대한세포병리학회지 제 16 권 제 1 호
The Korean Journal of Cytopathology
16 (1) : 41-46, 2005
ISSN 1017-0391

가슴샘 카르시노이드종양의 세침흡인 세포소견
- 1예 보고 -

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= **Abstract** =

Fine Needle Aspiration Cytology of a Thymic Carcinoid Tumor
- A Case Report-

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Carcinoid tumors of the thymus are vanishingly rare, and the characteristic cytologic findings of this condition have never before been reported in Korea. Recently, we encountered a 58-year-old woman who had been suffering from general weakness and weight loss for several months. Radiological imaging revealed a large anterior mediastinal mass. A fine needle aspiration biopsy (FNAB) of the mass showed predominantly scattered single cells, as well as some loose clusters of small cells with scanty cytoplasm. Some of these small cells exhibited plasmacytoid features, with moderately granular cytoplasm. We also discuss the cytological differential diagnosis between thymic carcinoid and other mediastinal tumors.

Key words: Carcinoid tumor, Thymus, Fine needle aspiration cytology

논문접수 : 2005년 3월 10일
게재승인 : 2005년 4월 20일

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INTRODUCTION

Thymic carcinoid is easily confused with thymomas, and was previously referred to as carcinoid tumor of the mediastinum, epithelial thymomas, mediastinal bronchial adenoma, parathyroid adenoma, or unclassified mediastinal tumor.[1] In 1972, Rosai and Higa initially identified thymic carcinoid as a specific entity, which was distinct from thymoma.[2] The histogenesis of this tumor was believed to originate from the neural crest or by the *in situ* development and differentiation of thymic neuroendocrine cells.[1]

Thus far, there have only been three cytologic reports of thymic carcinoid, including 7 cases in the English literature.[3-5] Here, we report a case of thymic carcinoid and its cytologic findings, with particular emphasis on the differential diagnosis of thymic carcinoid from other anterior mediastinal tumors.

CASE

A 58 year-old female patient was referred to our hospital due to an abnormal mass shown on a chest X-ray which had been performed at a local clinic. This patient presented with general weakness and weight loss, which had persisted for several months. The patient's physical examination proved unremarkable. Her laboratory tests also were unremarkable. Chest CT revealed a mass, which measured 10 × 9 × 5.5 cm, and exhibited heterogeneous density in the anterior mediastinum. This mass was attached to the aortic arch, pericardium, and the anterior chest wall. We also noted mediastinal lymphadenopathy adjacent to the mass (Fig. 1). Under the suspicion of thymic carcinoma or invasive thymoma, we conducted a computed tomography (CT)- guided fine needle aspiration cytology (FNAC). The patient subsequently underwent a surgical excision of the mass, and was also treated with postoperative radiation therapy.

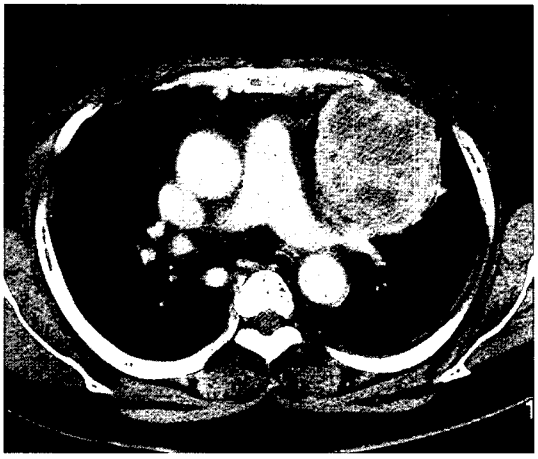

Fig. 1. Chest CT finding. It reveals 10 x 9 x 5.5 cm sized solid and heterogeneous mass with multiple lymphadenopathy. The mass is located in the anterior mediastimun and attached to the aortic arch, pericardium, and anterior chest wall.

Cytologic Findings

The FNAC revealed predominantly individually-scattered single cells, as well as some loose clusters of small cells, in a slightly bloody background (Fig. 2A & B). Focally, the tumor cells appeared to be arranged in a row, and assumed a rossettoid or acinar structure (Fig. 3A & B). The tumor cells were uniformly small, with round-to-oval contours. Although the cytoplasm in these cells was typically scanty, a few cells contained moderate amounts of granular cytoplasm. The nuclear / cytoplasmic ratio was determined to be rather high. The nuclei appeared eccentric and round, with stippled chromatin and inconspicuous nucleoli. Some of the tumor cells exhibited a plasmacytoid appearance (Fig. 3C). Our differential diagnosis included carcinoid tumor, lymphocyte predominant thymoma, small lymphocytic lymphoma, and plasmacytoma.

