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A Case of Thymic Carcinoid Tumour with Multiple Metastasis Including Bone Marrow

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= 국문초록 =

골수침범 및 다발성 전이를 나타낸 흉선유암종 1예

이화여자대학교 의과대학 부속병원 내과학교실, 흉부외과학교실*, 방사선과학교실**, 임상병리학교실***, 해부병리학교실****

이나영, 김화정, 천선희, 이순남, 원용순*, 김유경, 홍기숙***, 구혜수****

흉선 유암종은 전종격동 종양의 2.5-4%를 차지하는 매우 드문 종양으로 1972년 Rosai와 Higa에 의해 처음 기술되었다. 흉선 유암종은 악성의 임상경과, 조직학적 소견 및 불량한 예후등이 흉선암과 구별되며, 병리학적 진단은 광학 현미경 소견과 조직 생화학 검사 및 전자현미경 소견에 바탕을 둔다. 이 종양은 국소 침범과 다발성 전이가 흔하며, 종양의 절제와 방사선 조사를 치료의 근간으로 한다. 국내에서는 1983년 이 등이 보고한 이례 총 8예가 보고되었으나, 골수를 포함한 다발성 전이는 없었다.

저자들은 이화여자대학교 의과대학 부속병원 내과에서 62세의 남자에서 골수침범 및 폐, 늑막, 심낭, 복부대동맥 주위 임파절 및 피하 임파절 전이로 악성경과를 나타낸 흉선 유암종 1예를 경험하였기에 문헌고찰과 아울러 보고하는 바이다. (Tuberculosis and Respiratory Diseases 1999, 46 : 402-408)

Key words : Carcinoid tumour, Thymus, Bone marrow, Pleural effusion.

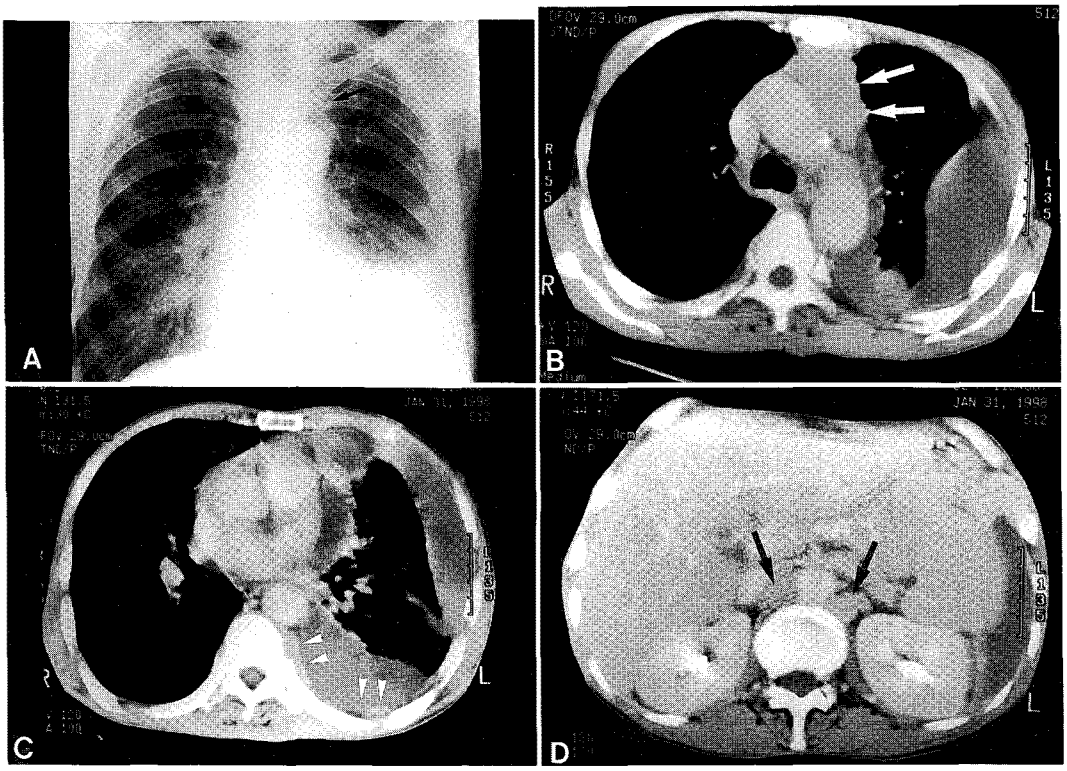

Fig. 1. A. 62-year-old man with thymic carcinoid and lymph node and pleural metastasis.
A. Posteroanterior chest radiograph shows mediastinal mass projecting to left side(arrows) and left pleural effusion.
B, C, D. Contrast-enhanced chest CT scan(mediastinal window) shows mass(B), left pleural effusion with pleural masses(arrow heads)(C), and paraaortic lymphadenopathies(arrows) in abdomen(D).

