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Fine Needle Aspiration Cytology of Follicular Neoplasm of the Thyroid

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=Abstract=

The major limitation of fine needle aspiration of the thyroid is in the evaluation of follicular tumors. It may be difficult or occasionally, impossible to distinguish on a cytologic basis, between hyperplastic nodular goiter, follicular adenoma and well differentiated follicular carcinoma. We reviewed cytologic presentations of 15 histologically confirmed follicular neoplasms of the thyroid. Aspiration smears of 6 follicular adenomas were cell-rich with ball-like or syncytial aggregates of monotonous follicular cells, in contrast to honeycomb-like flat sheets of adenomatous goiter. Mild nuclear pleomorphism and a small visible nucleolus were noted in 2 cases, respectively. Nine cases of follicular carcinoma showed very high cellularity, irregularly shaped cell clusters, and numerous isolated tumor cells. Nuclear pleomorphism and visible nucleoli were noted in 6 and 5 cases, respectively. Another characteristic finding, entrapped endothelial cells within the cell clusters, was noted in 7 carcinomas and 1 adenoma. The background of the smears of all follicular neoplasms was hemorrhagic, with no or scanty colloid. We confirmed that the cytologic features of follicular adenoma and carcinoma were similar in general, with subtle differences in cell morphology, but the presence of isolated tumor cells and entrapped endothelial cells was suggestive of malignancy.

Key words : Thyroid, Follicular neoplasm, Aspiration, Cytology

Introduction

Fine needle aspiration cytology is considered an accurate diagnostic method for most thyroid lesions[1-4]. However, it has been believed that there is a major limitation in the evaluation of follicular lesions. Differential diagnosis between hyperplastic nodular goiter, follicular adenoma, and well-dif-

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ferentiated follicular carcinoma may be very difficult or impossible[5-8]. This paper profiles the cytologic features of a small series of histologically confirmed follicular tumors of the thyroid.

Materials and Methods

From January 1989 to May 1993, 41 patients were diagnosed as follicular adenoma or carcinoma of the thyroid after surgery at the Korea Cancer Center Hospital. Fifteen cases among them, with adequate preoperative aspiration cytologic specimens, were included in the study. On histologic examination of 6 cases there were adenomas of macrofollicular, simple, and trabecular type in 2 cases each. Nine cases of follicular carcinoma, with definite invasion, showed a predominantly follicular pattern in 5, and a trabecular and solid pattern in 4. Three cases were only minimally invasive. Their alcohol-fixed and Papanicolaou-stained cytologic specimens were reviewed.

Results

The aspiration smears of follicular adenomas were generally cell-rich with collections of follicular cells(Fig. 1). The cell groups showed a syncytial or ball-like configuration with crowded and overlapped nuclei, in contrast to the flat honeycomb-like sheets of nodular goiter. The cells were monomorphic, and had bland round to ovoid nuclei with finely granular chromatin and indistinct nucleoli (Fig. 2). Follicle formation was rarely seen in one macrofollicular and one trabecular adenoma. Mild variation in nuclear size and small visible nucleoli were noted in 2 cases, respectively(Fig. 3). The background of the smears contained plenty of blood and scanty or no colloid(Fig. 1).

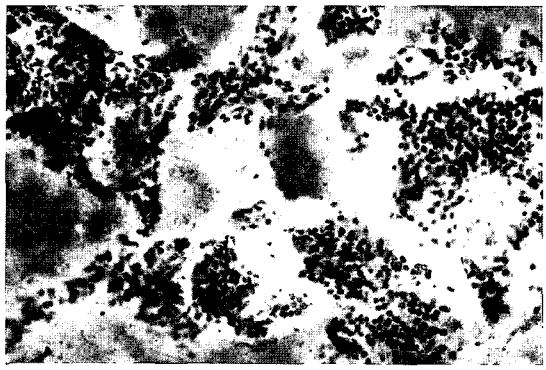

Fig. 1. Photomicrograph of aspiration cytologic smear of follicular adenoma, showing high cellularity with syncytial cell clusters. Background is hemorrhagic without colloid material(Papanicolaou, ×175).

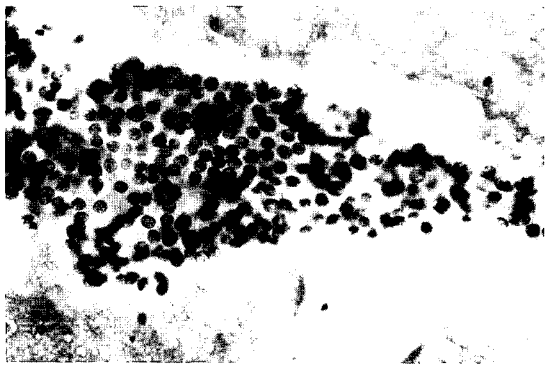

Fig. 2. Cell clusters of follicular adenoma, consisting of monomorphic cells with round bland nuclei in 3 dimensional arrangement. Focal follicle formation is observed(Papanicolaou, ×350).

