A Case of Cutaneous Metastasis Originating from Thymic Carcinoma

Suk-Jin Choi, M.D., Nark-Kyoung Rho, M.D., Jun-Mo Yang, M.D., Eil-Soo Lee, M.D.

Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

We report a case of cutaneous metastasis of thymic carcinoma in Korean. A 44-year-old female, who had been diagnosed as thymic carcinoma and treated with total thymectomy and postoperative radiation therapy, presented grouped erythematous papules on the left chest. CT scans revealed metastatic lesions in the left pleura and abdominal cavity. Histopathologic examination of skin biopsy showed extensive infiltration of malignant cells in dermis and subcutis. The morphology of infiltrating cells was similar to that of tumor cells from primary thymic carcinoma specimen. The results of immunohistochemical study for skin biopsy were consistent with the features of non-neuroendocrine thymic carcinoma. Histopathologic and immunohistopathologic similarity between cutaneous lesion and previous tumor suggested that malignant cells in the skin lesion could originate from progressing thymic carcinoma.

(Ann Dermatol 14(4) 230~234, 2002).

Key Words : Cutaneous metastasis, Thymic carcinoma

Thymic carcinoma is a rare thymic neoplasm that pursues an aggresive course and has a generally poor prognosis[1]. It is an epithelial tumor of the thymus but differs from thymoma in that it displays cytologically malignant features and extensive local invasion as well as distant metastases[1-3].

Since the early 20th century, cutaneous metastases of thymic carcinoma have been reported in western countries[4-6], but there has been no reported case in Korea to our knowledge. We present herein a case of cutaneous metastasis originating from thymic carcinoma in a middle-aged Korean woman.

Received April 2, 2002.
Accepted for publication May 28, 2002.
Reprint request to : Eil-Soo Lee, M.D., Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-Dong, Kangnam-Ku, Seoul, 135-710, Korea
Tel. (02)3410-6578, Fax. (02)3410-3869
E-mail : sjchoi1973@hanmail.net
*This case was presented at the 53rd Annual Meeting of the Korean Dermatological Association on April 19, 2001.

CASE REPORT

A 44-year-old female was presented with a 2-week history of multiple asymptomatic erythematous indurated papules on her left chest(Fig. 1). She had been diagnosed as thymic carcinoma 5 years before and treated with total thymectomy, left anterior chest wall resection with reconstruction, and postoperative radiation therapy. On follow-up CT scan and bone scan, systemic metastasis had been detected 3 years after previous surgery and three cycles of palliative chemotherapy had been done for 2 months. However, in spite of palliative radiation therapy, the patient's state had been continuously aggravated. Laboratory findings showed the following values: white blood cell count, 14,200/mm^3(normal, 3,150-8,630/mm^3); hemoglobin, 10.8g/dL(normal, 11.2-14.8g/dL); and alkaline phosphatase, 1221IU/L(normal, 30-115IU/L). Nodular thickening of left parietal pleura with relatively large amount of effusion on chest CT scan suggested recurrent disease in the left pleural space(Fig. 2A). Abdominal CT scan disclosed enlarged para-aortic and aortocaval lymph nodes, also indicating systemic metastases(Fig. 2B). Histopathologic examination

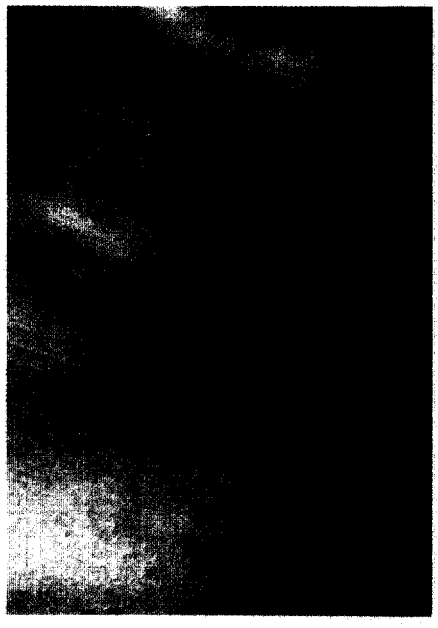

Fig. 1. Grouped erythematous indurated papules on the left chest.

of skin lesion revealed that dermis and subcutis were diffusely infiltrated by poorly-differentiated pleomorphic cells with hyperchromatic nuclei and scanty cytoplasm(Fig. 3A). The cellular morphology of skin specimen was quite similar to that of previous thymectomy specimen(Fig. 3B), which made us suggest cutaneous metastasis originating from thymic carcinoma. On the immunohistochemical studies for skin biopsy, tumor cells had the negative staining for chromogranin, synaptophysin, and vimentin. But malignant cells were positive for pan-cytokeratin, epithelial membrane antigen and CD5(Fig. 4). We lost the patient 4 months after the appearance of cutaneous metastatic carcinoma, and could not follow-up her ever since.