Gross Findings

On gross examination, the tumor appeared relatively circumscribed with several areas of adhesion. We also noted several enlarged lymph nodes adjacent to the mass, which measured up to 3cm in diameter. The cut surface revealed partially solid and cystic areas, and some irregular hemorrhaging (Fig. 4A). We detected no distinct fibrous bands, which are characteristic features of thymoma.

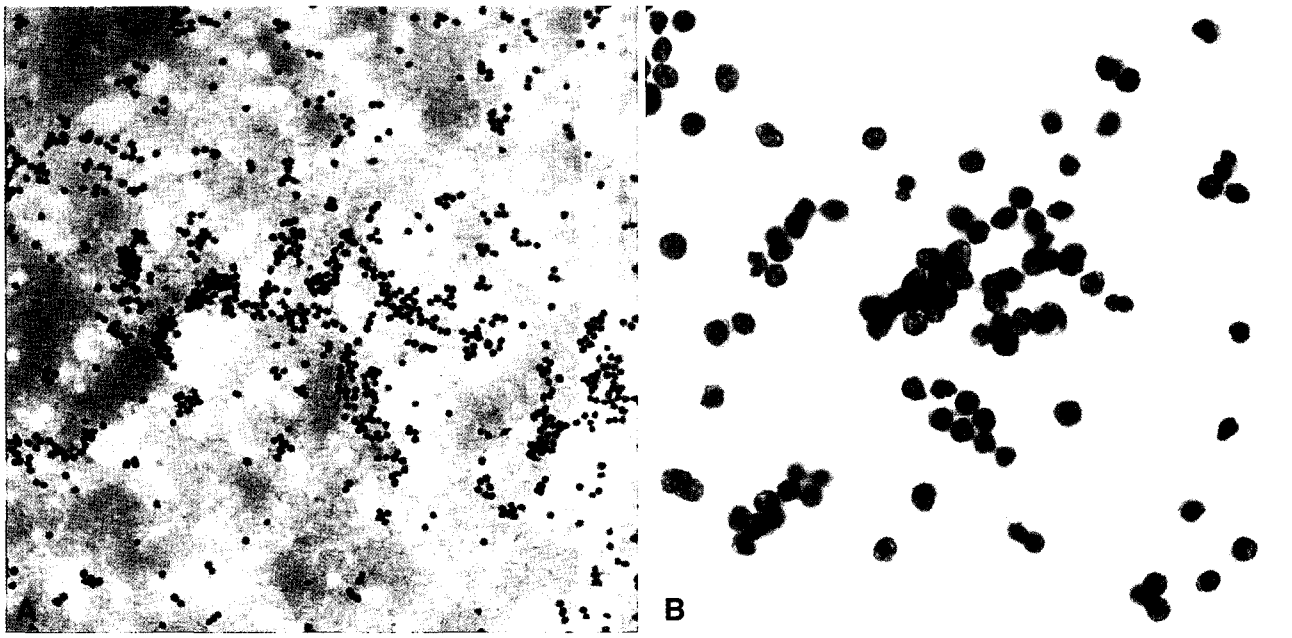

Fig. 2. Low power view of fine needle aspiration cytology. (A) Individually scattered single cells seen in the bloody background. (B) Some loose clusters of small round cells are also seen. (H-E)