Introduction

Carcinoid tumours arising in the thymus are rare, representing 2.5% to 4% of all anterior mediastinal tumours. In 1972, Rosai and Higa were first described carcinoid tumour of thymus as a specific entity[1]. Thymic carcinoid tumour is differentiated from thymomas by aggressive clinical behavior, histology and their worse prognosis[2]. Seperation from thymoma can be difficult and careful light microscopy as well as electron microscopy and immunohistochemistry may be necessary to distinguish them[3]. Local invasion and multiple metastasis are common. Excision of the tumour and subsequent radiation therapy is the treatment of choice[1,4,5]. In Korea, since Lee et al was first described in 1983, only 8 cases have been reported[6-13]. The tumour in this patient behaved in a highly aggressive fashion with metastasis to the lung, pleura, pericaridum, paraarotic and subcutaneous lymph-node and bone marrow. To our knowledge, this is the first report of a thymic carcinoid tumour in which multiple metastasis include bone marrow in Korea.

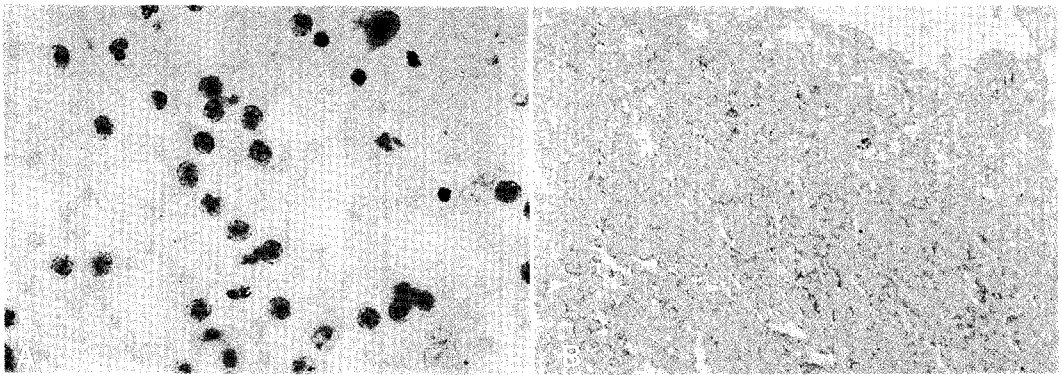

Fig. 2. A, B. Fine needle aspiration cytology of thymic carcinod reveals the characteristic uniform individual small round cells with scanty cytoplasm, round to oval nuclei and finely granular chromatin.(Hematoxylin and Eosin stain, ×400)(A) and positive for NSE in immunohistochemical stain(B).

Case Report

A 62-year-old man was referred to our hospital due to severe dyspnea. He was a heavy smoker(40 pack-year of tobacco use) and alcoholic. Physical examination revealed decreased breathing sounds in left lung field and enlarged liver without abnormal liver function and ascites. One and half months prior to being admitted, the left pleural effusion was diagnosed, tube thoracostomy was performed and antituberculous medication was done under the suspicion of tuberculous pleurisy at a local clinic. A chest X-ray at the time of admission showed a mediastinal mass projecting to left side and a massive left pleural effusion(Fig. 1-A). Thoracentesis was performed and revealed bloody fluid with glucose level 123mg/dL, protein level of 4.1g/dL, lactate dehydrogenase level of 186 U/L, and ADA value of 23 U/L. Cytologic examination of pleural fluid revealed inflammatory cells. Specimens from a pleural biopsy demonstrated fibrous exudates and chronic inflammation. Abdominal ultrasonographic examination revealed hepatosplenomegaly without mass, and left pleural effusion. A computed tomography scan of chest revealed a lobulated homogeneous gross mass in the anterior mediastinum, measuring 8×7×4cm, left pleural effusion with pleural mass and paraaortic lymphadenopathies(Fig. 1-B, C, D). A fine needle aspiration cytology of the mass was taken under tomographic control. Histological examination showed a number of uniform individual small round cells with scanty cytoplasm, round to oval nuclei and finely granular chromatin suggesting carcinoid tumour(Fig. 2-A, B). Bronchoscopy demonstrated no specific endobronchial lesion. Echocardiogram revealed normal findings except pericardial thickening.