As in Table 1, follicular carcinomas showed basically identical cytologic features to those of adenomas. But carcinomas generally showed higher cellularity, and larger and more irregular cell clusters than adenomas(Fig. 4). Nuclear pleomorphisms and visible nucleoli were more frequent, but the degree was as mild as adenomas. Follicle formation was also more frequently seen than in adenomas. The background was devoid of colloid. Two relatively characteristic findings in carcinoma cases were the

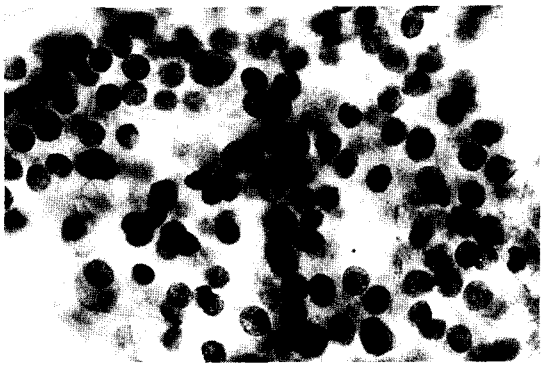

Fig. 3. Mild degree of nuclear pleomorphism and small visible nucleoli, seen in 2 cases of follicular adenoma(Papanicolaou, × 700).

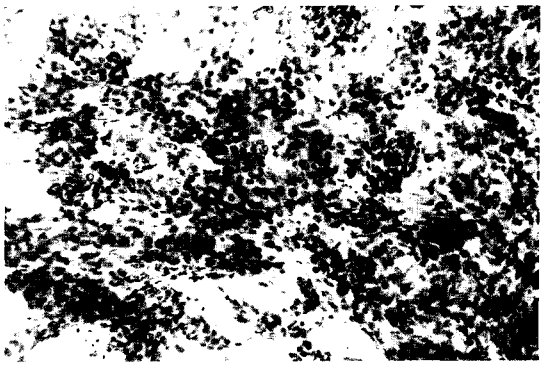

Fig. 4. Follicular carcinoma, showing higher cellularity and more irregular and crowded cell clusters than adenomas(Papanicolaou, × 175).

Table 1. Summary of cytologic features of follicular neoplasms

	Adenoma (6)	Carcinoma (9)
Cellularity	High	Very high
Cell groups	Syncytial, ball-like	Syncytial, irregular
Isolated cells	Rare (1)	Numegous(9)
Nuclear pleomorphism	Uncommon (2)	Frequent(6)
Chromatin	Finely granular	Finely granular
Nucleoli	Uncommon, small (2)	Frequent, small (5)
Entrapped endothelial cells	Rare (1)	Frequent(7)
Macrophage	Rare (2)	Absent
Colloid/blood	Scanty/ abundant	Scanty/ abundant

( ): Number of cases

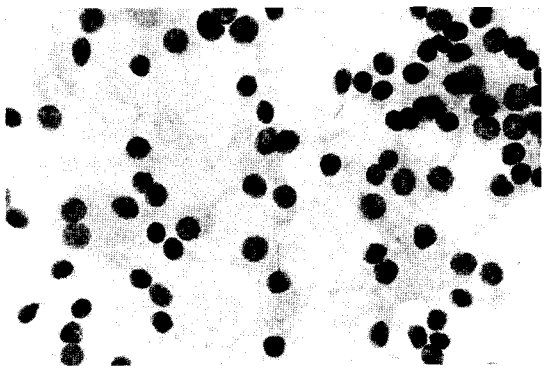

Fig. 5. Numerous isolated tumor cells in follicular carcinoma (Papanicolaou, × 700).

presence of individually isolated tumor cells and entrapped endothelial cells in between the cell clusters. Isolated tumor cells were a predominant or partial component of all cases of carcinoma (Fig. 5), and was observed in one case of adenoma. Endothelial cells adherent to the epithelial cells were seen in 7 out of 9 carcinomas and in one adenoma (Fig. 6).

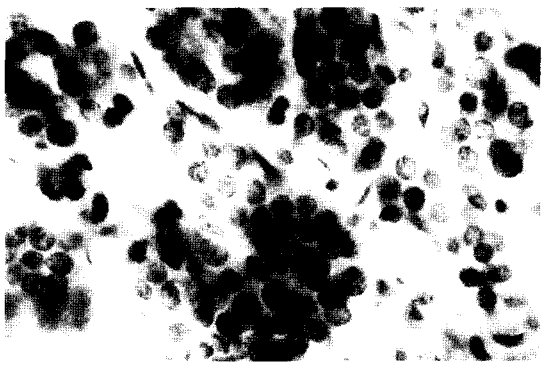

Fig. 6. Endothelial cells adherent to trabecular clusters of follicular cells (Papanicolaou, × 700).

