material was obtained from the round mass around right posterior triangle and stained by the Papanicolaou and H&E. Cytologic examination under low power showed a quite cellular smear arranged in trabeculae, solid or loose clusters (insular) of tumor cells (Fig. 1). Occasional presence of microfollicular structures containing scanty or little colloid and singly dispersed cells were evident (Fig. 2). Necrotic debris was observed in the background. Tumor cells were small and showed very little pleomorphism. No bizarre, giant, or multinucleated cell was found. The nuclei were round with regular border with finely dispersed chromatin, however, they showed definite atypical features including nuclear enlargement, overlapping and hyperchromasia (Fig. 3). Intranuclear inclusions and grooves were occasionally observed (Fig. 2). Nucleoli were not prominent.

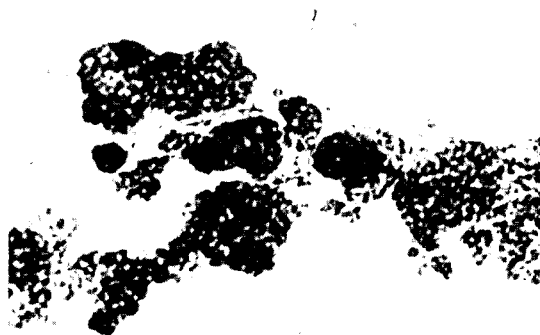


Fig 1. Typical hypercellular trabecular or nest pattern with individually scattered cells are recognized at low magnification (Papanicolaou,  $\times 40$ ).

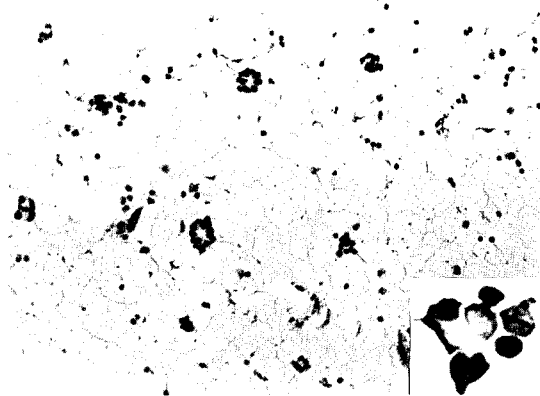


Fig 2. The neoplastic cells are singly dispersed or arranged in small follicles. The neoplastic cells share nuclear features of papillary carcinoma, such as nuclear grooving and optically clear nuclei (Papanicolaou,  $\times 100$ , inset,  $\times 400$ ).

The cytoplasm was usually scanty, pale, poorly outlined and almost amphophilic on Papanicolaou stain, but sometimes showed paranuclear cytoplasmic vacuoles. No papillae or psammoma body was seen.



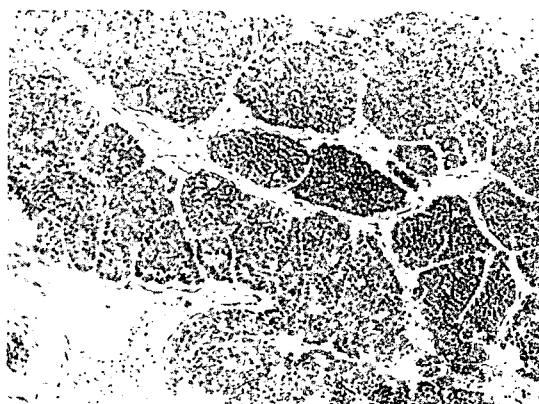
**Fig 3.** The neoplastic cells are arranged in high cellular trabeculae containing microfollicles and surrounded by thin fibrous septa. The neoplastic cells show uniform round hyperchromatic nuclei, nuclear overlapping, and scanty cytoplasm (Papanicolaou,  $\times 400$ ).

### 3. Histologic Features

The thyroid gland was totally resected weighing 75 g. The outer surface was multinodular. The cut surface showed a well circumscribed, solid grayish white mass, measuring 3.5cm in greatest diameter in the upper pole of the right lobe, which exhibited foci of necrosis and focally invasive margin. The other areas of thyroid showed varying sized multiple nodules some of which being calcified (Fig. 4). Microscopic sections showed well defined nests and trabeculae composed of round or oval monotonous population of small cells with round nuclei and scanty cytoplasm. The nests were separated by fine fibrovascular septae and artificially created clefts. Within the islands, a microfollicular pattern was apparent (Fig. 5). The cytologic detail was identical to that of the aspirate material. Occasional mitotic figures were noted but less than 1 per 10 high power fields and



**Fig 4.** A well circumscribed, solid grayish white mass, measuring 3.5cm in the right lobe. The remained thyroid shows typical gross feature of nodular hyperplasia.