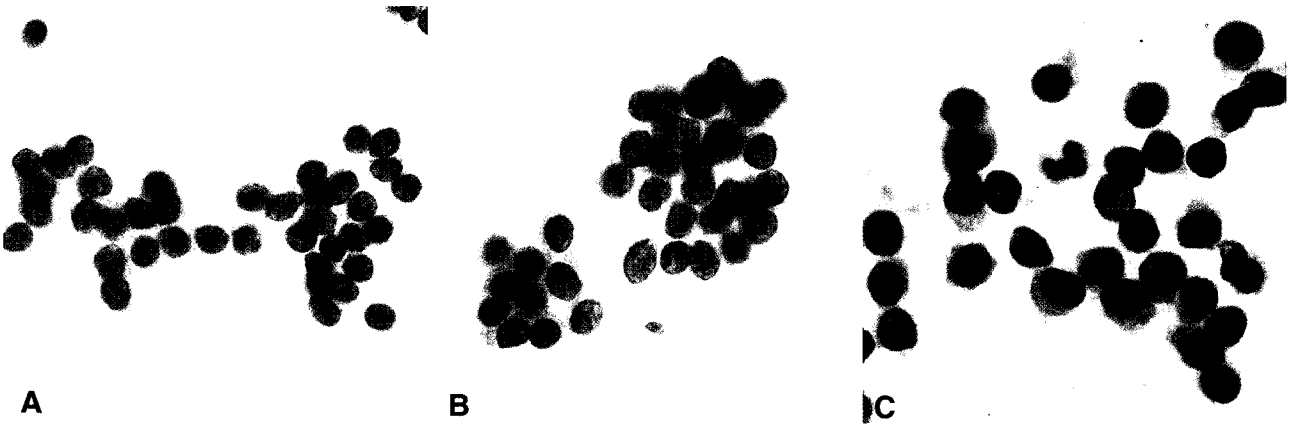

Fig. 3. High power view of fine needle aspiration cytology. (A) The tumor cells in the loose clusters are arranged in a row. (Papanicolaou) (B) The tumor cells also form rossettoid or acinar structure. (Papanicolaou) (C) The tumor cells are uniformly small with round to oval contour and show finely granular cytoplasm and stippled chromatin pattern. Occasionally, the tumor cells have a plasmacytoid feature. (H-E)

Histologic findings

Upon histological examination, we noted residual thymic tissue containing Hassall's corpuscles and small lymphocytes in the area adjacent to the tumor. The tumor was highly cellular, and revealed solid nests and a trabecular pattern, compartmentalized by delicate fibrovascular stroma (Fig. 4B). At the periphery of the mass, the tumor cells also assumed a ribbon-like or Indian-file appearance. We also observed some central coagulation necrosis and frequent hemorrhaging. We frequently noted lymphatic tumor emboli. The tumor cells in the sample were uniform, and exhibited granular eosinophilic cytoplasm. The nuclei were round, containing stippled powdery chromatin and inconspicuous nucleoli. We also occasionally observed mitotic figures. The tumor cells were positive for cytokeratin, neuron-specific enolase, synaptophysin, and chromogranin, but were negative for