Laboratory investigations showed that serum calcium, phosphorus, CEA, alpha-fetoprotein, gonadotropin, ACTH, and cortisol level were within normal limits. Urinary 5-HIAA was also normal. A thoracoscopy revealed that the tumour replaced the contents of the anterior mediastinum, extended to the left thoracic cavity and invaded the left upper lung, the pericardium, the parietal pleura and metastasized to regional lymph nodes. Only an incisional biopsy of mediastinal mass and pleura and excisional

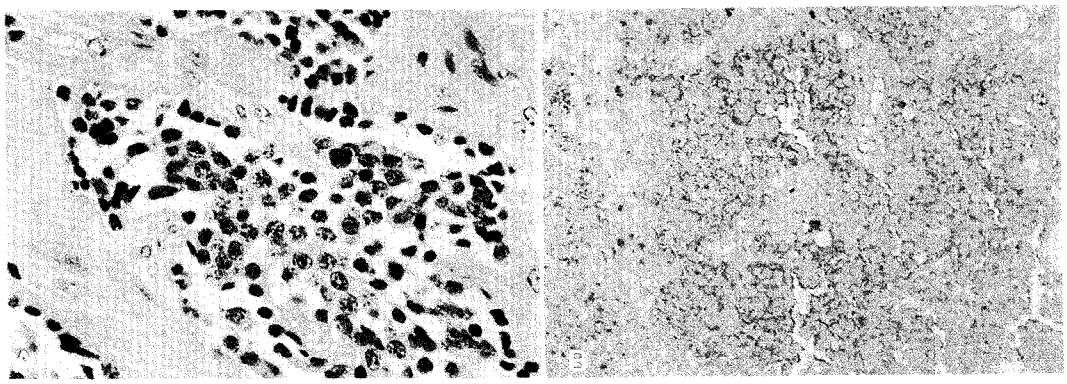

Fig. 3. A, B. Biopsy specimens of the midiastinum mass shows monotonous with round to oval nuclei and eosinophilic cytoplasm and group of tumour cells surrounded by fibrovascular septa(Hematoxylin and Eosin stain, ×400)(A) and immunohistochemical staining with the NSE of the mediastinal mass. Intracytoplasmic granules are positively stained(B).

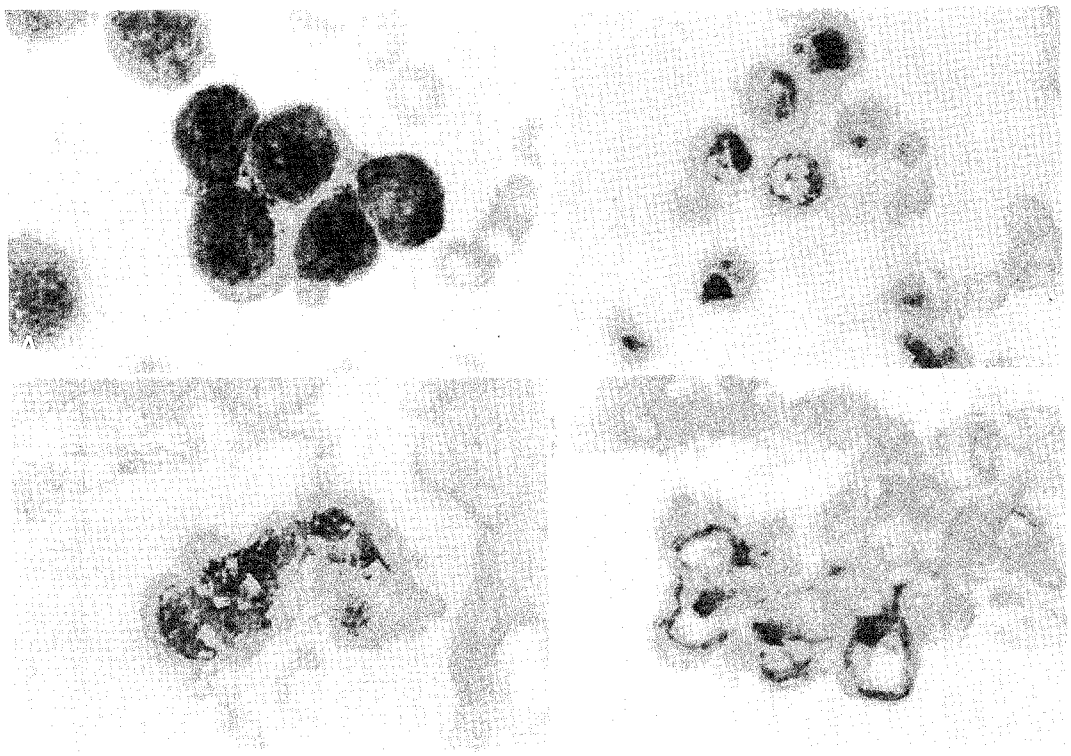

Fig. 4. A. Biopsy sepcimen of bone marrow showing sheets of monotonous round to oval cells with varying amounts of cytoplasm and stippled nuclear chromatin are seen.(Hematoxylin and Eosin stain, ×1000).

