Editorial

Thymic carcinoma *vs.* thymic neuroendocrine tumor

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Thymic neoplasm is a rare disease, accounting for <1% of all cancers. Among the thymic malignancies, thymic carcinoma (TC) including thymic neuroendocrine tumor (TNET) rarely occurs (1,2). Both TC and TNET appear to have an aggressive behavior (3). Interestingly, TNET develops distant metastasis and recurrence more frequently than neuroendocrine tumors originating from other organs (4). Although the incidence of TNET is increasing, which may be due to increased awareness of this disease among clinicians, information on TNET is limited due to the small number of cases (4,5).

Recently, Zhao *et al.* published an interesting paper in the *European Journal of Cardio-Thoracic Surgery* comparing the survival and clinical features between TC and TNET based on a relatively large number of patients from a single center (6). The largest retrospective clinical comparative study of TC and TNET was conducted by Filosso *et al.* on behalf of the *European Society of Thoracic Surgeons* and *the International Thymic Malignancy Interest Group* collaboration (7). They performed a multi-institutional study to determine long-term survival and to identify prognostic factors for survival and recurrence. It is noteworthy that the preoperative characteristics of TNET were similar in both reports: male predominance, larger tumor size, and less chemo/radiotherapy in the TNET group. Both studies found that long-term outcomes were similar in TC and TNET. Filosso *et al.* found that 10-year survival was 40% in TC *vs.* 39% in TNET, which included 32% of large-cell neuroendocrine tumors and small-cell carcinomas. In the study by Zhao *et al.*, which only included typical and atypical carcinoids, the 10-year overall survival (TNET *vs.* TC =52% *vs.* 48%) as well as the relapse rate (TNET *vs.* TC =52% *vs.* 48%) were similar between the two groups.

In contrast to Filosso *et al.*, Zhao *et al.* provided information on the recurrence patterns, nodal metastasis, and surgical management. Moreover, they showed the prognostic role of the newly proposed TNM staging system in addition to the traditional Masaoka-Koga staging system. Although there is a lack of sufficient data, several studies have emphasized the importance of lymph node dissection in TC. TC is prone to lymph node metastasis compared to thymoma. Our institution reported a 20% incidence of lymph node metastasis in the setting of intentional mediastinal lymph node dissection in TC, including high-grade neuroendocrine carcinoma (8). Furthermore, we found that the paratracheal area was the most frequently affected nodal station (9). Among cases of TC, TNET had a higher likelihood of harboring lymph node metastasis than other subtypes of TC (TNET *vs.* TC =63% *vs.* 33%) (10). Zhao *et al.* again reported similar findings of a higher rate of lymph node metastasis in TNET than TC. Currently, mediastinal lymph node dissection is not widely applied for thymoma, especially in minimally invasive procedures. However, since preoperative tissue diagnosis of thymic neoplasm is not routinely recommended, patients with an anterior mediastinal mass usually undergo surgery without knowing whether the mass is thymoma or TC. Given that TC or TNET present with a high prevalence of lymph node metastasis, the routine application of mediastinal lymph node dissection during surgery for thymic neoplasms may have to be reconsidered.

The only consistent prognostic factor for survival is complete resection, regardless of histology (11-14).

Therefore, complete resection is the treatment of choice for localized TC and TNET. Despite the high relapse rate, however, there is no consensus regarding systemic and local treatment for metastatic disease (15). While TC and TNET often metastasize, the response to chemotherapy is poor (16). Although ADOC (Doxorubicin-Cisplatin-Vincristine-Cyclophosphamide) and CAP (Cisplatin-Doxorubicin-Cyclophosphamide) regimens have been widely used for TC, carboplatin and paclitaxel (preferred for TC) are recommended by the National Comprehensive Cancer Network (17,18). TC harboring c-KIT mutations may be candidates for tyrosine kinase inhibitor treatment (19). More recently, PD-L1 expression was observed in up to 80% of TC cases and 10% of large-cell neuroendocrine carcinoma cases (20-23). Hence, immunotherapy may be promising for TC. Future randomized studies with immune checkpoint inhibitors for advanced or unresectable thymoma and TC may provide better evidence.