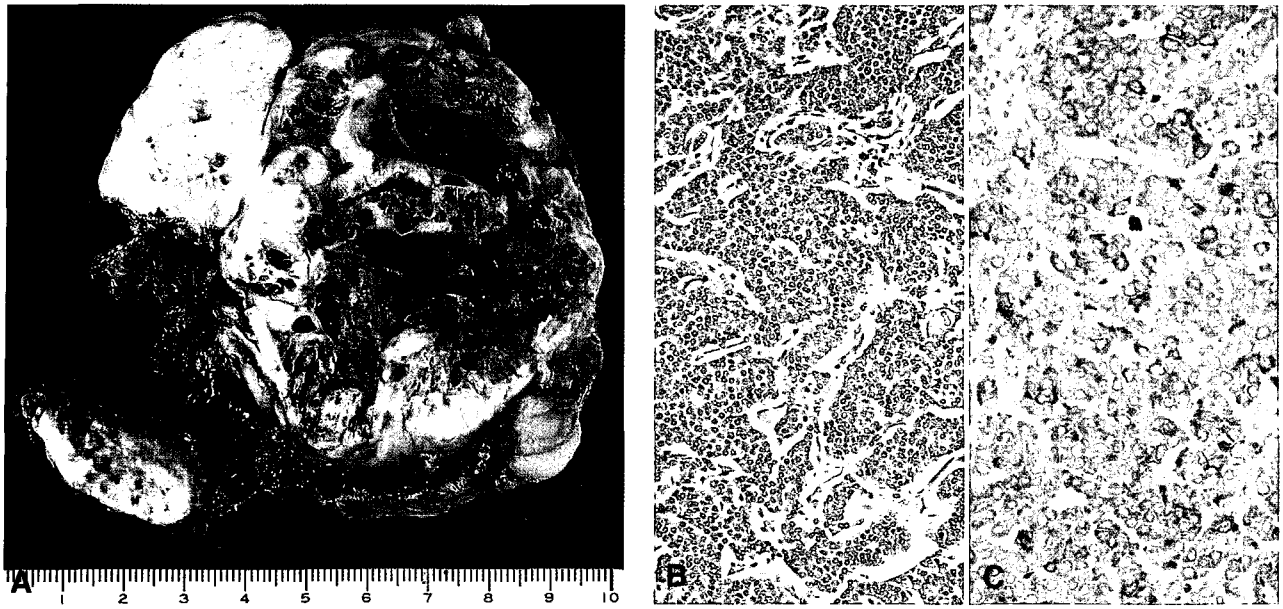

Fig. 4. Gross and histologic findings of the resected specimen. (**A**) The cut surface shows pale yellowish solid mass with cystic changes and hemorrhage. (**B**) The tumor is highly cellular and arranged in solid nests and trabecular pattern divided by delicate fibrovascular stroma. (**C**) The tumor cells are immunoreactive for chromogranin.

ACTH (Fig. 4C). A few small lymphocytes which stained positively for CD3 and CD45RO were scattered within the tumor nests. The tumor itself was diagnosed as a thymic carcinoid on the basis of the histologic and immunohistochemical findings described above. Histologically, though, the tumor was classified as an atypical carcinoid tumor of the thymus, according to the WHO classification.

DISCUSSION

Recently, CT-guided FNAC has been used extensively in the preoperative diagnostic procedures conducted for a mediastinal mass. This technique allows for the targeted sampling of the solid portion of the tumor. In cases in which an experienced cytopathologist is able to recognize each characteristic cytologic feature, it is possible to establish a preoperative cytologic diagnosis of the mediastinal mass.

Carcinoid tumors are a well-recognized disease entity, which occur primarily in the gastrointestinal tract, esophagus, and pancreas, but also, albeit rarely, in the lungs, bronchus, and breast.[3] Only about 100 cases of thymic carcinoid have been reported in the English literature.[1] Moreover, only 3 reports, encompassing 7 cases, have been described in the English literature which included the cytologic findings. However, no such reports have ever originated in Korea.[3-5] According to the aforementioned previous reports and our current case, we can conclude that thymic carcinoid has sufficiently distinct cytologic features to allow for correct diagnosis.[3-5]

Collins et al. reported the cytologic findings of 19 carcinoid tumors, including 2 cases of thymic carcinoid.4 However, the cytologic findings of thymic carcinoid were not described separately from those of the other carcinoid tumors in that report. Therefore, we were unable to precisely identify the characteristic cytological features of primary thymic carcinoid tumor on the basis of that report. However, in 1995, there was a report of four cases of thymic carcinoid which had been diagnosed by FNAC.[3] Hallmann et al. subsequently reported another case of thymic carcinoid which had been diagnosed by FNAC.[5] These two reports demonstrated that the aspirates of thymic carcinoid contained a predominantly noncohesive single cell population, as well as some loose cell clusters.[3,5] Our present case involved a similar smear

Table 1. Cellular features helpful in differential diagnosis between thymic carcinoid and other tumors

Feature	Thymic carcinoid	Thymoma (LP)	Lymphoma (SLL)	Plasmacytoma	Present case
Cell population	One	Two*	One	One	One
Smear Pattern	Single cell Loose cluster	Single cell	Single cell	Single cell	Single cell Loose cluster
Background	Hemorrhagic Absence of necrosis	Clear	Clear	Clear	Hemorrhagic
Cell					
Cytoplasm	Distinct Granular	Scanty**	Scanty	Distinct Cyanophilic	Distinct Granular
N/C ratio	Moderate	Almost 1:1**	Almost 1:1	Moderate	Moderate to high
Nucleus	Eccentric (Plasmacytoid) Round, Stippled	Cleft, Groove**	Cleft, Groove	Cart-wheel	Eccentric (Plasmacytoid) Round, Stippled
Nucleolus	Small, Inconspicuous	Variable**	Variable	Inconspicuous	Inconspicuous

LP: Lymphocyte predominant subtype
SLL: Small lymphocytic lymphoma
*: Two cell populations composed of lymphocytes and epithelial cells
**: Detailed cellular descriptions of mature lymphocytes in thymoma

pattern and cytological details, as was observed in the above reported cases. The tumor cells were monotonous, small, round-to-oval cells which contained granular cytoplasm and eccentrically-located round nuclei, which themselves harbored inconspicuous nucleoli. Some of the tumor cells assumed a plasmacytoid appearance. Therefore, we suggest that the cytologic findings described above are characteristic features of thymic carcinoid.