**Fig 5.** The insular pattern of poorly differentiated thyroid carcinoma. The nests are solid, but some small follicles are also seen (H-E,  $\times 100$ ).

scattered foci of necrosis were present. The tumor invaded blood vessels and surrounding thyroid tissue. The residual thyroid tissue showed histology of nodular hyperplasia. Immunohistochemically thyroglobulin was demonstrated as small intercellular or intracellular vacuoles, as opposed to the

diffuse type of distribution observed in most follicular or papillary carcinomas.

#### 4. Ultrastructural Features

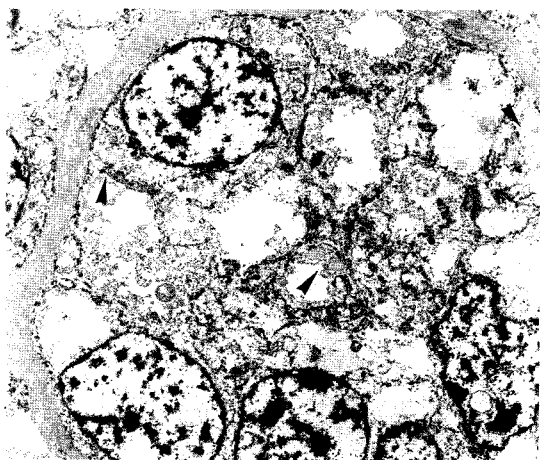
The tumor cells had abundant cytoplasm with endoplasmic reticulum and numerous free ribosomes. Dense granular material corresponding to thyroglobulin was occasionally observed in the lumen of microfollicles as well as in paranuclear globules in the tumor cells. The nuclei were round with homogeneously dispersed chromatin(Fig. 6). This pattern was similar to that described in embryonic thyroid tissue.

### Discussion

Insular carcinoma, proposed by Carcangiu et al.<sup>1)</sup> is a morphologically distinctive form of poorly differentiated carcinoma arising from follicular cells characterized by prominent or exclusive insular or trabecular pattern that had an aggressive clinical behavior. More recently, Popotti et al.<sup>5)</sup> described 32 cases of IC, in which the insular

component constituted more than 65% of the tumor and termed "primordial cell carcinoma" due to ultrastructural resemblance of the embryonic thyroid tissue. Insular carcinoma is viewed by the WHO Committee as a morphologic variant of follicular carcinoma, however, in some instances IC coexists with papillary carcinoma either of the conventional or the follicular variant and shows architectural progression from a papillary carcinoma to an insular pattern which paralleled by changes in cytologic features such as nuclear grooves and inclusions<sup>6)</sup>. IC constituted approximated 4~10% of all the thyroid carcinomas. Most cases occur in the fourth and seventh decades of life and is slightly more common in women. Metastases are common, both to regional lymph nodes and to distant sites including lung and bone. Microscopically, IC is heterogeneous in the sense that some cases have nuclear features similar to those of papillary carcinoma, others have an architectural configuration of follicular carcinoma, but exhibits prominent nests and uniform, small, hyperchromatic nuclei.

Fine needle aspiration cytology has been a well-documented and cost-effective method for the diagnosis of both benign and malignant lesions of the thyroid. The diagnostic criteria for papillary, follicular, medullary and anaplastic carcinoma have been established, however, cytologic features of poorly differentiated or "insular" carcinoma are not widely recognized. The FNA cytologic features of IC was first described by Flynn et al.<sup>1,2)</sup> in 1988 that characterized by "cytologically bland follicular cells". Recently, Pietribiasi et al.<sup>3)</sup> described cytologic features of six cases of IC, emphasizing cellularity, microfollicular pattern, scanty necrotic background, and nuclear grooves and inclusions without nuclear atypia. However, they



**Fig 6.** Dense granular material (arrow) is occasionally observed in the lumen of microfollicle and paranuclear intracytoplasm of tumor cells (×2,500).

described that definite preoperative diagnosis of IC was not feasible on the cytologic smears alone, but embedded fragments were highly helpful showing the diagnostically significant trabecular pattern<sup>3)</sup>. In our case, the aspirate showed some of the nuclear features of papillary carcinoma, however, its prominent trabeculae, microfollicles and absence of papillary structures were unusual for papillary carcinoma and excluded the diagnosis of papillary carcinoma despite the presence of optically clear and grooved nuclei.

In FNA cytology of the thyroid, microfollicles composed of relatively uniform tumor cells are rather common and can be considered in different kinds of lesions such as follicular adenoma, well differentiated follicular carcinoma, and the follicular variant of papillary carcinoma. The presence of loose sheets of follicular cells with small paranuclear vacuoles, crowding of uniform small nuclei with scanty cytoplasm, nuclear overlapping, and trabecular pattern can be considered different features from follicular neoplasm. In medullary carcinoma, another lesion for differential diagnosis, the tumor cells are more variable in size, contour and configuration and show granular cytoplasm. Amorphous hyaline material, that is amyloid, is another important diagnostic feature for medullary carcinoma. In the present case cellular pleomorphism was minimal and amorphous hyaline material was not observed, thus medullary carcinoma could be excluded, too. With anaplastic carcinoma, abundant necrotic background of a highly cellular smear and the presence of highly atypical nuclei are main differential features from IC. The trabecular pattern is present in both hyalinizing trabecular adenoma and IC, but IC appears to reveal higher cellularity, frequent necrosis, and more common trabecular pattern. It has been shown that the accu-