B, C, D. Immunohistochemial stain of bone marrow shows negative for leukocyte common antigen (B), positive for NSE(C) and positive for cytokeratine(D).

biopsy of subcutaneous node were performed. Microscopically, biopsy specimens showed typical features of carcinoid, such as monotonous with round to oval nuclei and eosinophilic cytoplasm and a group of tumour cells surrounded by fibrovascular septa(Fig. 3-A). Immunohistoche-mically, they were immunoreactive for neuron-specific enolase(NSE)(Fig. 3-B). Three times of pleurodesis with doxycycline were given due to the large amount of malignant effusion. A bone marrow examination was performed due to gradually decreasing platelet count and revealed metastasis(Fig. 4-A).

Immunohistochemical stain showed strong positive for cytokeratin and NSE, negative for leukocyte common antigen(LCA)(Fig. 4-B, C, D). He underwent a course of chemotherapy with cytoxan, vincristin, etopo-side. But, the patient showed unsatisfactory results and died of progressive disease after three months of diagnosis.

Discussion

Carcinoid tumour of thymus was first recognized in 1972 by Rosai and Higa[1]. Carcinoid tumours, including thymic carcinoid, arise from APUD neuroendocrine cells that contain neurosecretory granules. Carcinoid tumours are most common in the gastrointestinal tract and bronchus, often associated with other endocrine tumours[14-16].

Carcinoid tumours of thymic origin are rare, and occur predominantly in middle-aged male patients who used to be heavy smokers. They are usually discovered at their advanced stage.

Wick et al[16]. classified thymus carcinoid into three groups ; one involving tumours associated with Cushing's syndrome or other endocrino-pathies ; one involving tumours not associated with endocrine abnormalities ; and one including tumours associated with MEN syndrome. In the absence of endocrine abnormalities, carcinoid tumours of the thymus are either asymptomatic or they display symptoms of an expanding mass in the mediastinum. In the patient described in our present report, no other tumours of the endocrine system were clinically detected.

It is important to distinguish thymic carcinoid tumour from the thymomas because of the aggressive nature of the tumour, lack of effective treatment and their worse prognosis. Invasion of adjacent structures occurs in 30-50% cases. Intrathoracic lymph node metastasis were documented in over 40% and distant metastasis, commonly to the lung, bone, and liver, in 30%[4,6,17-19]. According to previous reports, local invasion of the adjacent tissues was found in 88 % of thymic carcinoid tumour at diagnosis[20].

Thymic carcinoid tumour can be diagnosed either by surgical exploration or by open biopsy of the tumour at mediastinoscopy. Ultrasound or CT-guided fine needle aspiration cytology may be helpful for diagnosis in selected patients.

Histologically, thymic carcinoid tumours is composed of monomorphic polyhedral or round cells arranged like rosettes, calcium deposits, areas of necrosis and sometimes lymphocytic infiltration[21,22].

Immunohistochemical techniques may show the presence of such markers as cytokeratin, desmosomial proteins, neuronal enolase, and human chorionic gonadotropin[23,24]. Isolating these markers may be useful in the clinical follow up of the disease, together with serial measurements of urinary 5-HIAA concentration[17,24]. In our patient the marker, NSE and cytokeratin, were present but the 5-HIAA concentration was within the reference range.

Differential diagnosis is accomplished by tissue identification, including thymoma, lymphoma, terato-

ma, germ cell tumour, tumour of ectopic parathyroid gland, paraganglioma, and metastatic disease[25,26].

Surgery, including the initial excision of the tumour and any recurrence, is the treatment of choice[1,5]. Long-term survival is possible with complete excision[27]. The effectiveness of adju-vant therapy has not been proved[28]. Chemotherapy and radiotherapy should be considered first if radical resection is impossible or if the tumour recurs[29].

Summary

This report describes the thymic carcinoid tumor behaved in a highly aggressive fashion metastasis. Anti-cancer chemotherapy was not effective, the patient died of progressive disease after three months of diagnosis.

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