Thymic large-cell neuroendocrine carcinoma: a disease neglected in the ESMO guideline?

Large-cell neuroendocrine carcinoma (LCNEC) of the thymus is a rare aggressive neoplasm. Its precise prognosis has not yet been determined. The recently published European Society of Medical Oncology (ESMO) clinical practice guidelines for neuroendocrine bronchial and thymic tumors [1] defined LCNEC and small-cell carcinoma (SCC) of the thymus as high-grade thymic carcinoids with a 5-year survival rate of <10%. However, the prognostic value of present classification of thymic lesions has not been proven [2].

We reviewed 8 English papers including 13 thymic LCNEC cases. Subjects comprised seven males and six females with a median age of 55 years (range, 44–75 years). Median duration of follow-up was 26 months (range, 2–95 months). Seven patients were asymptomatic. Patients who underwent complete surgical resection were 11 and 2 underwent partial resection. One patient with Masaoka stage I disease, one with stage II, six with stage III, one with stage IVa, one with stage IVb, and three patients with undocumented disease. During follow-up, four patients died and seven experienced recurrence of disease. The survival rates were calculated using the Kaplan–Meier analysis. The 5-year overall survival and 5-year disease-free survival of thymic LCNEC were 66% and 43%, respectively (Figure 1).

Thus, our results of 5-year survival rates for thymic LCNEC are considerably different from those stipulated in the ESMO guideline. However, publication bias cannot be ruled out and our sample size was small. The ESMO guideline cited Moran’s paper [3], which included the largest case series of thymic neuroendocrine carcinoma. In their study, 10 of 11 patients with high-grade (poorly differentiated) neuroendocrine carcinoma died of tumors during the follow-up. Later, Moran stated that the majority of poorly differentiated neuroendocrine carcinomas that they have observed were of the SCC type and that whether the so-called LCNEC is a true entity in the mediastinum remains unclear [4]. The exact number of LCNEC cases included in their study was not provided, but it appears that the survival rate in their study was representative of SCC of the thymus and not of thymic LCNEC.

Excess underestimation of the prognosis of thymic LCNEC could harm the quality of life of patients. Therefore, the definition of the prognosis of thymic LCNEC should be reconsidered in the next edition of the guideline.

Figure 1. Survival curves for thymic large-cell neuroendocrine carcinoma. Solid line, overall survival; dotted line, disease-free survival.

(The complete reference list for 13 cases of thymic LCNEC is provided in the supplementary data, available in Annals of Oncology online.)

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