Atypical carcinoids have been reported to constitute 5-10% of all pulmonary carcinoid tumors.[6] With regard to cytology, atypical carcinoids are generally characterized by a higher degree of cellular pleomorphism, and contain spindle-shaped tumor cells, a greater quantity of mitotic figures, increased hyperchromasia, prominent nucleoli, and even nuclear molding.[3,4,7] According to the previous reports, five cases have been histologically classified as typical carcinoid tumor.[3,5] However, our present case was histologically classified as an atypical carcinoid, owing to the occasional mitotic figures, multifocal necroses, and frequent lymphatic tumor emboli observed. In the present case, the cytologic findings of FNAC were quite similarto those of previous reports, and necroses and mitotic figures could not be detected in the aspirates. Therefore, we surmise that it may not be possible to determine the histologic subtype of thymic carcinoid simply on the basis of FNAC results.

Considering that the aspirates are predominantly composed of noncohesive small single cells, the results of FNAC could easily be misinterpreted as lymphocyte predominant thymoma, or even as small lymphocytic lymphoma.[3] In addition, plasmacytoma could be also included in this differential diagnosis, due to the plasmacytoid appearance observed in association with some tumor cells. The cytologic differences between thymic carcinoid tumor and other tumors are summarized in Table 1. The most pronounced characteristic cytologic features of thymoma are the observation of a biphasic cellular population, consisting of mature lymphocytes interspersed with variable proportions of elongated epithelial cells, even in cases of the predominant lymphocyte subtype. Carcinoid tumors can be distinguished from thymomas due to the absence of a biphasic cellular population, and also by the observations

of granular cytoplasm and a plasmacytoid appearance. Small lymphocytic lymphomas can also readily be confused with thymic carcinoids. However, small lymphocytic lymphomas exhibit some distinct cytological features, including dispersed single cells with less conspicuous cohesion formation, frequent nuclear clefts or grooves, and scanty cytoplasm which lacks cytoplasmic granularity. Moreover, as was observed in the present case, distinct organoid patterns, including rosettoid arrangements, acinar structures, and single rows of cells, exclude the possibility of lymphoma. Like malignant lymphoma, plasmacytomas also exhibit a dispersed single cell pattern with no organoid arrangement, which is probably the most important factor in differentiation plasmacytomas from thymic carcinoids. In addition, most plasmacytoma tumor cells show an even distribution of eccentrically-located nuclei, with a cart-wheel appearance. Although some plasmacytoid cells can also be observed in thymic carcinoids, a diagnosis of plasmacytoma can be excluded, due both to their rarity, and to the lack of a cart-wheel appearance in their nuclei.

In conclusion, we have described a case of thymic carcinoid tumor exhibiting characteristic cytologic features. We have also emphasized differential diagnosis, while providing useful criteria for an accurate diagnosis of thymic carcinoid tumors.

REFERENCES

1. Simosato Y, Mukai K. Tumors of the Mediastinum, 3rd Series. Washington, D.C.: Armed Forces Institute of Pathology, 1997;158-83.
2. Rosai J, Higa E. Mediastinal endocrine neoplasm, of probable thymic origin, related to carcinoid tumor. *Cancer* 1972;29:1061-74.
3. Wang DY, Kuo SH, Chang DB, Yang PC, Lee YC, Hsu HC, et al. Fine needle aspiration cytology of thymic carcinoid tumor. *Acta Cytol* 1995;39:423-7.
4. Collins BT, Cramer HM. Fine needle aspiration cytology of carcinoid tumors. Acta Cytol 1996;40:695-707.
5. Hallmann RS, Schneeweiss LG, Correa E, Zamora J. Fine needle aspiration biopsy of thymic carcinoid tumor: a case with immunocytochemical correlation. *Acta Cytol* 1998; 42:1042-3.
6. Fekete PS, Cohen C, DeRose PB. Pulmonary spindle cell carcinoid. Needle aspiration biopsy, histologic and immunohistochemical findings. *Acta Cytol* 1990;34:50-6.
7. 이연수, 박경신, 최영진, 김석진, 김병기, 심상인. 폐의 비정형 유암종의 세침흡인 세포학적 소견-2예 보고- 대한세포병리학회지 1997;8:76-82.