racy of cytologic diagnosis can be increased by using cell block and immunohistochemical study as an adjunct to routine cytologic procedures. Thus the accuracy and sensitivity of the FNA diagnosis of IC can be feasible, showing trabecular, insular and microfollicular structures with presence of thyroglobulin in paranuclear vacuoles of tumor cells. Clinically, IC shows conflicting evidence on the prognostic implications and responsiveness to radioiodine therapy in the literature. In Carcangiu and Rosai series<sup>6)</sup>, insular component had important clinical implications because of the markedly worse prognosis and high recurrence rate. Ashfaq et al.<sup>7)</sup> in 1994, however, demonstrated no adverse prognostic effect of the insular components and discouraged the use of the term "insular carcinoma" and suggested the diagnostic term follicular or papillary carcinoma with "insular component" whether it represents a minor or predominant component. In conclusion, the main cytologic features allowing diagnosis of IC of the thyroid are as follows: 1) presence of trabeculae containing microfollicles with or without thin fibrous bands along the margin of trabeculae, 2) uniform, small and hyperchromatic nuclei with low grade atypia and little cytoplasm, 3) optically clear and grooved nuclei, 4) paranuclear vacuoles containing thyroglobulin, and 5) necrotic background.

## References

1. Carcangiu ML, Zampi G, Rosai J: Poorly differentiated ("insular") thyroid carcinoma. *Am J Surg Pathol* 8:655-668, 1984
2. Flynn SD, Forman BH, Stewart AF, Kinder BK: Poorly differentiated ("insular") carcinoma of the thyroid gland. *Surgery* 104:933-970, 1988
3. Pietribiasi F, Sapino A, Papotti M, Bussolati G: Cytologic features of poorly differentiated 'insular' carci-

noma of the thyroid, as revealed by fine-needle aspiration biopsy. *Am J Clin Pathol* 94:687-692, 1990

4. Zakowski M, Schlesinger K, Mizrachi HH: Cytologic features of poorly differentiated "insular" carcinoma of the thyroid. *Acta Cytol* 36:523-526, 1992

5. Papotti M, Micca FB, Favero A et al: Poorly differentiated thyroid carcinoma. Primordial cell carcinoma. *Am J Surg Pathol* 17:291-301, 1993

6. Rosai J, Carcangiu ML, DeLellis RA: Atlas of Tumor Pathology, Tumors of the Thyroid Gland. 3rd ed, Armed Forces Institute of Pathology, Warhington DC, 1990, pp 123-133

7. Ashfaq R, Vuitch F, Delgado R et al: Papillary and follicular thyroid carcinoma with an insular component. *Cancer* 73:416-423, 1994

= 국문초록 =

## 갑상선 미분화 “도암종”의 세침흡인 세포학적 소견

- 1례 보고 -

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양영일·김찬환·강신광

갑상선 미분화 “도암종”은 예후가 나쁘고 희귀한 종양으로 이 종양의 세침흡인 세포학적 소견에 관한 보고는 1990년 Pietribiasi 에 의해 처음 기술된 이후 현재까지 8례가 있을 따름이다.

최근 저자들은 23세 여자의 좌측 경부의 갑상선 종괴로부터 세침흡인 세포검사를 시행하여 진단된 갑상선 도암종을 경험하여 그 세침흡인 세포학적 소견을 기술하는 바이다. 환자는 10년전부터 좌측 경부에 서서히 자라는 종괴를 호소하였으며 본 종괴에서 세침흡인 세포학적 검사를 시행하였다. 종괴의 세침흡인 도말은 세포밀도가 높았고 일정한 모양의 작고 둥근 세포들이 “도” 구조 혹은 “지주” 구조를 보이며 간혹 개개로 산재되어 있는 세포 및 소포형태도 보였다. “도” 구조 및 “지주” 구조 내에는 미세한 소포형태가 관찰되었고 종양세포들의 핵은 자주 중첩되어 있었다. 갑상선 여포상 선종에서 보이는 성글게 배열된 소포구조도 드물게 관찰 되었다. 세포간의 크기나 모양은 거의 일정하였고 유사분열은 거의 관찰되지 않았다. 핵은 둥글고 뚜렷한 핵막과 미세하게 뭉친 염색질을 가지며 핵소체는 뚜렷하지 않았으며 드물게 젓빛 유리모양의 핵과 핵구가 관찰되었으나 유두상 구조는 관찰되지 않았다. 세포질의 경계는 불명확하였고 간혹 세포질내에 공포가 관찰되었다. 이상의 도암종의 세포학적 소견은 여포상 종양이나 유두상 종양들과는 구분되는 특징적인 소견이라 생각되며 세포학적 소견으로도 도암종의 진단이 가능하다고 생각된다.