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Footnote

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References

1. Travis WD, Brambilla E, Burke AP, et al. WHO histological classification of tumours of the thymus. World Health Organization Classification of Tumours of the Lung, Pleura, Thymus and Heart, 2004. Lyon: IARC Press, 2015.
2. de Jong WK, Blaauwgeers JL, Schaapveld M, et al. Thymic epithelial tumours: a population-based study of the incidence, diagnostic procedures and therapy. Eur J Cancer 2008;44:123-30.
3. Ahmad U, Yao X, Detterbeck F, et al. Thymic carcinoma outcomes and prognosis: results of an international analysis. J Thorac Cardiovasc Surg 2015;149:95-100, 101.e1-2.
4. Yao JC, Hassan M, Phan A, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol 2008;26:3063-72.
5. Jia R, Sulentic P, Xu JM, et al. Thymic Neuroendocrine Neoplasms: Biological Behaviour and Therapy. Neuroendocrinology 2017;105:105-14.
6. Zhao Y, Gu H, Fan L, et al. Comparison of clinical features and survival between thymic carcinoma and thymic carcinoid patients. Eur J Cardiothorac Surg 2017;52:33-8.
7. Filosso PL, Yao X, Ruffini E, et al. Comparison of outcomes between neuroendocrine thymic tumours and other subtypes of thymic carcinomas: a joint analysis of the European Society of Thoracic Surgeons and the International Thymic Malignancy Interest Group. Eur J Cardiothorac Surg 2016;50:766-71.
8. Park IK, Kim YT, Jeon JH, et al. Importance of lymph node dissection in thymic carcinoma. Ann Thorac Surg 2013;96:1025-32; discussion 1032.
9. Hwang Y, Park IK, Park S, et al. Lymph Node Dissection in Thymic Malignancies: Implication of the ITMIG Lymph Node Map, TNM Stage Classification, and Recommendations. J Thorac Oncol 2016;11:108-14.
10. Weksler B, Holden A, Sullivan JL. Impact of Positive Nodal Metastases in Patients with Thymic Carcinoma and Thymic Neuroendocrine Tumors. J Thorac Oncol 2015;10:1642-7.
11. Sullivan JL, Weksler B. Neuroendocrine Tumors of the Thymus: Analysis of Factors Affecting Survival in 254

Patients. Ann Thorac Surg 2017;103:935-9.
12. Weksler B, Dhupar R, Parikh V, et al. Thymic carcinoma: a multivariate analysis of factors predictive of survival in 290 patients. Ann Thorac Surg 2013;95:299-303.
13. Filosso PL, Yao X, Ahmad U, et al. Outcome of primary neuroendocrine tumors of the thymus: a joint analysis of the International Thymic Malignancy Interest Group and the European Society of Thoracic Surgeons databases. J Thorac Cardiovasc Surg 2015;149:103-9.e2.
14. Gaur P, Leary C, Yao JC. Thymic neuroendocrine tumors: a SEER database analysis of 160 patients. Ann Surg 2010;251:1117-21.
15. Shepherd A, Riely G, Detterbeck F, et al. Thymic Carcinoma Management Patterns among International Thymic Malignancy Interest Group (ITMIG) Physicians with Consensus from the Thymic Carcinoma Working Group. J Thorac Oncol 2017;12:745-51.
16. Öberg K, Hellman P, Ferolla P, et al. Neuroendocrine bronchial and thymic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012;23 Suppl 7:vii120-3.
17. NCCN Clinical Practice Guidelines in Oncology. Thmomas and Thymic Carcinomas. J Natl Compr Canc Netw, 2017. Version 1. 2017-March 2.
18. Hirai F, Toyozawa R, Nosaki K, et al. Are Anthracycline-Based Regimens Truly Indicated To Be the Standard Chemotherapy Regimen for Thymic Carcinoma? J Thorac Oncol 2016;11:115-21.
19. Petrini I, Zucali PA, Lee HS, et al. Expression and mutational status of c-kit in thymic epithelial tumors. J Thorac Oncol 2010;5:1447-53.
20. Remon J, Lindsay CR, Bluthgen MV, et al. Thymic malignancies: Moving forward with new systemic treatments. Cancer Treat Rev 2016;46:27-34.
21. Yokoyama S, Miyoshi H, Nakashima K, et al. Prognostic Value of Programmed Death Ligand 1 and Programmed Death 1 Expression in Thymic Carcinoma. Clin Cancer Res 2016;22:4727-34.
22. Weissferdt A, Fujimoto J, Kalhor N, et al. Expression of PD-1 and PD-L1 in thymic epithelial neoplasms. Mod Pathol 2017;30:826-33.
23. Tsuruoka K, Horinouchi H, Goto Y, et al. PD-L1 expression in neuroendocrine tumors of the lung. Lung Cancer 2017;108:115-20.

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