DISCUSSION

Primary thymic epithelial neoplasms have been the source of much controversy over the years because of difficulties in their histopathologic classification and prognostication of clinical behavior[7]. Despite recent advances in understanding the immunopathology and molecular pathology of these neoplasms, there is no universally accepted system of classification for these tumors[8]. Suster and Moran[7,8] proposed the classification of these tumors into three diagnostic categories based on their degrees of differentiation: thymoma, atypical thymoma, and thymic carcinoma(corresponding to well-differentiated, moderately-differentiated, and poorly-differentiated neoplasms, respectively). Thymoma is a thymic tumor displaying obvious features of thymic organotypical differentiation and absence of cytological atypia. On the other hand, thymic carcinoma is a poorly differentiated thymic epithelial neoplasm showing obvious cytological evidence of malignancy with total or almost complete loss of the organotypical features of thymic differentiation[7]. Several clinicopathologic variants of thymic carcinoma have been described, which include keratinizing squamous cell carcinoma, nonkeratinizing squamous cell carcinoma, lymphoepithelioma-like carcinoma, neuroendocrine

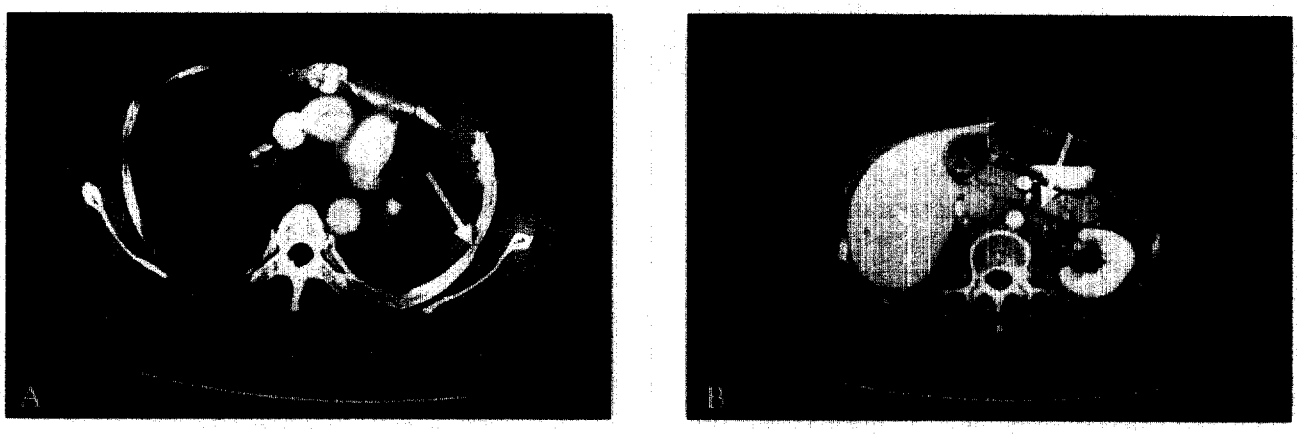

Fig. 2. (A) A CT scan of the chest revealed nodular pleural thickening(white arrow) with effusion in the left pleural space. (B) Abdominal CT scan showed para-aortic lymphadenopathy(white arrow).