Discussion

Fine needle aspiration cytology is very useful in the diagnosis of various thyroid lesions[2,6,7], especially in the diagnosis of neoplasm and thyroiditis[1,3,4]. One of the main criticisms against the use of aspiration cytology for thyroid nodules has been the difficulty in differential diagnosis of follicular lesions on a cytologic basis. Many authors recommended the use of 'follicular neoplasm' or 'follicular lesion' in the field of cytologic diagnosis[4,5,8-10]. This limitation cannot be solved completely since essential criteria for a microscopic diagnosis of follicular carcinoma is the presence of capsular and/or vascular invasion, which cannot be identified in cytologic specimens. Indeed, the cytologic features of follicular adenoma and carcinoma used to be very similar, in this series as well. However, efforts to discriminate malignant tumors from adenomas have constantly been made. Helpful criteria include increased size of the nuclei[10-13], increased number or size of the nucleoli[11,14], and severe nuclear overlapping with numerous single tumor cells[10,15-17]. Some authors emphasized the growth pattern over appearances of individual cells in the evaluation of follicular lesions[9,18,19]. Solid or microfollicular patterns of growth can be noticed without difficulty if we look more specifically for the pattern of cell clusters. But this pattern does not necessarily represent the malignant behavior of tumors, although follicular carcinomas tend to be more cellular and solid than adenomas. It is known that the growth pattern of follicular adenoma has no clinical implication.

In our study, the presence of isolated tumor cells and entrapped endothelial cells were more frequent in follicular carcinomas than in adenomas. The presence of numerous isolated cells is considered to reflect the dyshesiveness of tumor cells, supporting a diagnosis of malignancy. But the endothelial cells may be only showing the trabecular pattern and high vascularity of tumors. These features may not be specific for follicular carcinomas, but have been almost never seen in non-neoplastic follicular lesions.

In general, diagnostic accuracy for follicular tumors on the cytologic basis tends to be lower than that of other tumors of the thyroid[12]. Our original diagnoses were 2 follicular cell hyperplasia, 2 adenomatous goiter, 1 benign atypia and 1 negative for adenoma cases, and 2 follicular carcinoma, 2 follicular neoplasm, 1 carcinoma, 1 Hürthle cell tumor, 1 follicular cell hyperplasia, 1 suspicious papillary carcinoma, and 1 suspicious malignancy in cases of follicular carcinoma. It is important to understand the common cytologic features of follicular tumors, such as high cellularity, syncytial cell aggregates, and scanty colloid, and some special findings in relation with the growth pattern or aggressive behavior. High detection rates of follicular neoplasm up to 98~99% have been reported in several studies[3,9,11,20]. Some authors succeeded in diagnosing over 75% of the follicular carcinomas accurately[11]. By paying more attention to the cytology of follicular lesions, it would be possible to miss no more than 1~2% of follicular carcinomas.

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= 국문초록 =

갑상선의 여포상 종양의 흡인세포학적 소견

원자력병원 해부병리과

조 경 자 · 장 자 준

갑상선의 세침흡인 세포학적 검사에서 가장 문제가 되는 점은 여포상 종양의 진단이다. 세포학적 소견만으로는 증식성 결절성 갑상선종, 여포성 선종 및 분화가 잘 된 여포상 암종 간의 감별 진단이 매우 어려운 경우가 많다. 저자들은 최근 4년 5개월 간에 조직학적으로 확진된 여포상 종양 중 수술 전에 적합한 세포학적

검사가 시행된 15예를 대상으로 그 세포학적 소견을 재검토하였다. 여포상 선종 6예의 흡인 도말은 공 모양 또는 합포체를 형성하는 다량의 여포성 세포를 함유하고 있었고, 경도의 핵 다형성 및 작은 핵소체가 각각 2예에서 관찰되었다. 배경은 출혈성으로 교질 성분은 매우 적거나 없었다. 여포상 암종 9예도 기본적으로 선종과 유사한 세포학적 소견을 보였는데, 세포밀도가 좀더 높고, 세포집단의 모양이 더 크고 불규칙하였으며, 흩어진 개별 종양세포가 많은 것이 차이점이었다. 핵의 다형성 및 눈에 띄는 핵소체가 선종에서 보다 많은 6예 및 5예에서 각각 관찰되었으나 그 정도는 심하지 않았다. 대부분의 암종과 1예의 선종에서 종양세포 집단에 밀착한 혈관 내피세포가 관찰되었다. 전반적으로 여포상 선종 및 암종은 미미한 차이를 보여서 세포학적으로 확실히 구별하기는 어려웠으나, 많은 수의 개별 세포와 종양세포 간에 포착된 혈관내피세포의 존재는 양성보다는 악성을 시사하는 소견으로 생각되었다. 여포상 종양의 세포학에 좀더 관심을 가짐으로써 그 발견율을 현저히 높일 수 있다고 생각된다.