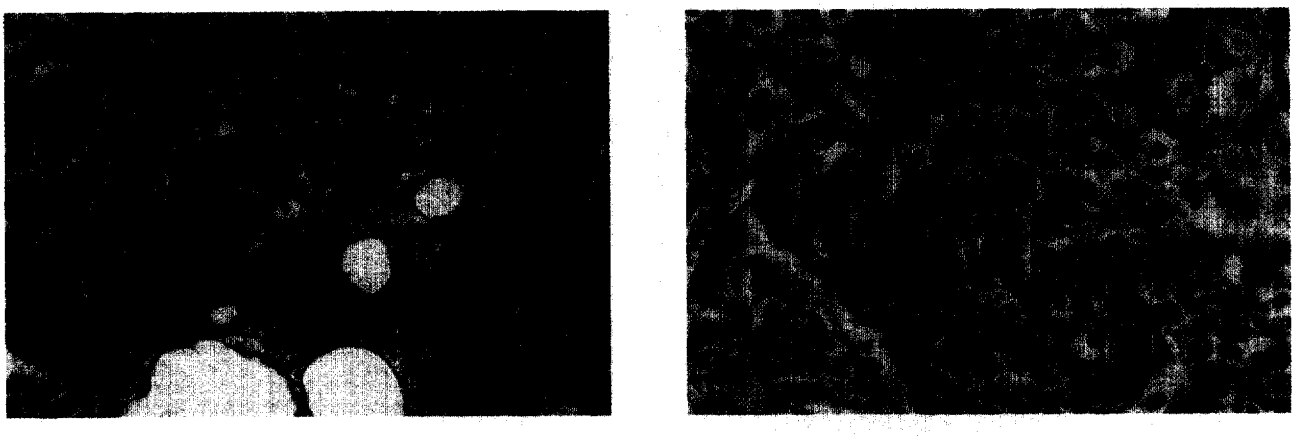

Fig. 3. (A) Histopathologic examination of skin biopsy revealed pleomorphic cells with hyperchromatic nuclei and scanty cytoplasm in lower dermis and subcutis(H&E, ×400). (B) The cellular morphology of previous thymectomy specimen(H&E, ×400).

A B

Fig. 4. On the immunohistochemical studies for skin biopsy, tumor cells showed the positivity for pan-cytokeratin and CD5(A: pan-cytokeratin, ×40, B: CD5, ×40).

carcinoma, adenosquamous carcinoma, mucoepidermoid carcinoma, clear cell carcinoma, adenocarcinoma, basaloid carcinoma, and sarcomatoid carcinoma[1-3,9]. The histopathologic findings from both thymectomy and skin biopsy specimens in our case were relatively consistent with those of nonkeratinizing squamous cell carcinoma.

Thymic carcinoma usually presents in adult men and is only rarely seen in children[2]. A number of patients have symptoms of an anterior medistinal mass, including cough, dypnea, chest pain, and superior vena cava syndrome[1,2]. This tumor has highly aggresive behavior, such as extensive local invasion as well as distant metastases[2,3]. In Korean patients with thymic carcinoma reported in several case reports[10-12], males were about twice as frequently affected as females, with a mean age of onset in the early fifties. Most common histologic type was squamous cell carcinoma, followed by undifferentiated carcinoma and lymphoepithelioma-like carcinoma. Local invasion was commonly detected, and about half of reviewed cases showed systemic metastasis[10-12]. Although the treatment necessitates a multimodality approach including surgical resection, postoperative radiotherapy, and chemotherapy[2,3,13,14], the overall 5-year survival is approximately 33.3%[3]. Even though clinical and demographic features have not proven useful as prognosticators, improved survival has been correlated with encapsulated tu-

mors, a lobular growth pattern, low mitotic activity, and low histologic grade[1,9,13]. Metastases from thymic carcinoma are most commonly seen in mediastinal, cervical, axillary lymph nodes, followed by bone(particularly spine), lung, and liver1. In addition, very rarely reported metastatic sites of thymic carcinoma include central nervous system[15], skin[4,5,13,14], pancreas[16], digit[17], and orbit[18]. Cutaneous metastases from thymic carcinoma have been reported in western countries since 1930[4,5]. Metastatic skin lesions from this tumor have been described sometimes in several clinical studies handling with the treatment and prognosis of thymic carcinoma[13,14], but the incidence and clinical patterns of skin metastasis are not yet exactly evaluated. To the best of our knowledge, our case is the first Korean case of cutaneous metastatic carcinoma originating from thymic carcinoma.

Immunohistochemical study of primary thymic carcinomas uniformly show reactivity for keratin proteins, and many of these tumors likewise are labeled by antibodies to EMA[9]. Carcinoembryonic antigen can be seen as well, especially in lesions with overt or ultrastructural glandular differentiation[19]. Vimentin is usually absent in all subtypes of thymic carcinoma except for sarcomatoid carcinoma[19]. Neuroendocrine markers, such as neuron-specific enolase, synaptophysin, chromogranin and neurofilament protein, are variably present in those neoplasms that have pure, mixed, or occult neuroendocrine differentiation[9]. A number of recent studies revealed the presence of CD5 in the epithelial cells of non-neuroendocrine thymic carcinoma, and have contended that CD5 is seen in overtly malignant epithelial tumors of the thymus[20]. The results of immunohistochemical stains for skin lesion were consistent with those for non-neuroendocrine thymic carcinoma with overt malignancy. On the basis of histopathologic and immunohistochemical findings, we concluded that cutaneous lesion of our patient was originated from thymic carcinoma.

REFERENCES

1. Blossom GB, Steiger Z, Stephenson LW: Neoplasms of the mediastinum. In DeVita VT, Hellman S, Rosenberg SA (eds): Cancer: principles & practice of oncology. 5th ed., Lippincott-Raven, Philadelphia, 1997, pp951-969.
2. Aisner J, Antman KH, Belani CP: Pleura and mediastinum. In Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE (eds): Clinical oncology. 2nd ed., Churchill Livingstone, New York, 2000, pp1478-1516.
3. Chahinian AP: Mediastinal neoplasms: thymic and cardiac tumors. In Holland JF, Frei E, Bast RC, Kufe DW, Morton DL, Weichselbaum RR (eds): Cancer medicine. 4th ed., Williams & Wilkins, Baltimore, 1997, pp1827-1837.
4. Bedford GV: A case of carcinoma of the thymus with extensive metastases in a new-born child. Can Med Assoc J 23:197-202, 1930(cited from reference 6).
5. Wasserman P, Epstein JW: Congenital carcinoma of the thymus with extensive generalized metastases. J Pediatr 14:798-804, 1939(cited from reference 6).
6. Schwartz RA: Cutaneous metastatic disease. J Am Acad Dermatol 33:161-182, 1995.
7. Suster S, Moran CA: Primary thymic epithelial neoplasms: spectrum of differentiation and histological features. Semin Diagn Pathol 16:2-17, 1999.
8. Suster S, Moran CA: Thymoma, atypical thymoma, and thymic carcinoma: a novel conceptual approach to the classification of thymic epithelial neoplasms. Am J Clin Pathol 111:826-33, 1999.
9. Ritter JH, Wick MR: Primary carcinomas of the thymus gland. Semin Diagn Pathol 16:18-31, 1999.
10. Joo YD, Kim JH, Sohn CH, Kim RH, Kim CH, Suh HS, et al: Thymic carcinoma; reports of eight cases. J Korean Cancer Assoc 30:743-751, 1998.
11. Kang YH, Jeon DS, Lee HJ, Park SM, Lee JH, Oh HM, et al: Three cases of thymic carcinoma. Korean J Med 54:278-284, 1998.
12. Lee EJ, Jung GS, Kim SM, Huh JD, Joh YD, Shin MJ, et al: CT differentiation of invasive thymoma and thymic carcinoma. J Korean Radiol Soc 39:941-946, 1998.
13. Yano T, Hara N, Ichinose Y, Asoh H, Yokoyama H, Ohta M: Treatment and prognosis of primary thymic carcinoma. J Surg Oncol Suppl 52:255-258, 1993.
14. Fornasiero A, Daniele O, Sperandio P, Morandi P, Fosser VP, Cartei G, et al: Chemotherapy of invasive or metastatic thymoma: report of 11 cases. Cancer Treat Rep 68:1205-1210, 1984.
15. Kato H, Mashiyama S, Fukawa O, Sasaki T, Yamane Y, Asano S: A case of thymic carcinoma with brain metastasis. Kyobu Geka 50:1059-1063, 1997.

16. Hoeffel C, Chelle C, Fornes P, Hoeffel JC: Pancreatic metastatic thymoma. Am J Gastroenterol 92:546-547, 1997.
17. Shannon FJ, Antonescu CR, Athanasian EA: Metastatic thymic carcinoma in a digit: a case report. J Hand Surg 25:1169-1172, 2000.
18. Stockl FA, Tucker N, Burnier MN: Thymic carcinoma metastatic to the orbit. Am J Ophthalmol 124:401-403, 1997.
19. Walker AN, Mills SE, Fechner RE: Thymomas and thymic carcinomas. Semin Diagn Pathol 7:250-265, 1990.
20. Dorfman DM, Shahsafaei A, Chan JK: Thymic carcinomas, but not thymomas and carcinomas of other sites, show CD5 immunoreactivity. Am J Surg Pathol 21:936-940, 1997.